Eur J Cancer, Vol. 29A, No. 15, pp. 2083–2089, 1993.
Printed in Great Britain

0959–8049/93 $6.00 + 0.00

The Cosmetic Outcome in Early Breast Cancer Treated With Sector Resection With or Without Radiotherapy

G. Liljegren, L. Holmberg, G. Westman and the Uppsala-Örebro Breast Cancer Study Group

In a randomised trial, the cosmetic results after sector resection and axillary dissection with or without postoperative radiotherapy for early breast cancer were evaluated. The evaluations were made at 3, 12, 24 and 36 months (357, 326, 302 and 255 women, respectively) after treatment. Good to excellent cosmetic results were achieved in 84–90% of those in the group randomised to radiation and in 91–95% in the group allocated to surgery only, as judged by the women themselves, and in 81–86% and 87–93%, respectively, according to other observers. At 12 months the results in 290 patients were photographically documented and evaluated by a panel. The results were good to excellent in 35–84% of the irradiated group and in 62–93% of the non-irradiated group. Poor results followed the development of contour differences, breast oedema and mamillary deviation, which were the most important mediators of a poor cosmetic result after radiotherapy. We conclude that sector resection and axillary dissection can be performed with good cosmetic results. Doses to 54 Gy of radiotherapy influence the result negatively, but from a clinical standpoint to a moderate extent.
Eur J Cancer, Vol. 29A, No. 15, pp. 2083–2089, 1993.

INTRODUCTION

IN THE LAST decade, prospective randomised trials have reported that conservative surgery and radiotherapy can achieve approximately 90% local control without any impairment of survival at 5–10 years, as compared to mastectomy in early breast cancer [1–3]. As a result, the acceptance of conservative procedures has increased considerably, and the cosmetic outcome has become an important endpoint. A number of retrospective evaluations of the cosmetic outcome, focusing on the effect of specific patient characteristics and treatment factors, has been published [4–17]. Good-to-excellent cosmetic results have been reported in up to 90% of the cases, as evaluated by the women themselves, compared to 60–80% evaluated by other observers. Among the factors that have been mentioned as influencing the results are the volume of the excised tissue [7, 10, 11, 16, 18, 19], the tumour size [4, 7, 8, 10], the type of incision [7, 9], whether an axillary dissection was conducted [4, 7, 17], the size of the breast [7, 10, 20], body weight [7], the location of the tumour [16], administration of chemotherapy [4, 6, 12–14] and the type and dose of radiation administered to the breast [11, 15–17]. In most of these studies, the methods and the time after treatment when the evaluations were made were not standardised. The surgical and radiotherapeutic procedures usually did not adhere to a specified protocol. The impact of radiotherapy on the cosmetic outcome has not been evaluated in a randomised series.

The following is an analysis of the cosmetic outcome after 3 years of follow-up in a prospective randomised trial comparing women who, after a standardised sector resection plus axillary dissection in breast cancer stage I, were randomised to postoperative radiotherapy routinely, with those who were allocated to treatment with surgery alone.

Correspondence to G. Liljegren.
G. Liljegren is at the Department of Surgery; G. Westman is at the Department of Oncology, Örebro Medical Center Hospital, S-701 85 Örebro; G. Liljegren is also at and L. Holmberg is at the Department of Surgery, University Hospital, S-751 85 Uppsala, Sweden.
Revised 21 June 1993; accepted 29 June 1993.

EJC 29:15-B

PATIENTS AND METHODS

Study design

In 1981, a prospective randomised multicentre study on early breast cancer was initiated in central Sweden. The study design has been described in detail [21]. Women below the age of 80 with unifocal breast cancers of maximum diameter 20 mm on the pre-operative mammogram were eligible. All patients were subjected to a standardised sector resection, as described earlier [22]. In short, both radial and curvilinear incisions of the skin were used. The mammary gland was dissected free of its periphery in the plane of Scarpa's fascia, down to the pectoral muscle with the pectoral fascia included in the specimen. A sector was excised with bi-digital control of the palpable or localised tumour. The excision aimed at a 1–2 cm lateral margin. Non-palpable lesions were localised with the wire-hook technique [23] or with stereotactic application of dye (coal or methylene blue) [24]. The decision of whether to suture the parenchyma or leave the defect open was left to the individual surgeon. The surgeon decided whether the breast needed to be drained. The axilla was dissected to levels I and II via a separate incision. A drain was usually placed in the axilla.

Randomisation

If the pathological report of the specimen showed radical excision, no multifocal lesions outside a margin of 20 mm of the index tumour and no axillary metastases, the women, after giving informed consent, were randomised either to receive postoperative radiotherapy (XRT group), a total dose of 54 Gy to the breast, or to control only (non-XRT group).

Table 1. Patients' characteristics

Characteristics	Treatment: XRT group n = 184	Treatment: Non-XRT group n = 197
Mean age (years) ±SD	59.0 ± 11.5	60.9 ± 11.0
No. of patients (%)		
Postmenopausal	118 (64.1)	144 (73.1)
Detected by screening	84 (45.7)	89 (45.2)
Largest tumour diameter ≤ 10 mm	79 (42.9)	94 (47.7)

XRT, postoperative radiotherapy received.

Radiotherapy

The breast parenchyma plus 1 cm was defined as the target volume. The contour was determined through the mammillary plane. Two opposing tangential fields with an open angle of 185° were applied. Radiotherapy was delivered by photons from a 2–6 MV linear accelerator (23.5%), a 7–10 MV linear accelerator (41.6%) or from ^{60}Co (23.5%). A total dose of 54 Gy in 27 fractions, five fractions a week, without boost or bolus was applied to the target. The isodose, representing the minimum target-absorbed dose, was defined as 95% of the specification dose. With this definition the target dose varied by ± 5%.

Patient accrual

Patient accrual started in October 1981. Six central county hospitals enrolled patients. Accrual terminated in September 1988, when 389 patients had been enrolled. When we received complete information, 8 were excluded because of ineligibility. Thus, the trial included 381 patients. Patients' characteristics are given in Table 1.

Follow-up

The protocol stipulated that the cosmetic evaluation should be carried out by the woman herself and two other observers, both health care professionals who were involved in the follow-up of the women at 3, 12, 24 and 36 months after treatment. At each evaluation, the observer judged the cosmetic result on a five-grade scale where excellent = no difference, very good = minimal difference, good = definite but slight difference, acceptable = major difference, or poor = marked difference was noted as compared to the untreated breast. At each evaluation, one of the observers (the physician at the outpatient clinic) considered the amount of pigmentation, telangiectasia, differences in contour, mammillary deviation and breast oedema as non-existent, moderate or severe, as compared to the untreated breast. At 12 months, a more extensive evaluation was performed. The cosmetic result was documented photographically in frontal and oblique views of the treated and untreated breast. The pictures were evaluated by two surgeons, one female and one male, who did not perform the operations on the breast, and two women who had previously undergone a cholecystectomy but had not undergone breast surgery. None of the four observers in the panel knew to which treatment group the patients belonged. No tattoos were conducted in the XRT group. They used the same scale as that used by the health care professionals and the women themselves.

Statistical methods

In the univariate comparisons, a χ^2 analysis was used. The results were considered to be statistically significant at the 5% level. The multivariate analyses were developed stepwise. Since a large number of variables were available, the final model was derived by chunkwise tests on models [25]. The explanatory variables were divided into four different groups or "chunks" in which the factors were logically related to one another—i.e. patient characteristics, treatment characteristics, tumour characteristics and factors related to the appearance of the breast (Table 2). The dependent variable was dichotomised as excellent, very good and good vs. acceptable or poor cosmetic results. The scores of the women, the health care professionals and the panel evaluating the photographic documentation were tested individually. In order to summarise the scores of the health care professionals and those of the panel evaluating

Table 2. Variables tested 12 months after treatment. Four different models were constructed, each based on the factors in one column and with the cosmetic outcome as the dependent variable. No contour difference, breast oedema and mamillary deviation used as reference categories, respectively.

Treatment variables	n	Patients' characteristics	n	Tumour characteristics	n	Factors related to the appearance of the breast	n
Radiotherapy	160	Age < 45 years	80	Tumour size ≤ 5 mm	13	Moderate-to-severe contour difference	120
Haematoma in breast	28	Age 45–59 years	81	Tumour size 6–10 mm	137		
Haematoma in axilla	10	Age 60–69 years	89	Tumour size 11–15 mm	134	Moderate-to-severe mammillary deviation	128
Seroma in breast	23	Age ≥ 70 years	89	Tumour size 16–20 mm	55		
Infection in breast	33	BMI < 20	15	Upper inner quadrant	80	Moderate-to-severe breast oedema	195
Infection in axilla	11	BMI 20–24	135	Inferior inner quadrant	35		
		BMI 25–29	111	Inferior outer quadrant	43		
		BMI ≥ 30	66	Upper outer quadrant	172		
		Married	222	Central	7		
		Widowed	68				
		Divorced	19				
		Single	16				
		Small breast size	47				
		Medium breast size	170				
		Large breast size	73				

BMI, body mass index.

the photographs, a mean value for each was determined. All explanatory variables were categorised, since it was not clear that their relationship to the cosmetic result should be linear. All models used were based on logistic regression, using the logist procedure in the SAS system [26].

RESULTS

Evaluation of XRT group vs. non-XRT group

357 of the 381 original patients were evaluated at 3 months. 24 women were not examined at 3 months, 7 of them because of death or an early local recurrence. The corresponding figure at 12 months was 326, with 39 patients non-evaluable, 13 with no data because of local or regional recurrences, and 3 died before that time. The number of patients evaluated at 24 months was 302, with a non-evaluable protocol in 36 patients, 28 patients with no data because of local or regional recurrences, and 15 patients died before that time. The number of patients evaluated at 36 months was 255 with a non-evaluable protocol in 77 patients, 30 patients had no data because of local or regional recurrences, and 19 patients died before that time. The number of patients evaluated by photographic documentation at 12 months was 290. In the XRT group, there were 13 non-compliers to radiotherapy, and in the non-XRT group, two women received postoperative radiotherapy.

The figures for good-to-excellent cosmetic results at 3, 12, 24 and 36 months are given in Fig. 1. In general, the degree of satisfaction was high. During the first year, one notes a tendency towards a better outcome in the non-XRT group, as judged by the other observers. At 24 months, this difference is no longer statistically significant. At 36 months, the trend is again in favour of the non-XRT group. The women's own evaluations did not differ substantially between the two groups at 12 months. At 3, 24 and 36 months, however, there was a tendency towards a slightly more favourable result in the non-XRT group, the difference being statistically significant at 3 months. On the whole, the patients tended to give more favourable ratings than did the observers. Ratings tended to be better over time during the first 2 years in the XRT group.

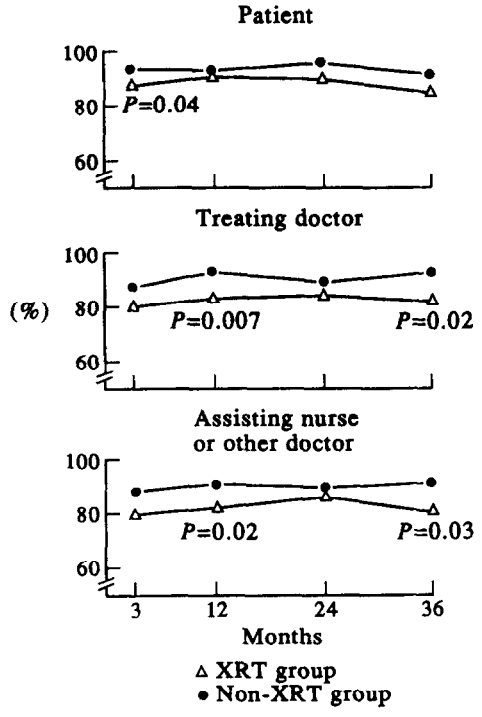

Fig. 1. Percentage excellent, very good and good cosmetic results at 3, 12, 24 and 36 months after operation. According to the patients, 42.8% in the non-XRT group and 25% in XRT group, had excellent cosmetic results at 12 months. Corresponding rates at 24 months are 36.6 and 29.9%, respectively.

The amounts of pigmentation, telangiectasia, differences in contour, mammillary deviation and breast oedema at the different times of examination are shown in Fig. 2(a–e). In all instances but two, the prevalence of these side-effects was higher in the XRT group. In the latter group, the high frequency of pigmentation was obvious during the first months of follow-up. At 3 years, there were no longer any differences between the two groups. No difference was noted in the overall low frequency of telangiectasia. In both groups, high frequencies of moderate-to-severe contour differences, mammillary deviation and breast oedema were observed. These frequencies were constantly and considerably less in the non-XRT group. In the XRT group, differences in contour tended to increase during the first 2 years of follow-up.

Photographic evaluation

The results of the photographic evaluation are given in Table 3. This evaluation revealed large differences in opinion between the observers. The female surgeon gave the most positive view and the male surgeon the least. The two cholecystectomised women had scores between these extremes. Three of the observers considered that the results were better in the non-XRT group.

Univariate analysis and exploratory multivariate models

The factors listed in Table 2 were analysed in a univariate fashion and in chunkwise models: one model each for treatment variables, patient characteristics, tumour characteristics and factors related to the appearance of the breast. Apart from the factors related to the appearance of the breast, the results were largely negative, with a few exceptions. Women in the XRT group had a 4.6 relative hazard (RH) [95% confidence interval (CI) 1.7–12.5] of having a less satisfactory result, according to the health care professionals. A postoperative infection also resulted in significantly worse ratings by the health care professionals. Concerning the tumour-related factors, the women gave significantly worse scores if the tumour was equal to or less than 5 mm in diameter. The women also tended to give better scores if the tumour was localised in the upper outer quadrant and if their breast was medium-sized (data not shown).

Concerning the analysis of the factors related to the appearance of the breast, statistically significant findings were more frequent. The results given in Table 4 indicate that marked differences in contour between the breasts resulted in less satisfaction with the cosmetic results in the three aspects evaluated—i.e. in the patients', health care professionals' and the panels' opinions. When severe oedema was present both health care professionals and the panelists gave less satisfactory scores.

Final multivariate model

The final multivariate model was based on the results mentioned above from the four different explanatory models (Table 5). Radiotherapy gave a statistically less favourable result only in the view of the health care professionals. Tumour size equal to or less than 5 mm, contour difference, mammillary deviation and breast oedema were also factors which produced significantly worse results.

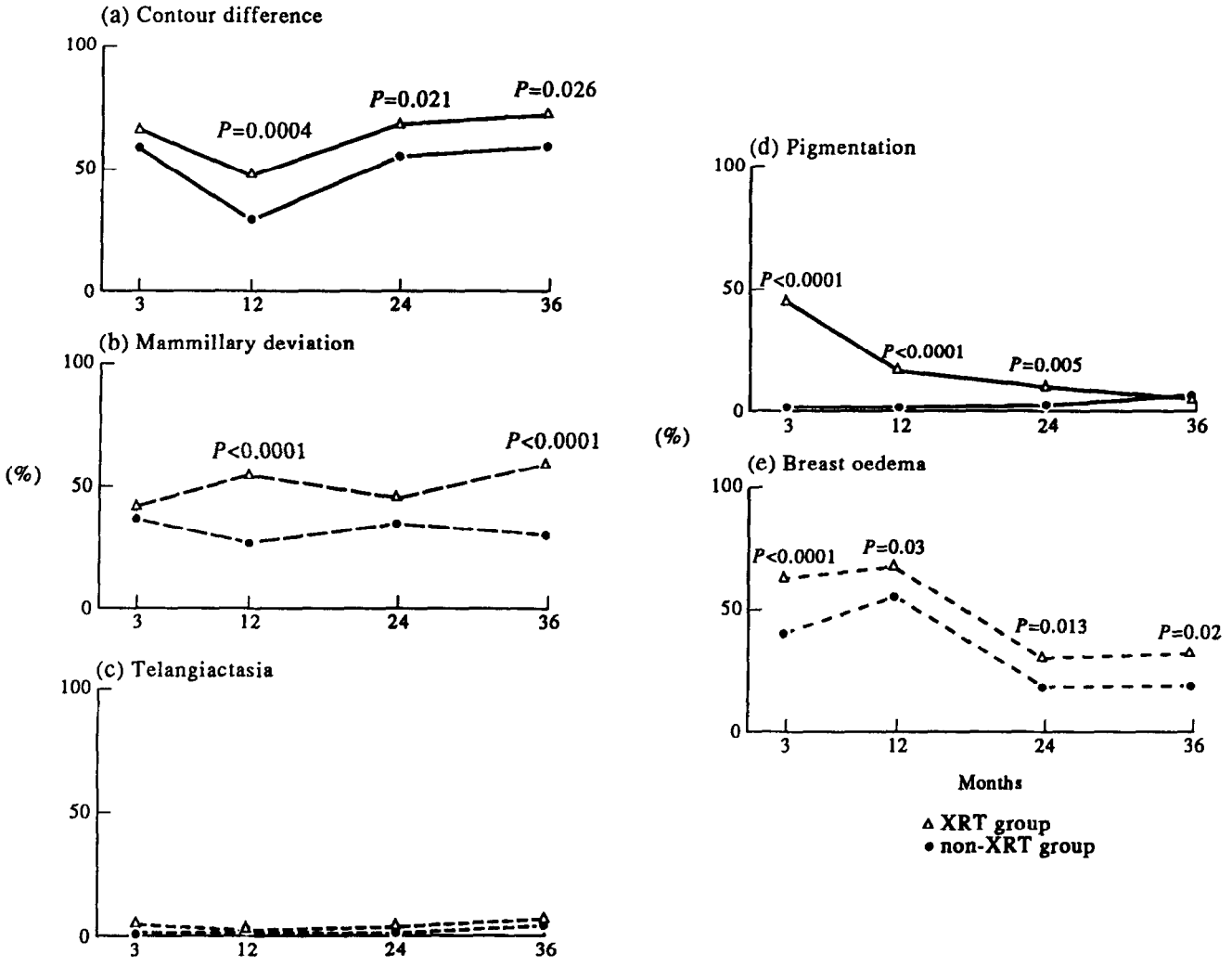

Fig. 2. Percentage moderate and severe contour difference, mammillary deviation, telangiectasia, breast oedema and pigmentation at 3, 12, 24 and 36 months after operation.

In a separate model (results not shown), we investigated how radiotherapy, tumour size, tumour location, patient's age and breast size influenced the occurrence of contour differences, mammillary deviation and breast oedema. Radiotherapy consistently gave worse results in the order of a RH = 1.3–3.8. The only other statistically significant results were that women aged over 70 or with small breasts had more breast oedema.

DISCUSSION

To our knowledge, this is the first prospective randomised trial in early breast cancer in which satisfaction with the cosmetic result after a sector resection with or without postoperative radiotherapy has been evaluated. The study protocol stipulated that standardised methods of surgery and of radiotherapy be performed, and it called for follow-up visits at fixed intervals when both the woman's view and that of other observers were recorded. An evaluation by an independent panel was also used to minimise observation bias.

Table 3. Evaluation of photographs 12 months after treatment. Percentage of good-to-excellent results related to treatment group

	XRT group (n = 138)	Non-XRT group (n = 152)
Female surgeon	84	93 (P = 0.02)
Male surgeon	35	62 (P < 0.0001)
Cholecystectomised woman (1)	59	62 (ns)
Cholecystectomised woman (2)	51	71 (P = 0.0006)

ns, not significant.

In this study, radiotherapy, at a total dose of 54 Gy, administered to the whole breast without a boost, had a negative effect on the cosmetic outcome after 3 years of follow-up. Several authors have previously found a clear relationship between the radiation dose administered to the breast and the cosmetic outcome. However, most reports have shown unsatisfactory cosmetic results only when higher doses than those given in this study have been used. Van Limbergen *et al.* [16] found that, when a dose of 50 Gy was administered, even an additional 1 Gy increased the mammillary deviation by 1 mm which, in this study, was found to be one of the principal factors producing a less satisfactory cosmetic result. Other reports in the literature state that doses higher than 60 Gy lead to a high frequency of poor cosmetic results [15, 17]. Some authors have reported less satisfactory results when cytotoxic therapy was combined with radiotherapy [4, 12, 13]. In this study, no cytotoxic therapy was given.

Table 4. Relative hazards (RH) with 95% confidence intervals (CI) for an adverse cosmetic outcome in a multivariate model with factors related to the appearance of the breast 12 months after treatment as determinants

	Patient		Mean score of observers		Mean score of panel	
	RH	95% CI	RH	95% CI	RH	95% CI
No contour difference	ref	ref	ref	ref	ref	ref
Moderate contour difference	2.5	0.9–7.1	3.3	1.0–10.4	2.4	1.0–5.9
Marked contour difference	18.0	4.7–69.0	17.8	4.1–78.5	4.81	1.3–18.0
No breast oedema	ref	ref	ref	ref	ref	ref
Moderate breast oedema	1.2	0.4–3.4	2.1	0.5–8.2	0.9	0.4–2.3
Marked breast oedema	1.7	0.3–8.6	24.3	4.6–146.9	5.1	1.3–19.5
No mammillary deviation	ref	ref	ref	ref	ref	ref
Moderate mammillary deviation	1.5	0.6–3.9	4.6	1.5–14.3	1.3	0.6–2.9
Marked mammillary deviation	4.6	1.0–20.6	1.7	0.2–16.1	0.3	0.0–3.6

ref, no contour difference, no breast oedema and no mammillary deviation were used as reference categories.

Table 5. Relative hazards (RH) with 95% confidence intervals (CI) derived from the final multivariate model. Factors influencing appearance of the breast 12 months after treatment

	Patient score		Mean score of observers		Mean score of panelists	
	RH	95% CI	RH	95% CI	RH	95% CI
Radiotherapy	0.8	0.3–2.1	4.1	2.1–8.2	1.5	0.7–3.5
Infection of breast	1.6	0.2–14.4	23.1	3.6–148.6	0.6	0.1–5.7
Tumour size ≤ 5 mm	8.3	1.6–42.7	8.7	1.1–71.3	6.7	1.4–31.9
Moderate contour difference	2.6	0.9–7.8	3.1	0.8–11.9	2.5	1.0–6.6
Marked contour difference	20.2	4.8–85.0	14.7	2.8–77.9	4.6	1.2–17.9
Moderate mammillary deviation	1.6	0.6–4.4	4.5	1.2–15.8	1.3	0.5–3.0
Marked mammillary deviation	7.2	1.5–34.1	2.3	0.2–26.9	0.3	0.0–3.5
Moderate breast oedema	1.3	0.4–3.9	2.7	0.6–13.3	1.0	0.4–2.5
Marked breast oedema	2.1	0.4–11.5	62.2	6.8–575.0	6.1	1.5–24.3

The sector resection in this study was highly standardised and more extensive than in most other studies that evaluate the cosmetic results [4–8]. Nevertheless, the cosmetic score is similar to that in patients who have undergone less extensive surgery in the breast but better than that reported after quadrantectomy [27]. The multivariate analysis reveals that important factors in patients with less satisfactory results include contour differences, breast oedema and mammillary deviation. Irradiation increases the risk of acquiring these changes. However, since the effect of irradiation diminished somewhat in the final multivariate model, although the effects of the changes in appearance were still important, it seems that irradiation is not the only factor that negatively influences the appearance of the breast. The development of postoperative complications, such as a haematoma, seroma or an infection in the breast or axilla, did not greatly affect the development of a less satisfactory result.

Patients' characteristics such as age, social status, body mass index or breast size were not found to be of importance, except that women with medium-sized breasts tended to be more satisfied. The finding of a less satisfactory cosmetic result in tumours ≤ 5 mm is based on 13 patients only, and should thus be interpreted cautiously. However, the relative hazards were statistically significantly elevated for all three modes of evaluation, and this is unlikely to be due to chance alone. Women with small tumours were asymptomatic at the time of diagnosis and might, therefore, be less able to accept a disfiguration of the breast. This explanation accords with our previous finding that women who underwent a sector resection for a benign lesion reported a less satisfactory cosmetic result [28]. This hypothesis does not, however, explain the ratings made by the health care professionals or the panel. Another reason may be that sometimes when the tumour is not palpable, a disproportionally large amount of breast tissue is removed in order to ensure that all affected tissue has been excised, as compared to when the tumour is palpable and the margins can be distinctly controlled by bidigital palpation.

Our results confirm Pezner's finding that when photographs are shown to a panel of observers they have large differences of opinion [29]. To overcome this difficulty several authors have tried to make an objective measurement of the cosmetic result [20, 29–30]. However, as compared to subjective quality scoring, these methods seem to give essentially the same results [20].

It is noteworthy that blind evaluation by other observers is more sensitive than evaluation by the patients themselves of differences due to, e.g. radiotherapy or postoperative infections. From a clinical standpoint, however, it is particularly relevant to learn as much as possible about the patient's view.

In this study and in several others, where both the patients' views and an observers' opinions have been given, the patients have given higher scores for satisfaction [6, 10, 19]. This finding may have several different or interacting explanations: patients, when asked by a person involved in their treatment about the cosmetic result, may not want to express any criticism. If this is thought to be a major problem, additional evaluations by an independent panel, such as that used in this study, may be a prerequisite for valid results. To retain the breast even if the treated breast differs clearly from the other, may be so essential for many women choosing conservative surgery that its appearance is of less importance to them.

In summary, sector resection, aiming at local radical surgery and axillary dissection, can be performed with a good cosmetic result in stage I breast cancer. Postoperative radiotherapy to a total of 54 Gy to the breast, given in two tangential fields over 5 weeks, without a boost, has a negative impact on the cosmetic result during the first 3 years after treatment. From a clinical standpoint, however, the negative effect is moderate and needs to be seen in a larger perspective of the total cost–benefit of postoperative radiotherapy [31].

Factors of importance which lead to less satisfaction with the cosmetic result are the development of differences in breast contour, breast oedema and mammillary deviation after treatment. When the results of radiotherapy are unsatisfactory, it seems to be mainly mediated through these factors.

1. Veronesi U, Saccozzi R, Del Vecchio M, *et al.* Comparing radical mastectomy with quadrantectomy, axillary dissection and radiotherapy in patients with small cancers of the breast. *New Engl J Med* 1981, **305**, 6–11.
2. Fisher B, Redmond C, Poisson R, *et al.* Eight-year results in a randomized clinical trial comparing total mastectomy and lumpectomy with or without radiation in treatment of breast cancer. *New Engl J Med* 1989, **320**, 822–828.
3. Atkins H, Hayward JL, Klugman OJ, Wayk AB. Treatment of early breast cnacer: a report after ten years of clinical trial. *Br Med J* 1972, **2**, 423–429.
4. Rose AM, Olivotto I, Cady B, *et al.* Conservative surgery and irradiation therapy for early breast cancer: long-term cosmetic results. *Arch Surg* 1989, **124**, 153–157.
5. Read PE, Ash DV, Thorgood J, Benson EA. Short-term morbidity and cosmesis following lumpectomy and radical radiotherapy for operable breast cancer. *Clin Radiother* 1987, **38**, 371–373.
6. Beadle GF, Silver B, Botnick L, Hellman S, Harris JR. Cosmetic results follow primary radiation therapy for early breast cancer. *Cancer* 1984, **54**, 2911–2918.
7. Clarke D, Martinez A, Cox RS. Analysis of cosmetic results and complications in patients with stage I and II breast cancer treated by biopsy and radiation. *Int J Radiat Oncol Biol Phys* 1983, **9**, 1807–1813.
8. Dewar JA, Behamou E, Behamou R, *et al.* Cosmetic results following lumpectomy, axillary dissection and radiotherapy for small breast cancers. *Radiother Oncol* 1988, **12**, 273–280.
9. Margolies R, Poisson R, Shibata R, *et al.* The technique of segmental mastectomy and axillary dissection: a syllabus from the National Surgical Adjuvant Breast Project Workshop. *Surgery* 1987, **102**, 828–834.
10. Ray GR, Fish VJ. Biopsy and definitive radiation therapy in stage I and II adenocarcinoma of the female breast: analysis of cosmesis and the role of beam supplementation. *Int J Radiat Oncol Biol Phys* 1983, **9**, 813–818.
11. Olivotto I, Rose MA, Silver B, *et al.* Late cosmetic outcome after conservative surgery and radiotherapy: analysis of causes of cosmetic failure. *Int J Radiat Oncol Biol Phys* 1989, **17**, 747–753.
12. Ray GR, Fish VJ, Marmor JB, *et al.* Impact of adjuvant chemotherapy on cosmesis and complications in stage I and II carcinoma of the breast treated by biopsy and radiation therapy. *Int J Radiat Oncol Biol Phys* 1984, **10**, 837–841.
13. Beadle GF, Come S, Henderson C, Silver B, Hellman S, Harris JR. The effect of adjuvant chemotherapy on the cosmetic results after primary radiation therapy for early breast cancer. *Int J Radiat Oncol Biol Phys* 1984, **10**, 2131–2137.
14. Seymour HL. Primary treatment of early breast cancer with conservation surgery and radiation therapy: the effect of adjuvant chemotherapy. *Cancer* 1985, **55**, 2140–2148.
15. Harris JR, Levene MB, Svensson G, *et al.* Analysis of cosmetic results following primary radiation therapy for stage I and II carcinoma of the breast. *Int J Radiat Oncol Biol Phys* 1979, **5**, 257–261.
16. Van Limbergen E, Rijnders A, Van der Schueren, *et al.* Cosmetic evaluation of conserving treatment for mammary cancer. 2: a quantitative analysis of the influence of radiation dose, fractionation schedules and surgical treatment techniques on cosmetic results. *Radiother Oncol* 1989, **16**, 253–267.
17. Delouche G, Bachelot F, Premont M, Kurtz JM. Conservation treatment of early breast cancer: long-term results and complications. *Int J Radiat Oncol Biol Phys* 1987, **13**, 29–34.
18. Pezner RO, Patterson MR, Hill LR, Vora NL, Desai KR, Lipsett JA. Breast retraction assessment: Multiple variable analysis of factors responsible for cosmetic retraction in patients treated conservatively for stage I and II breast carcinoma. *Acta Radiol Oncol* 1985, **24**, 327–330.
19. Dubois JB, Gary Bobo J, Pourquier H, Pujol H. Tumorectomy and radiotherapy in early breast cancer: a report on 392 patients. *Int J Oncol Biol Phys* 1988, **15**, 1275–1282.
20. Van Limbergen E, van der Schueren E, van Tongelen K. Cosmetic evaluation of breast-conserving treatment for mammary cancer. 1: proposal of a quantitative scoring system. *Radiother Oncol* 1989, **16**, 159–167.
21. Holmberg L, Liljegren G, Adami HO *et al.* Sector resection with or without postoperative radiotherapy for stage I breast cancer. A randomized trial. *J Natl Cancer Inst* 1990, **82**, 277–282.
22. Aspegren K, Holmberg L, Adami HO. Standardization of the surgical technique in breast-conserving treatment of mammary cancer. *Br J Surg* 1988, **75**, 807–810.
23. Frank HA, Hall FM, Steer ML. Preoperative localization of nonpalpable breast lesion demonstrated by mammography. *New Engl J Med* 1976, **295**, 259–260.
24. Raininko R, Linna MI, Räsänen O. Preoperative localization of non-palpable breast tumors. *Acta Chir Scand* 1976, **142**, 575–578.
25. Kleinbaum DG, Kupper LL, Muller KE. *Applied Regression Analysis and Other Multivariable Methods*, 2nd edition. Boston, PWS-Kent Publishing Co., 1988, 327–328.
26. SAS Institute Inc. *SAS/STAT Software. CALIS and Logistic Procedures*. Release 6.04. NC, 1990.
27. Sacchini V, Luini A, Tana S, *et al.* Quantitative and qualitative cosmetic evaluation after conservative treatment for breast cancer. *Eur J Cancer* 1991, **27**, 1395–1400.
28. Holmberg L, Zarén E, Adami HO, *et al.* The patient's appraisal of the cosmetic result of segmental mastectomy in benign and malignant disease. *Ann Surg* 1988, **207**, 189–194.
29. Pezner R, Lipsett JA, Vora NL, Desai KR. Limited usefulness of observer-based cosmesis scales employed to evaluate patients treated conservatively for breast cancer. *Int J Radiat Oncol Biol Phys* 1985, **11**, 1117–1119.
30. Tsoukas LI, Fentiman IS. Breast complicance: a new method for evaluation of cosmetic outcome after conservative treatment of early breast cancer. *Breast Cancer Res Treat* 1990, **15**, 185–190.
31. Liljegren G, Holmberg L, Adami HO, *et al.* Sector resection with or without postoperative radiotherapy for stage I breast cancer: five-year results of a randomized trial. Submitted.

Acknowledgements—Our sincere thanks are due to Ms Anne Jennische for devoted and high quality secretarial assistance and to Ms Frida Liljegren for skilful assistance in collecting the data. We are also indebted to Drs Ö. Selking, M. Svensson, Ms E. Rääf and E. Larsson who examined the photographs. Financial support was received from the Örebro County Medical Research Fund and the Swedish Cancer Society.

APPENDIX

The Uppsala-Örebro Breast Cancer Study Group

Protocol committee: HO Adami, S Graffman, L Holmberg.
Principal investigators: HO Adami, L Holmberg, G Liljegren.
Study coordinator: L Holmberg, G Liljegren.
Preparation of manuscript: G Liljegren, L Holmberg, G Westman.
Participating investigators:
Central Hospital, Falun: A Cohen, U Ljungqvist, Department of Surgery.
Central Hospital, Västerås: L Bergkvist, Department of Surgery; L Johansson, Department of Oncology.
University Hospital, Uppsala: L Holmberg, Department of Surgery; HO Adami, Cancer Epidemiology Unit.
Central Hospital, Eskilstuna: Å Rimsten, Department of Surgery; B Stenstam, Department of Oncology.
Central Hospital, Karlstad: T Jahnberg, Department of Surgery; M Söderberg, Department of Oncology.
Örebro Medical Centre Hospital: G Liljegren, Department of Surgery; G Westman, Department of Oncology.
Consulting radiologist: L Tabar, Department of Mammography, Central Hospital, Falun.

Eur J Cancer, Vol. 29A, No. 15, pp. 2089–2093, 1993.
Printed in Great Britain

0959–8049/93 $6.00 + 0.00
Pergamon Press Ltd

Grading of Soft Tissue Sarcomas: Experience of the EORTC Soft Tissue and Bone Sarcoma Group

J.A.M. van Unnik, J.M. Coindre, C. Contesso, Ch.E. Albus-Lutter, T. Schiodt, R. Sylvester, D. Thomas, V. Bramwell and H.T. Mouridsen

A practical grading system for soft tissue sarcomas was developed, based on 282 eligible patients entered in an EORTC adjuvant clinical trial. The primary tumours in this trial had to be adequately treated. Histopathological parameters, which appeared significant in two preceding studies, were tested. These parameters were differentiation of the tumour, presence and amount of necrosis, the presence and amount of myxoid areas and the number of mitoses. In addition, the size of the tumour was also analysed. The quantitative data (mitotic count and size of the tumour) were not *a priori* grouped, but were divided into categories based on the results of the statistical analysis. Based on a multivariate analysis only mitotic count, the presence or absence of necrosis and the size of the tumour were significantly correlated with the duration of survival or the time to distant metastases. Of these parameters, the mitotic count was the most important.
Eur J Cancer, Vol. 29A, No. 15, pp. 2089–2093, 1993.

INTRODUCTION

THE HISTOLOGICAL typing of soft tissue sarcomas gives only limited information about their clinical behaviour. Most soft tissue malignancies, and particularly the most frequent entities, cover a large spectrum of aggressiveness and metastatic potential [1].

Hence the grading of these tumours is an essential adjunct to the histological typing. It would be ideal if we could arrive at a grading system adapted to all known prognostic factors, such as the histological (sub)type, the localisation and the size of the tumour and its relation to vital structures. To obtain statistically meaningful figures in this way, one would have to study a very large number of uniformally treated patients. It is understood that this is hardly ever possible, taking into account the rarity of this group of malignancies. Moreover, the histogenetic typing of soft tissue sarcomas, even with the aid of modern immunochemical markers, still has a non-negligible degree of uncertainty.

The pathological subcommittee of the Soft Tissue and Bone Sarcoma Group of the EORTC was asked to develop a practical grading system which could be used in the framework of a multicentre clinical trial. Members of this subcommittee participated in two previous studies.

In the study of Albus-Lutter [2], based on 400 cases at the Netherlands Cancer Institute, soft tissue sarcomas were typed according to Enzinger and Weiss [1], and a grading system was worked out for the different histological types when the number of cases of a particular type was sufficient. Also, a grading system was developed irrespective of the histogenetic type of the tumour. The parameters tested were the number of mitoses, presence and degree of necrosis and myxoid components, grade of differentiation, localisation (superficial versus deep; anatomical localisation) and the size of the tumour. Also, patient

Correspondence to J.A.M. van Unnik at the Department of Pathology, HO4.212, University Hospital, P.O. Box 85500, AZU, 3508 GA Utrecht, The Netherlands.
J.M. Coindre is at the Fondation Bergonie, Bordeaux, France; C. Contesso is at the Institute Gustave-Roussy, Villejuif, France; Ch. E. Albus-Lutter is at the Department of Pathology, Eemland Hospital, Amersfoort, The Netherlands; T. Schiodt is at the Department of Pathology, Rigshospitalet, Copenhagen, Denmark; R. Sylvester and D. Thomas are at the EORTC Data Center, Brussels, Belgium; V. Bramwell is at the OCTRF London Regional Cancer Centre, London, Ontario, Canada; and H.T. Mouridsen is at the Rigshospitalet Finsen Institut, Copenhagen, Denmark.
Revised 19 May 1993; accepted 13 Aug. 1993.