Int. J. Radiation Oncology Biol. Phys., Vol. 19, pp. 235–242
Printed in the U.S.A.

0360-3016/90 $3.00 + .00

● *Original Contribution*

EXTERNAL IRRADIATION OF EPITHELIAL SKIN CANCER

RICHARD D. LOVETT, M.D., CARLOS A. PEREZ, M.D., SUSAN J. SHAPIRO, M.D. AND DELIA M. GARCIA, M.D.

Radiation Oncology Center, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO 63110

A total of 339 consecutively treated, biopsy proven squamous and basal cell carcinomas of the skin treated from January 1966 to December 1986 were retrospectively analyzed to determine the patterns of local recurrence. There were 242 basal cell carcinomas, 92 squamous cell carcinomas, and 5 variants of squamous cell carcinoma in various locations. Radiotherapy was the initial treatment modality in 212 patients and 127 were treated after failing initial surgical excision. Lymph nodes were involved in 1/242 patients (.4%) with basal cell carcinoma, 14/92 patients (15%) with initially treated squamous cell carcinoma, and 20/51 (39%) with recurrent squamous cell lesions. Distant metastasis was found in one patient. Superficial X rays were given to 187 patients, electrons to 57 patients, megavoltage photons to 15, and a combination of modalities to the remainder. Overall local tumor control was achieved in 292 of 339 patients (86%), 220 of 242 (91%) with basal cell and 73 of 97 (75%) with squamous cell carcinoma. Tumor control was closely related to the size of the primary lesion. For lesions < 1 cm tumor control was 97% (86/89) for basal cell and 91% (21/23) for squamous cell carcinoma. For 1 to 5 cm, tumor control was 87% (116/133) for basal cell and 76% (39/51) for squamous cell carcinoma and for lesions greater than 5 cm, the tumor control was 87% (13 of 15) and 56% (9/16), respectively. Tumor control was related to the modality used to treat the patient in spite of stratification of primary lesion size. For superficial X rays, tumor control was 98% (81/83) for lesions < 1 cm, 93% (94/101) for lesions 1–5 cm and 100% (5/5) for lesions greater than 5 cm. For electrons tumor control was 88% (14/16), 72% (23/32), and 78% (7/9), respectively. For mixed beams tumor control was 90% (9/10), 76% (32/42), and 64% (9/14), respectively, and for ^{60}Co-4 MV X rays, tumor control was 100% (3/3), 67% (6/9), and 33% (1/3), respectively.

Cosmesis and complications were analyzed in 261 patients. An excellent or good cosmetic result was found in 92% (239/261) of the patients. There were 8 of 261 patients (3.1%) with fair and 19 of 261 (7.3%) with poor cosmesis. Cosmesis had an inverse relation to the primary lesion size with 97 of 99 patients (98%) with tumors 1 cm or less, 123 of 140 patients (88%) with lesions 1 to 5 cm and 13 of 16 patients (82%) with larger tumors having excellent or good cosmetic results. Cosmesis is also related to treatment modality. Excellent or good cosmesis was seen in 161 of 169 patients (95%) with superficial X rays, 37 of 46 patients (80%) with electrons, 39 of 51 patients (76%) with mixed beams, and 7 of 10 patients (70%) with megavoltage photons. The overall complication rate was 5.5% (17/310); this was directly related to the primary tumor size. For lesions 1 cm or less, the complication rate was 0.9% (1/108), for lesions 1 to 5 cm 7.1% (12/169), and for lesions > 5 cm 13.6% (3/22). Undoubtedly, this is related to larger volumes and higher irradiation dose used to treat them. We conclude that radiotherapy is an excellent treatment modality for epithelial skin cancer. Local tumor control, cosmesis, and complications are related to size of the primary lesion and thus treatment at an early stage is strongly recommended. Since tumor control and cosmesis also correlated with technical factors, careful attention to radiotherapy technique is required.

Skin cancer, Irradiation.

INTRODUCTION

Epithelial skin cancer is a common neoplasm which affects about 500,000 Americans each year (14). Seventy-five percent to 90% of these nonmelanomatous lesions are basal cell carcinoma and the majority of the remainder are squamous cell carcinomas. The most common etiology of epithelial skin cancer is ultraviolet light, an agent to which we are all exposed (4). Treatment of these cancers may be performed with many modalities: surgical excision (7), Moh's chemosurgery (10, 16), electrocautery (7), or radiotherapy (7, 11). The superficial nature of epithelial skin cancer makes it readily accessible to examination thus offering a potential for early diagnosis and cure. The

Presented at the 31st Annual ASTRO Meeting, San Francisco, CA, 1–6 October, 1989.

Reprint requests to: Carlos A. Perez, M.D., Radiation Oncology Center, Suite 411, 4511 Forest Park, St. Louis, MO 63108.

Acknowledgements—The authors would like to thank Alice Becker, Nancy A. Kucik, and Leslie McConnell-Clubbs for their valuable assistance in preparing this manuscript as well as the physicians of the Mallinckrodt Institute of Radiology whose patients were included in this paper.

Accepted for publication 13 February 1990.

superficial nature of this disease places emphasis on the cosmetic result of treatment.

Radiotherapy is a logical choice as a treatment modality for epithelial skin cancer particularly in the head and neck region. Its ability to treat a wide area with little alteration of normal tissues allows it to produce excellent cosmetic results as well as a high chance of treatment success. In the use of radiotherapy, consideration must be given to technical parameters such as total dose, dose per fraction, type of beam used, bolus use, and field size, which have an impact upon the final treatment results.

This report is a retrospective review of patients treated at our institution for epithelial skin cancer, examining treatment parameters and their impact on freedom from local relapse, cosmesis, and complication rate.

METHODS AND MATERIALS

Patient material

During a 20-year period from January 1966 to December 1986, a total of 339 consecutively treated and histologically confirmed basal cell and squamous cell skin cancers were treated at the Mallinckrodt Institute of Radiology. Radiotherapy records, referring physician reports, autopsies and hospital records were examined to gain data on the cosmesis, complication rate, and local recurrence rate for the patients. All patients were followed for a minimum of 2 years or until death or until lost to follow-up.

Of the 339 patients, there were 203 men (60%) and 136 women. There were 242 basal cell carcinomas (71%) and 97 squamous cell carcinomas (29%). Men comprised 76% of the basal cell population and 54% of the squamous cell patients. The age distributions for basal cell and squamous cell patients are similar with the peak incidence occurring from age 70 to 80 and the range extending from the third to ninth decade. The anatomic location of the basal cell and squamous cell lesions is shown in Figure 1. Ninety-three percent of the basal cell lesions are located on the head, with 45% occurring on the nose or in a periorbital location. Eighty-seven percent of squamous cell carcinomas are located on the head with 48% on the ear, scalp, or nose. One-hundred and seventy-one basal cell lesions (71%) were untreated and 71 (29%) were recurrent at presentation. Of the squamous cell lesions 46 (47%) were untreated and 51 (53%) recurrent. Squamous cell lesions, both untreated and recurrent, tended to be larger than basal cell carcinoma. The percent of lesions larger than 5 cm for squamous cell carcinoma untreated and recurrent was 11% and 24%, respectively, versus 8% and 3% for a basal cell carcinoma.

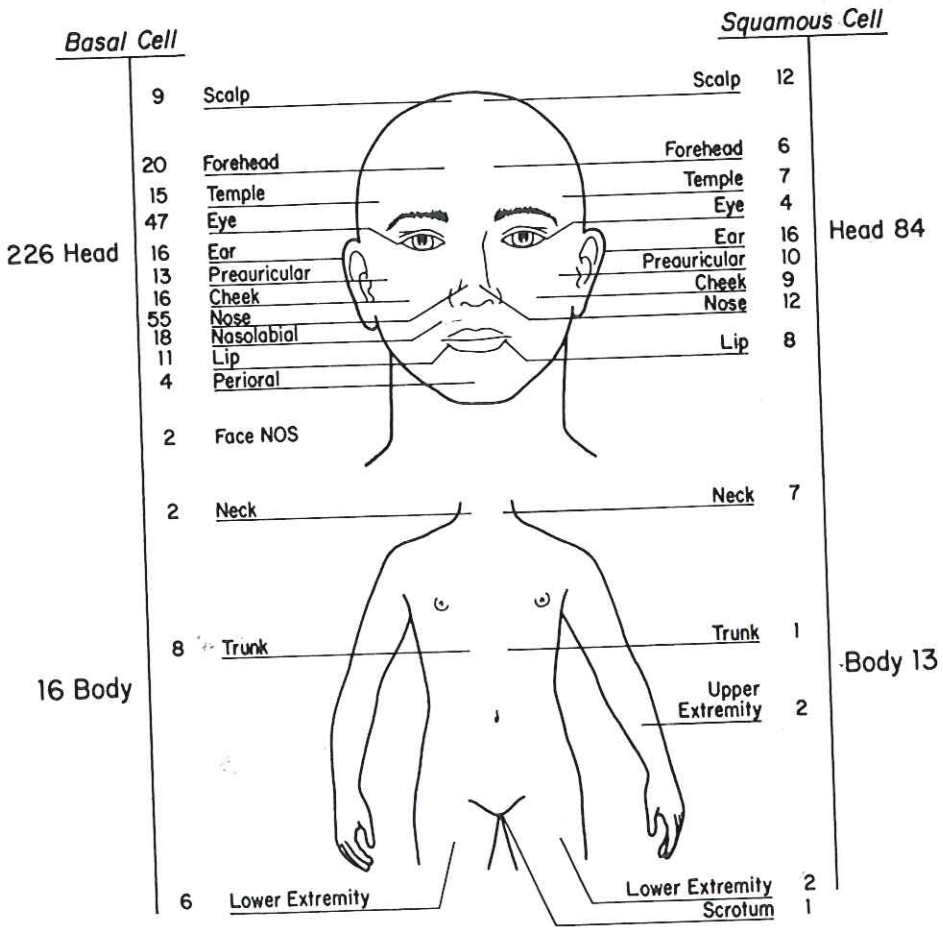

Fig. 1. Anatomic location of squamous cell and basal cell carcinomas treated at Mallinckrodt Institute of Radiology (1966–1986).

Table 2. Carcinoma of the skin—tumor control by size, histology, and presentation

Size	Basal cell untreated	Basal cell recurrent	Squamous cell untreated	Squamous cell recurrent
<1 cm	64/66 (97%)	22/23 (96%)	11/11 (100%)	10/12 (83%)
1.1–3 cm	71/75 (95%)	27/36 (75%)	19/21 (90%)	7/13 (54%)
3.1–5 cm	11/13 (85%)	7/9 (78%)	7/8 (88%)	6/9 (67%)
>5 cm	12/13 (92%)	1/2 (50%)	3/5 (60%)	6/11 (55%)
Size not specified	4/4 (100%)	1/1 (100%)	0/1 (0%)	4/6 (67%)
Total	162/171 (95%)	58/71 (82%)	40/46 (87%)	33/51 (65%)

and greater than 5 cm had 96%, 86%, 79%, and 71% freedom from local recurrence, respectively.

When the lesions are stratified by histology, tumor control showed the same negative correlation with increasing tumor size (Table 2). For basal cell lesions, the tumor control was 97% (86/89) for lesions less than 1 cm, 87% (116/133) for lesions 1.1 to 5 cm, and 86% (13/15) for lesions larger than 5 cm. For squamous cell carcinoma tumor control was 91% (21/23), 76% (39/51), and 56% (9/16), respectively.

Tumor control was analyzed according to type of external beam used in the treatment. Table 3 shows this data for basal cell lesions and Table 4 shows the data for squamous cell lesions. Overall tumor control for superficial x-ray beam treatment was 98% (81/83) for lesions less than 1 cm, 93% (94/101) for lesions 1.1 to 5 cm, and 100% (5/5) for lesions greater than 5 cm. For electron beam treatment, the tumor control was 88% (14/16), 72% (23/32), and 78% (7/9), respectively. For mixed beams tumor control was 90% (9/10), 76% (32/42), and 64% (9/14) and for megavoltage photon beams tumor control was 100% (3/3), 67% (6/9), and 33% (1/3).

Tumor control was examined according to histology and tumor diameters, total dose and dose per fraction. Basal cell carcinomas (Table 5) 1 cm or smaller had tumor control greater than 95% with all dose fraction schemes used. Basal cell lesions 1.1–5 cm exhibited a trend for better tumor control as the fraction size increased from ≤200 cGy to 301–400 cGy with 71%, 92%, 100%, and 100%, respectively. These lesions were also controlled more often as total dose increased until doses > 6000 cGy when a 76% tumor control was seen. Basal cell lesions > 5 cm showed greater tumor control as the total dose increased. The differences found in tumor control vs dose per fraction are not statistically significant.

In squamous cell lesions (Table 6), again with lesions 1 cm or less there was no dose response to fraction size or total dose; this group achieving 91% tumor control. In the 1.1–5 cm squamous cell group there is a dose response when fraction size is increased, 71% and 79% tumor control for ≤200 cGy per fraction and 201–300 cGy per fraction. When examining total dose there is an inverse dose response with lesions receiving ≤5000 cGy having 100% tumor control and >5000 cGy having 70% ($p = 0.048$). The same inverse dose response is seen with squamous cell tumors > 5 cm in diameter. For ≤5000 cGy total dose 100% tumor control was seen and for lesions receiving >5000 cGy 42% tumor control was seen ($p = 0.089$). This is probably related to the usual clinical practice of using higher tumor doses for larger lesions and for those which show poor regression with standard radiation doses.

In the patients with squamous cell carcinoma having nodal metastases at presentation the primary tumor control of lesions ≤ 1 cm was 100% (5/5), in the 1.1–5 cm lesions 69% (9/13), and for lesions > 5 cm or of unspecified size 56% (5/9). A separate publication will further describe the results in these patients (Shapiro, SJ, personal communication, 1989).

A multivariate analysis of factors possibly contributing to the tumor control was performed. Variables examined were the type of external beam used, dose per fraction, type of presentation, age, maximum tumor diameter, pathology, total dose, and the sex of the patient. The type of beam ($p < 0.001$) and the dose per fraction ($p = 0.001$) as well as primary (untreated) versus recurrent presentation ($p = 0.01$), and tumor diameter ($p = 0.043$) were

Table 3. Carcinoma of the skin—basal cell carcinoma local tumor control by modality and size

Modality	Size			
	<1 cm	1.1–5 cm	>5 cm	Not specified
Superficial X ray	69/71 (97%)	84/90 (93%)	4/4 (100%)	3/3 (100%)
Electron beam	11/12 (92%)	16/22 (73%)	4/5 (80%)	1/1 (100%)
Combination	5/5 (100%)	13/16 (81%)	5/6 (83%)	0/0
Photons (1.2–4 MV)	1/1 (100%)	3/5 (60%)	0/0	1/1 (100%)

$p = 0.013$

Table 4. Carcinoma of the skin—squamous cell carcinoma local tumor control by modality and size

Modality	Size			
	<1 cm	1.1–5 cm	>5 cm	Not specified
Superficial X ray	12/12 (100%)	10/11 (91%)	1/1 (100%)	0/0
	$p = 0.17$	$p = .41$		
Electron beam	3/4 (75%)	7/10 (70%)	3/4 (75%)	0/1 (0%)
Combination	4/5 (80%)	19/26 (73%)	4/8 (50%)	2/4 (50%)
Photons (1.2–4 MV)	2/2 (100%)	3/4 (75%)	1/3 (33%)	2/2 (100%)

highly significant prognostic factors. Histology, total tumor dose, and the patient's sex were not significant.

Cosmesis

Cosmesis was evaluated by the presence of telangiectasia, pigmentation change or fibrosis. Radiation therapy records, clinic notes, hospital records, and autopsy records were used to evaluate cosmesis in 261 patients with available information. The scale used was described previously. One hundred and thirty-two of the patients (51%) in which cosmesis was described had excellent, 41% (107 patients) good, 3.1% (8 patients) fair, and 7.3% (19 patients) poor cosmesis.

The patients were stratified according to total dose and dose per fraction. Neither parameter had a significant relation with cosmesis. When total dose and dose per fraction are examined together (Fig. 2), the majority of poor and fair cosmesis results occur in the patients treated with total doses > 5000 cGy and a dose per fraction less than 300 cGy.

Patients were also examined for cosmetic result after stratifying for pathology and type of presentation (Fig. 3). There was no significant relation overall between untreated or recurrent lesions; however, when stratified by histology, squamous cell lesions did have a higher incidence of fair and poor cosmetic results. In the squamous group, recurrent lesions did have poorer cosmesis with 29% (10/34) having a fair or poor cosmetic result.

Lesion size appeared to have an inverse relationship with cosmesis larger lesions having poorer results (Fig. 4). For all lesions ≤ 1 cm there were 55% excellent and 43% good results. For 1.1–3 cm lesions there were 45% excellent and 38% good results. For lesions > 3 cm, there were 40% excellent and 29% good results.

Patients were also stratified into groups by the type of radiation beam used in treatment. Excellent or good cosmesis was seen in 97% (159/164) of the patients treated with superficial X rays, 78% (32/41) of the patients treated with electrons, 78% (40/51) of the patients treated with mixed beams, and 80% (8/10) of the patients treated with megavoltage photons.

Complications

The overall complication rate for the 310 patients with available information treated over the 20 years studied was 5.5% (17/310). This group was composed of 15 pa-

Table 5. Carcinoma of the skin—basal cell carcinoma local tumor control by total dose, dose per fraction, histology, and tumor dose

Lesions	Dose/fraction (cGy)				
	<200	201–300	301–400	>400	
<1 cm					
<4000 cGy	1/1	2/2	1/1	1/1	5/5 (100%)
4001–5000 cGy	12/13	22/23	6/6	8/8	48/50 (96%)
5001–6000 cGy	7/7	17/18	4/4	2/2	30/31 (97%)
>6000 cGy	0/0	2/2	0/0	1/1	3/3 (100%)
	20/21 (95%)	43/45 (96%)	11/11 (100%)	12/12 (100%)	
1.1–5 cm					
<4000 cGy	3/6	5/5	1/1	4/4	13/16 (81%)
4001–5000 cGy	10/14	19/20	6/6	8/8	43/48 (90%)
5001–6000 cGy	13/15	25/28	1/1	6/6	45/50 (90%)
>6000 cGy	4/7	8/9	1/1	0/0	13/17 (76%)
	30/42 (71%)	57/62 (92%)	8/8 (100%)	18/18 (100%)	
>5 cm					
<5000 cGy	1/1	2/3	0/0	0/0	3/4 (75%)
5001–6000 cGy	3/4	5/5	0/0	0/0	8/9 (89%)
>6000 cGy	1/1	1/1	0/0	0/0	2/2 (100%)
	5/6 (83%)	8/9 (89%)	0/0	0/0	

Table 6. Carcinoma of the skin—squamous cell carcinoma local tumor control by total dose, dose per fraction, histology, and tumor size

Lesions	Dose/fraction (cGy) <200	201–300	301–400	>400		
<1 cm						
<5000 cGy	2/2	1/1	1/1	3/3	7/7 (100%)	
5001–6000 cGy	2/4	4/4	1/1	0/0	7/9 (78%)	
>6000 cGy	5/5	2/2	0/0	0/0	7/7 (100%)	
	9/11 (81%)	7/7 (100%)	2/2 (100%)	3/3 (100%)		
1.1–5 cm						
<4000 cGy	3/3	3/3	0/0	0/0	6/6 (100%)	
4001–5000 cGy	1/1	4/4	0/0	0/0	5/5 (100%)	$p = 0.048$
5001–6000 cGy	10/16	4/6	3/3	0/0	17/25 (68%)	
>6000 cGy	6/8	4/6	1/1	0/0	11/15 (73%)	
	20/28 (71%)	15/19 (79%)	4/4 (100%)	0/0		
>5 cm						
<5000 cGy	2/2	1/1	1/1	0/0	4/4 (100%)	
5001–6000 cGy	2/5	0/0	0/0	0/0	2/5 (40%)	$p = 0.089$
6000 cGy	2/3	1/4	0/0	0/0	3/7 (43%)	
	6/10 (60%)	2/5 (40%)	1/1 (100%)	0/0		

tients with soft tissue necrosis, two patients with soft tissue and bone necrosis, and one patient with bone necrosis. Only 1 patient of 64 (1.6%) who received treatment to the scalp, forehead or temple suffered from brain necrosis. This patient received treatment with a combination of beams to a total dose of 61.6 Gy for a basal cell carcinoma of the temporal region.

The complication rate is related to the primary lesion size: for lesions < 1 cm, 0.9% (1/108), for lesions 1–5 cm 7.1% (12/169), and for lesions > 5 cm 13.6% (3/22).

In our patient population there were 166 lesions of the periorbital region, which encompassed the forehead, periorbital area, nasal area or temple. Of these 152 lesions there were six patients who developed cataracts (3.9%). The locations of the tumors for these patients were: two in the nose, two in the lower eyelid, one in the upper eyelid, and one lesion in the cheek.

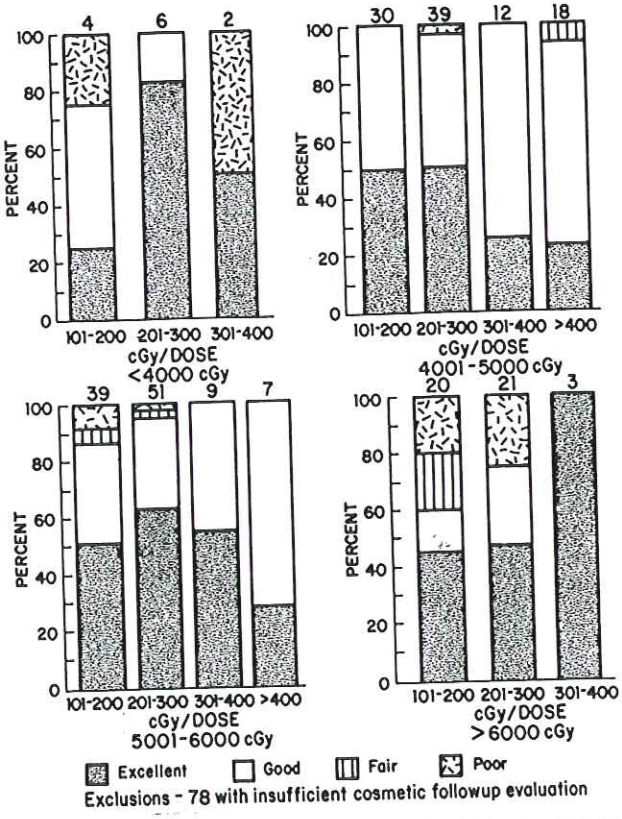

Fig. 2. Cosmetic results for squamous cell and basal cell carcinomas according to total dose of irradiation and average dose per fraction.

DISCUSSION

Epithelial skin cancer is a malignancy which is readily diagnosed through routine physical examination and as

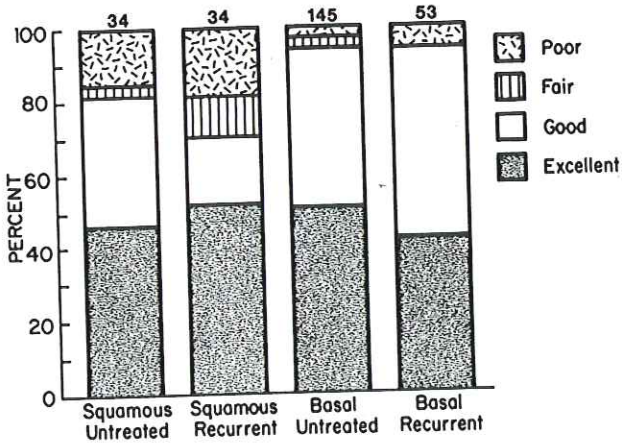

Fig. 3. Cosmesis for epithelial cancer according to histology and status at presentation.

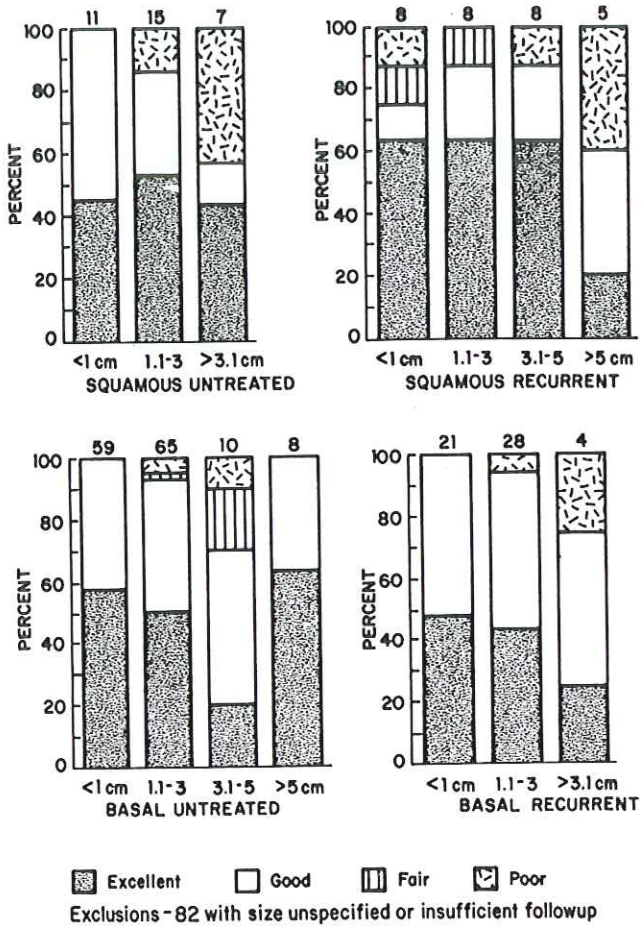

Fig. 4. Cosmesis for epithelial cancer according to histology status at presentation and maximum tumor diameter.

such it should be easily cured through treatment with any one of many modalities. Radiotherapy has the theoretic advantage of being able to treat a wide area encompassing the gross tumor, the area of subclinical spread and a margin of normal tissue with a minimum of normal tissue loss. It should be emphasized that patients should be treated adequately at the time of initial diagnosis. In our study 122 (36%) had failed a previous treatment, either surgery, electrodesiccation, or previous radiotherapy at another institution. These patients with recurrent tumors were shown to have poorer rates of tumor control (82% and 65% for basal cell or squamous cell carcinoma, respectively). If only untreated patients are considered, the tumor control rates were 95% in the basal cell carcinomas and 87% of the squamous cell carcinomas. Tumor control in previously untreated patients is comparable to the 94% rate seen by Fitzpatrick (6).

In Menn's *et al.* study of recurrent basal cell lesions he found a tumor control rate of 53% for all modalities and 73% with radiotherapy (8). There have been studies which have shown a high rate of control of recurrent basal cell lesions (89%) (13).

Often a patient will present initially for treatment with an extensive lesion through years of neglect, misdiagnosis, or self-treatment with home remedies. In this study, 7.5% of all untreated lesions (7.8% of basal cell carcinomas and 6.7% of squamous cell carcinomas) were larger than 5 cm in diameter. For these large basal cell lesions 92% were controlled if this was the initial treatment, but for large squamous cell lesions, only 60% were controlled even at their initial presentation. Our rates of control are comparable to those of Petrovich *et al.* (12), who showed tumor control in 93% of lesions < 2 cm but only 50% of lesions > 5 cm.

Tumor control has been studied in relation to total dose per fraction extensively as skin cancer results being superficial can be monitored without modern imaging devices. Strandquist examined total dose and the length of treatment time in his classic paper (15). He found that patients receiving various doses and fractionation schedules would have similar skin reactions which when plotted would fall on parallel isoeffect lines (11). Others have confirmed these relations (19). Von Essen examined skin necrosis and tumor control by total dose, dose per fraction and the area of the lesion treated to yield isoeffect planes when graphed 3-dimensionally (21). By increasing the total dose and the total time of treatment the 99% tumor regression plane can be surpassed while remaining below the 3% skin necrosis isoeffect plane (21). Others have observed acute reactions and cosmesis by examining prospectively multiple dose fraction combinations delivering the same minimal standard dose. There was no difference in cosmesis between 3 and 10 fractions (1).

In our study we have examined tumor control by stratifying by total dose and dose per fraction and found no significant pattern. However, when further stratified by histology and tumor size, patterns developed. Both basal and squamous lesions ≤ 1 cm had rates of tumor control over 90%. Larger basal cell lesions showed the expected dose response, however, larger squamous cell lesions showed tumor control decreasing with increased total dose. This may be an effect created by extensive squamous cell lesions involving deep structures receiving higher doses, or it could be an artifact caused by the retrospective nature of the study.

Cosmesis was examined in this study retrospectively, using subjective descriptions of telangiectasia, skin pigmentation change, and fibrosis. Whenever available we used photographs or slides to assess cosmesis and verify the subjective description. Objective means have been used by previous authors to document cosmetic alterations. Turesson and Notter (20) used reflectance spectrophotometry to examine telangiectasia and pigmentation changes in patients undergoing internal mammary radiation for breast cancer. We found a correlation between lesion size and cosmesis with larger lesions having poorer results. Patients treated with electron beam have poorer cosmesis than those treated with superficial X rays (excellent results in 78% and 97% of patients, respectively). We are currently analyzing our electron beam treated patients to determine the cause of this poorer cosmesis, since

technical factors such as the amount of bolus or beam energy selection or tumor size may bear on the results.

In our study the total number of complications was 18 of 310. This was mainly due to soft tissue necrosis with only three patients having bone necrosis. No patient suffered from cartilage necrosis although 32 patients received treatment to the ear (16 with basal cell and 16 with squamous cell carcinoma). Six of the scalp necroses occurred in areas being treated for recurrent lesions. Of the 217 previously untreated patients, seven (3.2%) suffered a complication. One of the soft tissue necroses was in the brain (diagnosed by excisional biopsy) in a patient receiving 6160 cGy with ^{60}Co and 10 MeV electrons for a large basal cell carcinoma of the scalp. The patient is alive with no residual neurologic deficit 4 years later. The remaining soft tissue necroses included nine cases of scalp necrosis, one case of ear canal necrosis and two cases of non-healing lower leg ulcers. These leg ulcers formed on one patient after areas of moist desquamation became infected.

In summary, radiation therapy provides excellent treatment to patients with epithelial skin cancers. There is a higher chance of tumor control in previously untreated than in recurrent lesions. Smaller tumors also have a higher control rate, regardless of the histological type. Although squamous cell lesions tended to be larger, however, when stratified by size, basal cell carcinomas were more easily controlled. Patients treated with electron beam therapy seem to have poorer control rates. This may be due to technical factors such as the use of bolus and the collimation of field sizes. Further analysis is ongoing to clarify this issue. Cosmesis has a relationship with pathology as squamous cell lesions in general have poorer cosmesis than basal cell lesions. Larger lesions and recurrent lesions also had poorer cosmetic results.

The rate of complications is within tolerable range of 5.3%. Patients receiving their initial treatment had a lower rate (3.2%) and the complication rate appears to be related to the lesion size, which determines the volume treated (larger) and the dose of irradiation (higher).

REFERENCES

1. Brennan, D.; Young, D. M.; Hopewell, J. W.; Wiernick, G. The effects of varied numbers of dose fractions on the tolerance of normal human skin. Clin. Radiol. 27:27–32; 1976.
2. Cox, D. R. Regression models and life tables. J. Roy. Stat. Soc. 34(Series B 72):187–220; 1972.
3. Cutler, S. J.; Ederer, F. Maximum utilization of the life table method in analyzing survival. J. Chron. Dis. 8:699–713; 1958.
4. Eastcott, D. F. Epidemiology of skin cancer in New Zealand. NCI Monog. 10:141–151; 1963.
5. Fisher, R. A. The use of multiple measurements in taxonomic problems. Ann. Eugenics 7:179–188; 1936.
6. Fitzpatrick, P. J. Skin cancer of the head—treatment by radiotherapy. J. Otolaryngol. 17:535–538; 1964.
7. Freeman, R. G.; Knox, J. M.; Heaton, C. L. The treatment of skin cancer. A statistical study of 1341 skin tumors comparing results obtained with irradiation, surgery and curretage followed by electrodesiccation. Cancer 17:535–538; 1964.
8. Menn, H.; Robins, P.; Kopf, A. W.; Bart, R. S. The recurrent basal cell epithelioma. Arch. Dermatol. 103:628–631; 1971.
9. Miller, R. G. Jr. Survival analysis. New York: John Wiley and Sons; 1981.
10. Mohs, F. E. The chemosurgical method for microscopical controlled excision of cancer of the skin. NY State J. Med. 56:3486–3492; 1956.
11. Orton, C. I. The treatment of basal cell carcinoma by radiotherapy. Clin. Radiol. 4:317–322; 1978.
12. Petrovich, Z.; Kulsk, H.; Langholz, B.; Astrahan, M.; Luxton, G.; Chak, L.; Rice, D. Treatment results and patterns of failure in 646 patients with carcinoma of the eyelids, pinna and nose. Am. J. Surg. 154:447–450; 1987.
13. Sakkura, C. Y.; Calamel, P. M. Comparison of treatment modalities for recurrent basal cell carcinoma. Plast. Reconstr. Surg. 63:492–496; 1979.
14. Silverberg, E.; Lubera, J. A. Cancer statistics 1989. CA 39: 3–39; 1989.
15. Strandquist, M. Studien uber die kumulative urkung der roentgenstrahlen bei fractionerung. Acta Radiol. 55(Suppl.): 1–292; 1944.
16. Swanson, N. A. Moh's surgery: technique, indications, applications, and the future. Arch. Dermatol. 119:761; 1983.
17. Tarone, R. Tests for trend in life table analysis. Biometrika 62:679–682; 1975.
18. Tarone, R.; Ware, J. On distribution free tests for equality of survival distributions. Biometrika 64:156–160; 1977.
19. Traenkle, H. L.; Hulay, D. Further observations on late radiation necrosis following therapy of skin cancer. Arch. Dermatol. 81:908–912; 1960.
20. Turesson, I.; Notter, G. The influence of the overall treatment time in radiotherapy on the acute reaction: comparison of the effects of daily and twice-a-week fractionation on human skin. Int. J. Radiat. Oncol. Biol. Phys. 10:607–618; 1984.
21. von Essen, C. F. A spatial model of time dose area relationships in radiation therapy. Radiology 81:881–883; 1963.