

Results of Prophylactic Irradiation in Patients with Resected Keloids

A retrospective analysis

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The data of 139 patients with 166 keloids treated postoperatively between 1962 and 1996 were evaluated for prognostic factors and outcomes. Treatment commenced within 48 h after surgery. Radiotherapy was carried out as brachytherapy, using an integrated radionuclide ⁹⁰Sr-⁹⁰Y surface applicator. The median dose delivered to the subcutis amounted to 14 Gy (range 7.5–28.5 Gy). The overall recurrence-free response rate was calculated to be 80% for all keloids. Response rates differed significantly ($p < 0.001$) between the different anatomical regions. The recurrence rate was lowest (2%) with keloids of the face and neck and highest with keloids of the thorax (49%). Outcome also differed significantly, depending on the etiology. Keloids following burns had a poorer success rate than those developing after surgery or mechanical trauma ($p < 0.001$). We were unable to demonstrate any significance in outcome related to gender, age or size. No direct correlation was found between total doses and response rates. In our patients there were no signs of secondary malignancies in the irradiation area within a median follow-up period of 12 years. Two new prognostic factors have been identified: keloid etiology and localization of the disorder.

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Keloids can be the result of a pathological wound-healing process, in which case the region becomes hypertrophic, and a soft tissue mass develops in the surrounding area of the wound, which can extend beyond the former wound margin (1). Like malignancies, keloids have rapid growth phases and phases with little or no growth activity (2). The maximum extension of the disorder is usually reached 2–3 months after the onset of keloid formation (3). Spontaneous regression of these benign tumors has been observed but is infrequent (4). Clinically, it can sometimes be difficult for the physician to differentiate between keloids and hypertrophic scars (5, 6).

In the past, many different treatment modalities have been used, especially surgical excision. Nevertheless, the recurrence rate after surgery alone is calculated to be as high as 50–80% (7–9). Therefore, adjunctive procedures have been proposed in the literature to improve therapeutic outcomes. Intralesional injection of corticosteroids has been widely used for example, but the published 5-year response rates are only around 50% (10, 11). Another approach that has been described is the use of pressure

bandages, but these dressings must be worn for a long time (10).

In our opinion, postoperative irradiation seems to be the best treatment modality. Numerous references in the literature demonstrate that the rate of side effects of this treatment modality is low and response rates are high (12–14).

There has been a considerable turnover of medical investigative staff at our institutes between 1962 and 1996, and the techniques (especially total doses and single doses) have been modified as well. We therefore have sufficient data to establish a dose-response profile for this kind of therapy.

MATERIAL AND METHODS

Between 1962 and 1996, 194 patients with keloids were treated postoperatively with ⁹⁰Sr-⁹⁰Y brachytherapy at the University of Münster and the Paracelsus-Strahlenklinik.

Because keloids are benign disorders, there were no regular follow-up examinations at the institutes and we

could only evaluate the outcome of therapy by using a questionnaire, which was sent to all patients and then analysed. Only the 139 patients with 166 keloids who answered the questionnaires were taken into consideration in this study.

Median ages of patients were 29 years for the female patients and 20 years for the male patients. In 60% of all patients, keloids developed before the third decade of life; 85% of all the keloids had become manifest before the end of the third decade and only 15% of all treated keloids had developed later in the fourth decade. Most of the keloids developed in the region of the thorax anterior (27%). Almost the same incidence was documented for the facial region (25%), followed by manifestations involving the neck (22%) and the abdomen (11%). The rest of the disorders involved the back, extremities, hand and ear (Table 1). All keloids were resected, and irradiation was begun within the first 48 h after resection.

Irradiation was carried out using an integrated Sr-90 surface applicator. The advantage of using contact brachytherapy can be seen in the minimal invasion depth of the β -rays. This means that the 80% isodose penetrates only 2–3 mm below the skin surface. Dosimetric measurements were carried out periodically, using film dosimetry.

Evaluation of disease etiology shows that most keloids developed following surgical resection ($n = 66$), traumatic lesions ($n = 45$) or burns of different degree ($n = 28$). The etiology of the remaining keloids ($n = 27$) was unknown at the time of evaluation. The median extension of the keloids was 6 cm (range: 2–24 cm).

Altogether, there were only 5 keloids larger than 10 cm. Keloids larger than the diameter of an applicator were treated using a special handle, in which up to four applicators could be fixed next to one another.

Twenty-four keloids were exposed to a total dose of between 7.5 Gy and 10 Gy; 30 keloids between 10.5 Gy and 12 Gy; 36 keloids between 12.5 Gy and 14 Gy; 30 keloids between 15 Gy and 17 Gy; 23 keloids between 18 Gy and 20 Gy; 11 keloids between 21 Gy and 25 Gy; and 12 keloids between 26 Gy and 28.5 Gy. The median single dose was 3 Gy (range 1.5–4 Gy). Irradiation was carried

Table 2*Total doses of therapy and recurrence rates*

Gy	No. of keloids	No. of recurrences (n)	Recurrence rate (%)
7.5–10	24	2	8
10.5–12	30	6	20
12.5–14	36	9	25
15–17	30	5	17
18–20	23	7	30
21–25	11	1	9
26–28.5	12	4	33
Total	166	34	20.5

out every day with the exception of Saturdays and Sundays. The median follow-up was 12 years and the statistical evaluation was done using χ^2 analysis.

RESULTS

Pain, discomfort or tension was experienced by 75% of the patients before surgical extirpation. Only 25% of all patients were completely symptom-free; 67% of the patients suffering from symptoms attributable to keloid manifestation were female; 85% of the initial patients were totally symptom-free 6 weeks after the end of combined therapy (resection and irradiation). No change in symptoms was documented in 15%, but most of these patients had developed recurrences by this time. Only two patients complained about pain after therapy, but without any signs of recurrences.

In 79.5% of all patients there was no evidence of recurrence and we were unable to document a significant difference between male and female patients (82.4% recurrence-free response rate for the female patients vs. 71.8% recurrence-free response rate for the males). We found that 15% of all recurrences developed within the first 2 months after therapy, 60% within 6 months, 76% within 12 months and 100% within 24 months after the end of therapy. We did not find any recurrences later than 2 years after therapy. Hence, half of all recurrences developed within the first 6 months after therapy. After the end of the first year, about 75% of all recurrences were manifest. However it is worth mentioning that about a quarter of all recurrences developed more than one year after irradiation. We have not seen any correlation between success rates or recurrence rates and total doses (Table 2).

The differences were not statistically significant, but there was a significant difference in treatment outcomes in relation to the anatomical region of the keloids. Patients with keloids in the region of the face and neck had a response rate of nearly 100%, in contrast to patients with disorders in the region of the thorax (Table 3). At the thorax the response rate was only 51%, representing a recurrence rate of 49% ($p < 0.001$).

Table 1*Localization of the keloids*

Localization	Total no. of keloids	Female	Male patients
Thorax	45	15 (41.67%)	21 (58.33%)
Face	42	25 (62.5%)	15 (37.5%)
Neck	37	15 (60%)	10 (40%)
Abdomen	18	13 (81.3%)	3 (18.7%)
Leg	10	5 (55.6%)	4 (44.4%)
Arm	7	5 (71.4%)	2 (28.6%)
Back	3	1 (33.3%)	2 (66.7%)
Ear	2	1 (50%)	1 (50%)
Hand	2	–	1 (100%)

Table 3
Different rates of manifestations dependent on anatomical regions

Localization	Total no. of keloids	Recurrence-free success rate	Recurrence-rate after treatment
Thorax	45	23 (51.1%)*	22 (48.9%)*
Face	42	40 (95.2%)	2 (4.8%)
Neck	37	35 (94.6%)	2 (5.4%)
Abdomen	18	13 (72.2%)	5 (27.8%)
Leg	10	8 (80%)	2 (20%)
Arm	7	5 (71.4%)	2 (28.6%)
Back	3	3 (100%)	– (0 %)
Hand	2	1 (50%)	1 (50%)
Ear	2	1 (50%)	1 (50%)

* $p < 0.001$

Furthermore, we identified a significant correlation (Table 4) between response rate and etiology. Keloids resulting from burns had a significantly poorer outcome than keloids developing after surgical intervention or mechanical trauma ($p < 0.001$). There was no significant correlation between response and the duration of the condition, nor was there a significant correlation between response rate and keloid size.

Keloids existing for more than 2 years before therapy had a recurrence-free response rate of 78.9% in comparison to 68.8% for keloids existing between only 1 and 6 months.

We were unable to document any significant differences in outcome in relation to gender and age.

As far as side effects are concerned, acute erythema was seen in 24% of patients and hypopigmentation in 11%, especially in patients receiving higher total doses. Thus far, no secondary malignancies in the irradiated areas have been reported.

DISCUSSION

Our study identified a response rate of about 80% after keloid resection and irradiation. As already stated, this corresponds to the data from other published work (9, 15, 16). We did not identify a significant difference between response rate and total dose in our patient population, which suggests that lower doses of irradiation may be sufficient (8 Gy–10 Gy). This is also well documented in the literature (11, 17).

We did not observe any difference in therapeutic outcome in relation to gender and age. This fact is discussed controversially in other published studies (11, 14).

Furthermore, we documented a significantly different outcome, depending on the anatomical localization of the keloid. Patients with keloids on the face and neck had a significantly better response rate than those with keloid manifestation on the thorax. This is a point that has not been stressed in the literature in the past. This may be related to traction forces active in the region of the female breast and the décolleté, which can be conducive to the development and recurrence of keloids, but the exact reason for this significant difference remains unclear so far.

We have demonstrated a correlation between keloid etiology and recurrence. Keloids following burns had a significantly poorer outcome than those developing after mechanical trauma or surgical excision. This might be a new prognostic factor in keloid therapy which should be considered in further studies. The observation that keloid manifestations at the thorax and keloids following burns had a poorer outcome was unrelated to the size of the keloids. We did not establish any significant difference in size between keloids on the face and neck and keloids elsewhere on the body.

Acute side effects as well as late side effects were slight and within the area of irradiation, no signs of secondary malignancies could be found. This corresponds to the data from the literature and emphasizes the important role of this therapy modality (9, 12, 13).

Table 4
Impact of etiology on success rate

Cause of keloids	Total no. of keloids	Recurrence-free success rate	Recurrence-rate
Surgery	66	55 (84%)	11 (16%)
Traumat. lesion	45	33 (74%)	12 (26%)
Burns	28	9 (32%)*	19 (68%)*
Unknown	27	24 (88.9%)	3 (11.1%)

* $p < 0.001$

In conclusion, postoperative irradiation of keloids is an effective therapy modality with very few side effects. In our retrospective analysis we were able to confirm some results from other investigators, such as independence from total radiation dose, the high overall success rates and the low incidence of acute and late side effects, too. Furthermore, there were no secondary malignancies within the area of irradiation after a long median follow-up time.

In addition to other reports, we have documented two new prognostic factors. These are the etiology of the keloids and the localization of the disorders. If other investigators could confirm these results, total doses could be increased in the region of the thorax and perhaps in keloids after burns.

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