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Breast-Conserving Therapy in the Management of Early-Stage Breast Cancer: Our Experience in 103 Cases

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Abstract

Purpose: The aim of this study is to determine whether our results in breast-conserving therapy of 103 patients with early-stage breast cancer are comparable to those of other facilities or not.

Materials and methods: From January 1990 to October 1999, 103 patients with early-stage breast cancer were treated by breast-conserving surgery and whole breast irradiation. All patients were of Stages I or II, and the greatest dimensions of primary tumor were less than 3 cm. The median follow-up time was 47 months from the completion of postoperative radiotherapy. Local, regional and distant failure rates, and survival rate were presumed using the Kaplan-Meier method.

Results: One patient suffered from local recurrence 30 months later. She was followed by simple mastectomy and kept from further recurrence. No regional relapse occurred. Distant metastases were seen in three patients: two patients in bones, and one patient in a bone and the liver after 19, 35, and 32 months, respectively. One patient died from disseminated cancer in 41 months. Only one patient died due to intercurrent disease. Both 5-year and 10-year disease-free survival rates were 94.2%, and both 5-year and 10-year cause-specific survival rates were 98.3%.

Conclusion: Our results were comparable to previously reported data. In this stage although the follow-up time was too short to define the long-term outcome, it suggested that breast conserving therapy was acceptable and effective in the management of early-stage breast cancer. (J Nippon Med Sch 2002; 69: 24–30)

Key words: breast cancer, breast-conserving therapy, surgery, radiation therapy

Introduction

Conservative treatment for early stage breast cancer is now widely acceptable as standard treatment in Europe and North America¹, while in Japan some

long-term results of breast-conserving therapy (BCT) have been reported^{2,3,4}. This means BCT is a well-recognized standard option for treatment of early-stage invasive breast cancer and has also been performed in Japan. Therefore also in our institute BCT began in 1990⁵. In this article, we determine

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the outcome of the patients with early-stage breast cancer treated by BCT in our institute over ten years and compare our results with those of other institutes.

Materials and methods

Patients' eligibility and characteristics

We considered that the indication for BCT was as follows: primary tumor 3 cm or less, not-palpable axillary nodes, absence of distant metastasis and patient's consent. From July 1990 to October 1999 (Fig. 1), one hundred and three women underwent BCT. The median age was 53 years with a range of 29 to 86 years. Eighty-three patients were pathological stage I (pT1pN0), and twenty patients were stage IIA (seven pT2pN0, thirteen pT1pN1). The breast-conserving surgery was performed in four departments (Table 1), but all the patients underwent

postoperative irradiation (RT) in the Department of Radiology of Nippon Medical School Hospital. Tumor localization and pathohistological results are shown in Table 2 and Table 3, respectively.

Therapy

Breast conservation surgery consisted of quadrantectomy (Qx) or lumpectomy with a gross surgical margin from 1 cm to 3 cm with axillary lymphadenectomy. Although these techniques were not distinguished exactly, they were selected based on each patient's breast size or tumor location. Postoperative RT began within four weeks in most of the patients. Negative-surgical-margin breasts were treated with two opposing tangential fields of total 50 Gy given in 5 weeks with a daily target of 2 Gy, while the breasts with positive surgical margin treated with 46-Gy tangential fields followed by 10-Gy boost using suitable-energy electron beams.

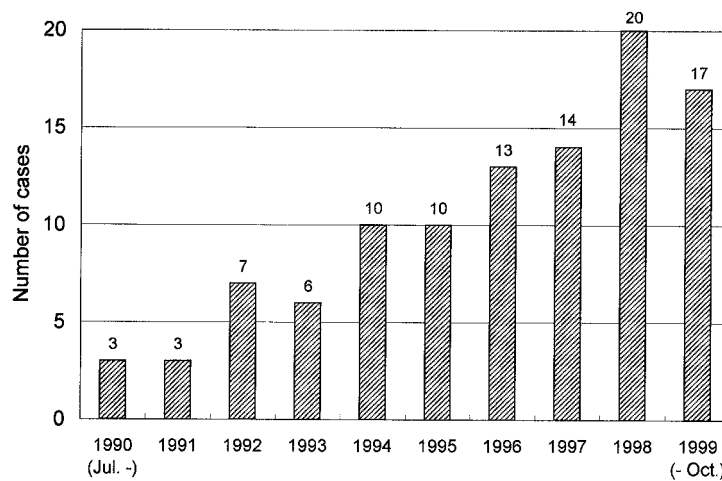


Fig. 1 Change in patient numbers treated with breast-conserving therapy by year

Table 1 Introductory departments

Introducers	Patients #
First Department of Surgery, NMS	81
Second Department of Surgery, NMS	12
Department of Surgery, Shitaya Hospital	3
Department of Surgery, Sato Hospital	7
TOTAL	103

NMS : Nippon Medical School Hospital

Table 2 Anatomical sites of the primary tumors

Sites	Patients #
Nipple	0
Central portion	0
Upper inner quadrant	20
Lower inner quadrant	9
Upper outer quadrant	57
Lower outer quadrant	9
Axillary tail	0
Not otherwise specified	8
TOTAL	103

Table 3 Pathologic results of 103 patients

Pathohistology	(n)
Noninvasive ductal carcinoma (=Ductal carcinoma in situ)	4
Invasive ductal carcinoma	7
Papillotubular carcinoma	40
Papillotubular carcinoma with scirrhus change	2
Solid tubular carcinoma	13
Scirrhus carcinoma	20
Mucinous carcinoma	2
Adenocarcinoma, NOS	15
TOTAL	103

NOS : not otherwise specified

Japanese and international classifications are intermingled in pathologist's reports.

In 1990~1997, x-ray simulation with fluoroscopy was used and only in central plane dose distribution was calculated for suitable adequate wedge filter choice using personal-computer-based simulation (ARCS-EX version 4.5, NIHON DENSHI OHYO CO., LTD., Tokyo). In 1998~1999, a CT-based treatment planning system (REXXAM version 3.00.00, GE-Yokogawa Medical Systems, Tokyo) became available and was utilized for semi-three-dimensional dose distribution optimization and radiation field verification (**Fig. 2**). For most of the patients, the oral antineoplastic and/or hormonal agents were prescribed adjuvantly. The adjuvant chemo-hormonal therapy regimen was 20 mg daily of tamoxifen citrate (Nolvadex®) for five years with/without daily 600 mg of doxifluridine (Furtulon®) for two years.

Follow-up time and analysis

The median follow-up time for the series was 47 months (range from 16 to 127 months, mean 56 months) from the completion of postoperative RT. Local, regional and distant failures, and survival rate were evaluated using the Kaplan-Meier method. The results were compared with those of major foreign and domestic facilities.

Informed consent

All patients were informed of the therapeutic options and they selected BCT consisting of breast-conserving surgery and whole breast irradiation.

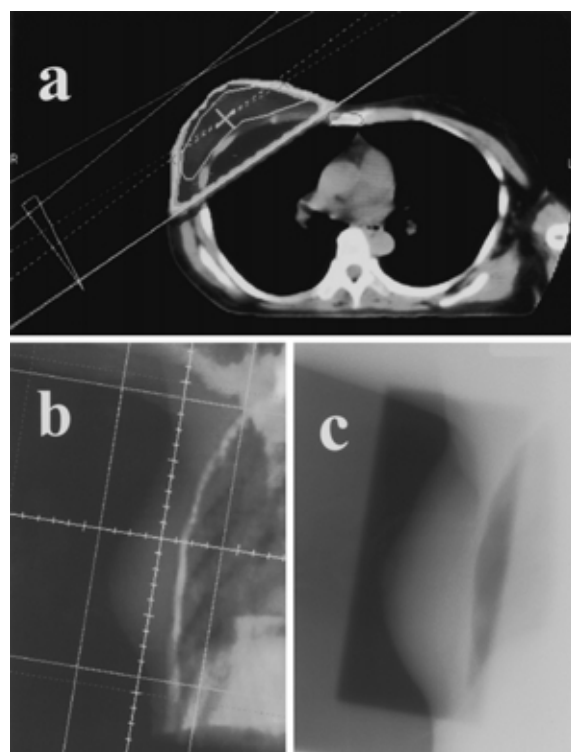


Fig. 2 Irradiation techniques using the CT-based radiation therapy planning system

a) A whole-breast tangential irradiation field on CT image. Note the medial and lateral borders that indicate approximately mid-thoracic line and medial axillary line, respectively (arrows).

b) A planned "beams-eye-view" image obtained by the CT-based simulation system

c) An actual irradiation field on verification film (Linacgraphy) acquired by the therapeutic machine (Linear accelerator: Linac). This Linacgraphy corresponds to the "beams-eye-view" mentioned above.

Results

Therapeutic outcome

After breast-conserving therapy, four patients suffered recurrent diseases: one local recurrence and three distant metastases. A local recurrence patient, who had been diagnosed with solid tubular carcinoma, pT1c N0 M0 after initial breast-conserving surgery without axillary lymphadenectomy, underwent simple mastectomy and has survived without cancer. In this patient, no particular intrinsic or therapeutic characteristics were found. The characteristics and prognoses of the patients with distant

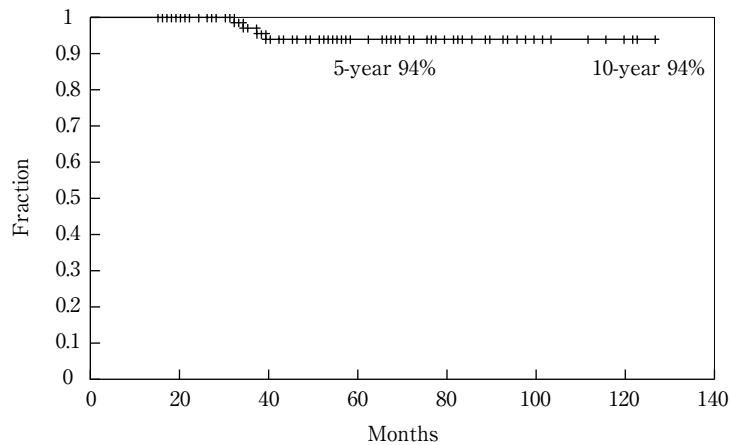


Fig. 3 Relapse-free survival curve of 103 patients with Stage I and II breast cancer treated with breast-conserving therapy calculated by the Kaplan-Meier method

metastases were as follows: all three patients were prescribed a daily dose of 20-mg tamoxifen adjuvantly without doxifluridine; the first patient (scirrhous carcinoma, pT1b pN0 M0) suffered metastatic disease in the iliac bone 19 months after initial therapy, and died from a disseminating tumor a further 21 months later; the second patient (papillotubular carcinoma, pT1c pN0 M0) had skeletal metastasis in the sacrum and the fifth lumbar spine treated with RT and chemotherapy, and remains alive with disease; and the third patient (papillotubular carcinoma, pT1c pN1bii (metastasis to six axillary nodes) M0) had been treated with adjuvant intravenous chemotherapy, but she relapsed into bone and liver metastases, underwent repeating chemotherapies and remains alive with disease. Only one patient died of senility and a cardiovascular disorder.

The actuarial relapse-free survival rates at both 5 and 10 years in these patients were 94.2% (Fig. 3). Both the 5- and 10-year actuarial local control rates were estimated at 98.6%. There was no statistically significant difference between pathological stage I and stage II ($p > 0.1$).

Radiation therapy related complications

Moderate to severe acute radiation-related complications occurred in only one patient who suffered from acute painful moist desquamation within the irradiation field during and four weeks after RT. She needed oral NSAID and ointment therapy

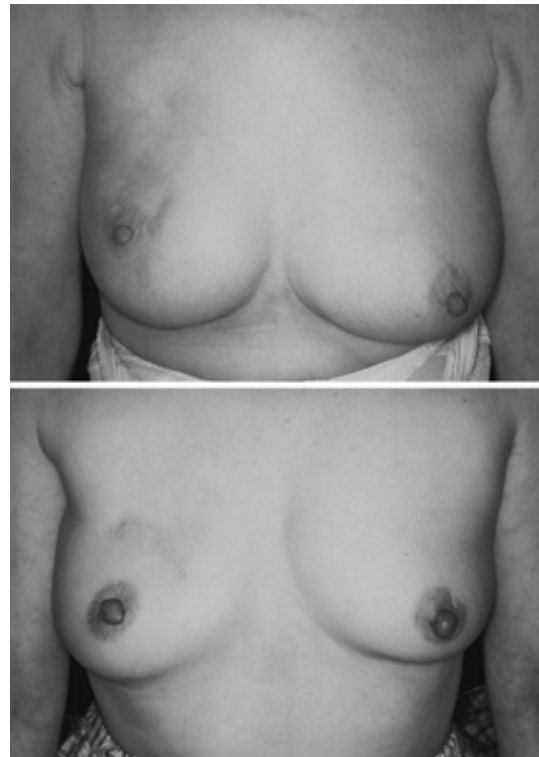


Fig. 4 Long-term aesthetic outcomes.

Case 1: A 65-year-old lady underwent quadrantectomy and whole breast irradiation for right upper-outer quadrant papillo-tubular carcinoma (pT1pN0M0) six years ago with moderate deformity. Case 2: A 56-year-old woman who received right-sided lumpectomy and whole breast irradiation for right upper-inner quadrant papillo-tubular carcinoma (pT1pN0M0) three years ago. She is satisfied with this result. The left breast underwent a previous negative biopsy for the palpable nodule near the nipple.

of corticosteroids and antibiotics. In other patient without comorbidity, a delayed healing of a skin infection from a surgical suture was seen, followed by observation.

Most patients had slight or moderate skin pigmentation and mild dry dermatitis with slight itching, but needed no particular treatment. Though post-RT subcutaneous edema and fibrosis were seen in 1–2 years, most of them were mild and few of them demanded therapy. A complaint of mastalgia was relatively common in the delayed stage, but severe cases were rare. The long-term aesthetic results of two typical patients are shown in **Fig. 4**.

Discussion

It has been firmly established that BCT is an appropriate primary therapy for the majority of women with Stage I and II breast cancer^{1,2}. **Table 4** shows literature on the outcomes in other facilities. In the United States and Western Europe, the 6-year to 15-year overall survival rates were 62% to 79%^{6–11}. In Japanese literature, a paper from Kyoto University recorded that the overall 5-year survival of 243 patients was 95%², and a Hokkaido group documented one local and one distant relapse of their 51 patients treated with Qx and RT³. A report from Aichi Cancer Center stated that the 5-year and 8-year overall survival rates of 295 patients treated by BCT were 93.2% and 91.5%, respectively⁴. And in this study, the five-year local control rate was approximately 95%. We presume that the figures in our results are comparable with those reported by

others^{2–4,6–11}. The goal of this study was to record the outcomes of BCT in our institute and to compare them with those of others. From this point of view, though the follow-up time was still short and patients' satisfaction with BCT was not estimated, we obtained satisfactory results and our methods and techniques are possibly adequate at this stage. Some problems in the specific points of detail, however, were made clear from this study.

Most patients in our series underwent Qx or wide excision, but the current standard surgery tends toward smaller lumpectomy. Two reports reached a conclusion that local recurrence rates between Qx with RT and lumpectomy with RT did not differ significantly^{13,14}. Moreover, Qx involved risks such as severer deformity in the affected breast than lumpectomy. But, on the other hand, good outcomes in Japanese facilities may depend on quadrantectomy with radiation therapy. Furthermore, in standard therapy, breasts treated by lumpectomy need 45-Gy to 50-Gy whole breast RT plus electron local boost: NIH Physician Data Query (NIH Physician Data Query: http://cancernet.nci.nih.gov/pdq/pdq_treatment.shtml) states that "Radiation therapy (as part of breast-conserving local therapy) consists of postoperative external-beam radiation to the entire breast with doses of 45 Gy to 50 Gy. A further radiation boost is commonly given to the tumor bed". But, local electron boost may bring about poorer cosmetic results¹⁵. Considering the above-mentioned points, we should change the range of excision after careful consideration and discussion between surgeons, radiation oncologists and clinical oncologists in our

Table 4 Overall survival rates of breast conserving therapy

Institution or trial[ref. #]	Years	No. of patients	Overall survival %
Milan[6]	1973–1980	352	71 (13 yrs)
NSABP-B06[7]	1976–1984	629	62 (12 yrs)
Denmark 82TM[8]	1983–1989	430	79 (6 yrs)
WHO[9]	1972–1979	88	73 (15 yrs)
NCI[10]	1979–1989	121	77 (10 yrs)
EORTC 10801[11]	1980–1986	456	77 (8 yrs)
Kyoto University[2]	1987–1993	243	95 (5 yrs)
Hokkaido group[3]	1988–1993	51	98 (5 yrs)
Aichi Cancer Center[4]	1989–1977	295	92 (8 yrs)

LR : local recurrence, DM : distant metastasis

institute.

The avoidance of axillary lymphadenectomy is a current topic. Axillary dissections have been done for prognostic information. As the rule of axillary lymphadenectomy is still controversial^{16,17,18}, it may be avoidable in breast cancer patients with ductal carcinoma in situ, microinvasive cancer, pure tubular carcinoma (less than 1 cm in diameter), and certain invasive carcinoma¹⁹. Studies of sentinel node biopsy^{20,21} are ongoing. Examination and dissection of the sentinel lymph node will provide sufficient information on diagnosis and staging of disease in order to avoid total axillary lymphadenectomy that is often involved with not a few complications and the cost.

RT related late effects of normal tissues include pulmonary fibrosis and myocardial damage in left-side whole breast irradiation²². These complications are controlled minimally using a CT-guidance RT planning system.

The last subject of this discussion is an expansion of BCT indication. In Japan, the target of BCT is thought to be a primary tumor of 3 cm or less in size considering Japanese women's breast size. Consequently the overall survival rates in Japanese reports are better than those in foreign countries by about twenty points (**Table 4**). In the future, large breasted patients with Stage T3 cancer will be candidates for BCT with or without neoadjuvant chemotherapy^{23,24}. Though indication of BCT for the positive surgical margin is still controversial²⁵, all patients with positive or close margins in our series are survivors without recurrence. Contrary to extended tumors, this series included four patients (4%) with non-invasive carcinoma. NSABP trials in the United States concluded that RT after lumpectomy was more beneficial than lumpectomy alone for localized intraductal carcinoma in situ (DCIS). It reduced the incidence of ipsilateral breast tumors: non-invasive tumors from 13.4% to 8.2% ($p=0.007$); invasive tumors from 13.4% to 3%²⁶. Therefore, selected non-invasive breast cancer should be included among candidates for post-lumpectomy RT.

In conclusion, breast-conserving surgery and whole breast RT for patients with early-stage breast cancer offer excellent local control and survival rates. Despite these results, some unsolved problems

such as reduction of surgical degree, an electron beam boost and an adoption of Stage III remain.

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