

## Radiation Therapy for Operable Breast Cancer after Conservative Surgery

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**Purpose:** To evaluate the result of conservative management on recurrence, survival and prognostic factors of patient with operable breast cancer.

**Materials and Methods:** Fifty three patients, treated for localized breast cancer by lumpectomy or quadrantectomy followed by radiotherapy between January 1985 and December 1996, were retrospectively studied. All patients followed up for at least five years. Their median age was 43 years (range 24~72). The tumor stages were as follows: T1 in 30 patients, T2 in 21, Tis in 2. Thirty-eight patients had negative and 15 had positive axillary nodes. The histological types were 42 infiltrating ductal, 2 infiltrating lobular, and 2 intraductal carcinomas with 7 other histologies. The tumor locations were the outer quadrant in 38 breasts, the inner quadrant in 13 and central in 2. Radiation doses of 46~50 Gy were given to the entire breast areas with additional doses of 14~18 Gy delivered to the tumor bed areas.

**Results:** The overall five and 10 year actuarial and disease free survivals were 94.3 % and 92.4%, 91.2 and 81%, respectively. The overall five year survivals were 100% in stage I and IIa, and 66.7% in stage IIb and IIIa tumors. Seven patients failed either locally or distantly. Incidence of local failure and distant metastasis for the first failure were 7.5% and 5.7%, respectively. Local recurrence appeared within 2 years of treatment at the primary site and after more than 8 years outside of primary lesion, whereas distant metastasis appeared between 2 and 6 years following treatment. The overall recurrences were high at a young age (< or = 35 years), with 5 out of 12 (2 local, 3 distant), and in T2 lesions with 5 out of 21 (1 local, 3 distant, and 1 in both). Distant metastasis was high in the positive axillary lymph node group with 4 out of 15 (26.6%). A high incidence in the axillary node was noted at a young age with 7 out of 12 (58.3%) and in T2 lesions with 8 out of 21 (38.4%). A young age, positive axillary node and large tumor size were all related with poor survival.

**Conclusion:** Based on this study, lumpectomy or quadrantectomy, followed by radiation appears to be an adequate therapeutic method in operable breast cancer. A long term follow-up is necessary because a recurrence of breast can occur long time after treatment. The poor prognostic group, especially young patients with an aggressive biological behavior needs more effective treatment modalities to improve their survival.

**Key Words:** Breast cancer, Conservative surgery and radiation

### Introduction

Treatment with radiation after lumpectomy or quadrantectomy in operable breast cancer has been extensively studied in Western country. Most data of prospective and retrospective studies

show no difference in survival of patients treated with breast preservation compared with those who underwent radical surgery.<sup>1~5)</sup> High local control and good cosmetic results are achieved in most patients. At Hanyang Univeristy Hospital conservative surgery and radiation was done case by case who had problems in anesthesia until 1992 when planned treatment was initiated. Before 1992, early breast cancer was treated with modified radical mastectomy. Since 1992 patients could have chosen treatment options of conservative surgery plus radiation therapy or modified radical mastectomy in tumor size 3 cm or less than 3

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cm with clinically negative axillary lymph nodes.

The present study is retrospective review of the results of operable breast cancer patients treated with radiotherapy after limited surgery at our hospital. The aim of study is to evaluate pattern of recurrence, survival and prognostic factors.

### Materials and Methods

Fifty three patients were treated with radiotherapy following lumpectomy or quadrantectomy between January 1985 and December 1996. All patients had a minimal follow up of five years. Their mean age was 43 years (range 24~72 years). The tumor was staged according to the American Joint Committee on Cancer (AJCC,1997) guidelines. The tumor stages were as follows : T1 in 30 patients, T2 in 21, Tis in 2. Thirty-eight had negative and 15 had positive axillary nodes. The tumor locations were the outer quadrant in 38 breasts, the inner quadrant in 13 and central in 2. The histological types were : 42 infiltrating ductal, 2 infiltrating lobular, and 2 intraductal carcinomas with 7 other histology (3 colloid, 1 papillary, 1 mucinous, 1 medullary, 1 apocrine carcinoma). Five patients had tight (<5 mm) margin

from resection margin. The characteristics of patients are shown in Table 1.

Surgery consisted of lumpectomy in 45 and quadrantectomy in 8 patients. All patients except 2 had axillary dissection at the level I and II. Mean number of removed axillary nodes was 19. Hormonal receptor and flow cytometric analysis were not routinely studied during that period.

Postoperative radiotherapy was performed at average 21 day after surgery. All patients were treated with Cobalt 60 or 6 MV X-ray. Tumor doses of 46~50 Gy were delivered to entire breast areas using tangential field with wedge compensator .An additional doses of 14~18 Gy were given to primary tumor bed areas with electron beam except 2 patients who received tangential boost with Cobalt 60. Daily doses of 2 Gy with total tumor dose of 60~66 Gy were given over 6~7 weeks. For early T1N0 or T2N0 lesions, radiation was given to the breast tissue alone. Radiation doses of 46~50 Gy were delivered to the supraclavicular node for the all patients except above mentioned. We did not give radiation with posterior field boost to the axilla in patients who underwent adequate level I and II axillary dissection.

Further management with adjuvant chemotherapy was based on information obtained surgical staging. Concurrent chemotherapy was given to the patients who had tumor size more than 2 cm or positive axillary lymph nodes in premenopausal or perimenopausal patients. In addition patients also received systemic

Table 1. Patients' Characteristics

No of patients		53
Follow-up period (months)	Median	72
	Median (range)	43 (24~72)
Age (years)	≤35	12
	>35	41
Stage	0	2
	I	23
	IIa	18
	IIb	7
Tumor size (cm)	IIIa	3
	≤1	9
	1~2	23
	>2	21
Axillary lymph node	cN*	2
	pN <sup>†</sup>	36
	≤3	8
	>3	7
Location	Outer quadrant	38
	Inner quadrant	13
	Central	2
Histology	Infiltrating ductal	42
	Infiltrating lobular	2
	Intraductal carcinoma	2
	Others	7
Margin	Tight (<5 mm)	5

\*clinically node negative, †pathologically node positive

Table 2. Treatment Methods

Surgery	Lumpectomy	45
	Quadrantectomy	8
	Axillary dissection	
	No	2
	Yes	51
Chemotherapy	No	22
	Yes	
	CMF*	22
	FAC <sup>†</sup>	3
	TAM <sup>‡</sup>	6
Radiation field	Tangential only	29
	Tangential/scl <sup>§</sup>	22
	Tangential+scl+axilla	2

\*Cyclophosphamide, Methotrexate, 5-fluorouracil

<sup>†</sup>5-fluorouracil, Adriamycin, Cyclophosphamide

<sup>‡</sup>Tamoxifen

<sup>§</sup>supraclavicular

chemotherapy in the case of tumor emboli in lymphatic vessel or high grade in pathologic findings with negative axillary nodes. Hormonal therapy was given to the patients with positive estrogen receptor. Twenty two patients had adjuvant CMF (Cytosine, Methotrexate, 5-fluorouracil) regimen and 3 had FAC (5-fluorouracil, Adriamycin, Cytosine) regimen. Six patients received Tamoxifen alone. The treatment data is shown in Table 2.

Survival and disease free survival curve were calculated by using Kaplan-Meier method. Comparison tests of significance for survival difference between group in the univariate analysis were based on the log rank test.

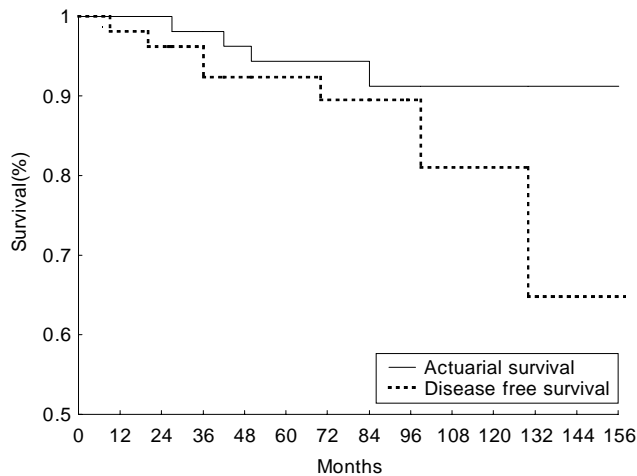


Fig. 1. Actuarial survival & disease free survival of breast cancer patients.

### Results

The overall five and 10 year actuarial and disease free survival were 94.3% and 92.4% 91.2% and 81%, respectively (Fig. 1). The overall 5-year survival were 100% in stage I and IIa, and 66.7% in stage IIb and IIIa tumors. Seven patients (13.2%) failed either locally or distantly. The patients who failed were younger than 45 years. Four patients (7.6%) had local recurrence, 3 patients (5.7%) had distant metastasis for first site of failure. One patient who had local recurrence developed distant metastasis later. Four local failure patients underwent salvage mastectomy. Three patients were alive and one had distant metastasis later. One patient whose recurrence was detected by high CEA level without detectable mass by mammography or ultrasound underwent salvage surgery and local recurrence was confirmed by electron microscopy. Two local recurrence occurred within 2 years following treatment and other two recurrence was found after 8 years. Two late local recurrences were developed in the different quadrant of breast from primary site and their age was less than 30 years. Four distant failure occurred between 2~6 years. All patients died within 14 months after distant failure. The list of patients with local and distant failure is shown in Table 3.

Prognostic factors including age, stage, size, lymph nodes status, histology of tumor, tumor location, and adjuvant chemotherapy were evaluated. The overall survival rates were lower in patients with young age, positive axillary nodes, high T stage.

Table 3. Patient's List with Recurrence

Age	Stage	Axillary LN status (involved LN/total LN)	Histology	Time of recurrence	Recurrence site	Last follow-up status
33	T2N1M0	9/15	Infiltrating ductal Extracapsular invasion	26 months	Lung, pericardium Brain	27 months dead
34	T2N2M0	7/23	Infiltrating ductal	70 months	Femur	95 months dead
43	T2N1M0	3/28	Infiltrating ductal	20 months 26 months	Local Bone Brain, liver	42 months dead
41	T2N0M0	—	Infiltrating lobular Margin : lobular in situ	9 months	Local	MRM, alive
29	T2N2M0	17/20	Infiltrating ductal	36 months	Brain	50 months dead
24	T1N0M0	—	Infiltrating ductal	99 months	Local (other quadrant)	MRM, alive
28	T1N0M0	—	Infiltrating ductal	130 months	Local (other quadrant)	MRM, alive

LN : lymph node, MRM : modified radical mastectomy

**Table 4. Prognostic Factors of Overall Survival**

Factors	Groups	No	5 yr*	10 yr.	p- value
Age	≤35	12	80.2	53.4	0.031
	>35	41	97.5	97.5	
Tumor size (cm)	≤1	9	100.0	100.0	0.040
	>1 and ≤2	23	100.0	100.0	
Stage	>2	21	84.8	63.6	0.004
	0&I	25	100.0	100.0	
	IIa	19	100.0	100.0	
	IIb	6	66.7	66.7	
Axillary node	IIIa	3	66.7	33.3	0.030
	-	38	100.0	100.0	
Chemotherapy	+	15	80.4	64.0	0.045
	No	31	100.0	100.0	
Histology	Yes	22	76.5	59.5	0.638
	Infiltrating ductal	41	92.2	83.0	
	Infiltrating lobular	2	100.0	100.0	
Tumor location	Others	8	100.0	100.0	0.260
	Outer quadrant	36	91.5	82.3	
	Inner quadrant	15	100.0	100.0	
	Central	2	100.0	50.0	

\*year survival rate

**Table 5. Relationship between Tumor Size and Axillary Node Involvement**

Tumor size (cm)	Axillary node	
	Negative (%)	Positive (%)
T1 ≤1	9 (100.0)	0 ( 0.0)
1> and ≤2	19 ( 82.6)	4 (17.4)
T2	13 ( 61.9)	8 (38.1)

**Table 6. Relationship between Age and Axillary Node Involvement**

Age	Axillary node	
	Negative (%)	Positive (%)
≤35	5 (41.7)	7 (58.3)
35~45	19 (95.0)	1 ( 5.0)
>45	18 (69.2)	8 (30.7)

Patients who received systemic chemotherapy had low overall survival. All patient with negative axillary lymph nodes is alive. Three out of four (75%) dead patients had more than 3 positive axillary lymph nodes. Tumor location and histology were not significant factor on survival. The data of prognostic factor is shown in Table 4.

Eight (38.1%) out of 21 T2 patients revealed positive axillary lymph nodes. The relationship between tumor size and axillary

involvement is shown in Table 5. The number of positive axillary lymph nodes (58.3%) was more at the young age group (< or =35 years) from initial diagnosis. The relationship between age and axillary lymph nodes involvement is shown in Table 6.

Postoperative wound problem developed in 2 patients. One patient had delayed wound healing at postoperative period and the other had axillary hematoma 2 years after the treatment.

## Discussion

There are extensive evidences to show that tumorectomy followed by adequate dose of radiation results in a local control and survival at 5- and 10-years similar to those obtained by radical surgery for patients with localized breast cancer.<sup>1-5)</sup> Because of increasing public awareness of alternative treatment to radical surgery, more women are seeking breast preserving modalities. The aim of present retrospective study was to evaluate the outcome of our treatment. Locoregional failure was 7.5 % in our experience, and result was similar to that reported by other series. Following tumorectomy and adequate radiation, 5-year local failure rate for T1 and T2 lesions generally approximated 5~10%.<sup>6-11)</sup> Locoregional failure was acceptable for early cancer since salvage surgery was successful with acceptable morbidity.<sup>12)</sup> In this study two local recurrence in primary site occurred within 2 years. One patient had high CEA level on follow-up study and salvage mastectomy showed microscopic tumor detected by electron microscopy at 20 months. The other patient had histology of lobular carcinoma with in situ component with negative re-excised margin. She received total 66 Gy to the tumor bed, but the microscopic tumor was not controlled and recurred at 9 months after lumpectomy. It was reported that surgical margin was important factor for local recurrence.<sup>7-9)</sup> NSABP investigator was not able to determine presence of carcinoma in situ as prognostic value for local recurrence among patients with uninvolved resection margins.<sup>13)</sup> If there is unclear resection margin, it is very important to perform re-excision prior to radiation therapy especially with in situ component. Patients with extensive intraductal component (EIC) had a greater incidence of locally extensive intraductal involvement in the vicinity of tumor.<sup>14-16)</sup> For EIC negative patient with focal involvement margin, acceptable low recurrence rate was reported.<sup>14)</sup> In this study, no patient had EIC component and 4 patients with tight

margin less than 5mm had good local control. Two patients had local recurrence at the other quadrant lesions 8 years after radiation. Recht et al<sup>17)</sup> reported that local recurrence with some distance from primary area was considered to be a new primary breast cancer and was rare within 5 years. Distant metastasis for the first time of failure was 5.7%. Distant metastasis developed more in positive axillary node group. Four (26.6%) of 15 positive axillary patients developed distant metastasis suggesting involvement of axillary lymph node was major predictor of distant failure. Five year survival rate of patients in this study was about 90%, but we did not compare with the result obtained by radical surgery in our institution. Above finding was similar to the studies reported by others.<sup>6~11)</sup>

Tumor size influences on the prognosis. In this study, median size of tumor was 2 cm. There was statistically significant difference in overall survival between T1 and T2 lesions. But there was no difference in overall survival between less or equal to 1cm and more than 1 cm. T2 lesions with negative lymph nodes had good prognosis (100% 5-year survival) whereas T2 with positive axillary lymph nodes had very poor outcome (50% 5-year survival) Other study showed prognostic significance of tumor size is valuable indicator with node negative disease and independent of axillary node status.<sup>18)</sup> But our study did not show any difference in survival with increasing tumor size in nodes negative patients. Linear relationship between tumor size and axillary nodal involvement was reported.<sup>19, 20)</sup> Our data revealed the trend of more axillary nodal involvement with increased tumor size. Tumor location and histology did not have effect on the survival, but the histology other than infiltrating ductal carcinoma was too small to have any significance. No patients have axillary recurrence since most patient underwent axillary dissection at level I and II. Fowble et al<sup>21)</sup> reported a 1.5% isolated axillary recurrence with limited axillary dissection and most recurrence occurred within 27 months. That study showed the number of removed axillary nodes was associated with axillary recurrence. The average number of removed axillary nodes in our study was 19 (range 11~41) and low recurrence in the axilla might be due to the adequate dissection which did not have a need for further radiation therapy to the axilla. We avoided to give routine axillary irradiation who underwent level I and II dissection with adequate number of removed lymph nodes. In this study patients who received ad-

juvant systemic chemotherapy had lower overall survival with statistical significance. Above results could be predictable since patients who received systemic chemotherapy were higher stage group compared to patients who did not have any chemotherapy.

Patients at a young age less than or equal to 35 years had decreased survival rate similar to other reported studies.<sup>22, 23)</sup> Several studies reported high local recurrence rate in young age.<sup>13, 24)</sup> In this study, local and distant metastasis was high at the young patients with 16.6% and 25% respectively (Table 3 and Table 4). All distant failure was found to be patients with positive axillary lymph nodes. Stage at the time of diagnosis was advanced in young patients with high incidence of positive axillary lymph nodes (58.3%) suggesting that young age had more aggressive clinical course.

Lumpectomy or quadrantectomy followed by radiation appears to be an adequate therapeutic methods in early breast cancer in our institution Long term follow-up is necessary because a recurrence of breast cancer can occur long time after treatment. Poor prognostic group, especially young patients have who has an aggressive clinical course needs more effective treatment modalities to improve their survival.

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국문초록

**유방암환자의 유방보존수술 후 방사선 치료 성적**

한양대학교 의과대학 치료방사선과학교실

이 명 자 · 전 하 정

**목적 :** 유방암 환자에서 국소적 절제 수술 후 방사선 치료 후 재발 양상, 생존율 및 예후 인자를 평가하기 위해 후향적으로 분석을 하였다.

**대상 및 방법 :** 1985년 1월부터 1996년 12월까지 한양대학교병원 치료방사선과에서 유방보존수술 후 방사선치료를 위해 의뢰된 유방암 1기, 2기 및 3기 53명을 대상으로 후향적 분석을 하였다. 추적기간은 평균 84개월이었고 최소 5년이였다. 연령분포는 24세부터 72세였고 중앙연령은 43세였다. 2명을 제외한 51명이 액와 림프절 광정술을 받았고 조직병리상 42명이 침윤성 선암이었고 2명이 소엽 세포암 2명은 선관내 선암이었고 7명은 그 외 병리소견을 가졌다. 병기로 T0 2명 T1 30명, T2 21명이었고, 53명 중 15명이 액와 림프절 침윤이 있었다. 원발 종양위치로 내측이 13명, 외측이 38명 유두 하 부위가 2명이였다, 방사선 조사는 전체유방에 46~50 Gy와 원발 종양 주위에 14~18 Gy 추가조사를 시행하였다.

**결과 :** 5년 생존율은 94.3% 5년 무병생존율은 92.4%였다. 10년 생존율은 91.2% 10년 무병생존율은 81%였다. 병기 별로 I 100%, IIa는 100%, IIb 및 IIIa는 66,7%의 5년 생존율을 보였다. 4명(7.5%)에서 국소 재발이 있었고 3명(5.7%)에서 원격전이가 있었다. 원발 병소 내 국소 재발은 2년 이내였고 원발 병소 밖의 국소 재발은 8년 후에 보였다. 원격전이는 2년에서 6년 사이였다. 35세 이하의 환자에서 국소 및 원격전이가 높아 12예 중 5예의 재발율을 보였고 (국소재발 2명, 원격전이 3명) 종양크기가 2 cm 이상인 환자 21예 중 5예(국소재발 2명, 원격전이 3명)에서 재발율을 보였다. 액와 림프절 침윤이 있는 15명 중 4명(26.6%)에서 원격전이가 있었다. 종양의 크기 2 cm 이상인 환자에서 임파선 전이율이 38.1%였고 35세 이하의 젊은 연령에서 임파선 전이율이 58.3%였다. 예후 인자로는 연령과 액와 림프절 침윤과 종양이 클수록 생존율이 유의하게 낮았다.

**결론 :** 유방 보존 수술 후 방사선 치료를 받은 조기 유방암환자의 치료결과는 양호함을 알 수 있었다. 국소 재발율은 추적기간이 길수록 증가함으로 보다 더 장기적인 추적이 필요하고 젊은 연령층의 치료 결과를 향상시키기 위해 보다 효과적인 치료법의 개발이 필요하리라 생각된다.

**핵심용어 :** 유방보존술 후 방사선치료