Treatment of Keloids by Surgical Excision and Immediate Postoperative Single-Fraction Radiotherapy

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The authors report the outcomes of patients with keloid scars treated with a protocol of extralesional excision and immediate single-fraction adjuvant radiotherapy. The design of the study was a retrospective analysis with up to 5-year outcome data. The setting was a single treatment team, University Teaching Hospital in London, United Kingdom. Participants ($n = 80$) were treated for 80 keloid scars (59 percent female patients, 76 percent nonwhite), and 44 percent of keloids were located on earlobes. For all patients, prior treatment without radiotherapy had failed. The salvage treatment reported in this article is combined extralesional excision and immediate postoperative external-beam radiotherapy. A 10-Gy dose of superficial 60-kV or 100-kV photon irradiation was given within 24 hours of the operation. The main outcome measure was freedom from recurrence of keloid scars. Results were that all keloid scars were controlled at 4-week follow-up. Probability of relapse at 1 year was 9 percent; at 5 years, probability of relapse was 16 percent. The earlobe showed no greater chance of relapse than other sites on the body. The authors' report shows that extralesional excision of keloid followed by early, single-fraction, postoperative radiotherapy is both simple and effective in preventing recurrence at excision sites. (*Plast. Reconstr. Surg.* 111: 1853, 2003.)

Keloid is defined as a healed human skin wound that extends beyond the confines of the original wound and is characterized by overabundant collagen deposition.[1] Keloids occur in all races, with a preponderance in Africans.[2] The disease appears to run in families, but the mode of inheritance is not clear.[3] Keloids form in both sexes equally within the same age group. Regional susceptibility to keloids is also recognized, with the presternal area, the back, and the posterior neck being the most common sites.[4] Keloids are clinically different from hypertrophic scars in that they are not confined to the wound and have a thicker and glassy appearance. The distinction is frequently difficult but is important to make before treatment, because the natural history of hypertrophic scars is that of spontaneous softening and flattening, whereas keloids remain thick and raised for years.[1,5]

The variety of treatments for keloids suggests that none are satisfactory. Surgery alone leads to recurrence rates of 45 to 100 percent.[6] Other treatments in current practice are application of silicone gel,[7] pressure dressing therapy,[8,9] and intralesional steroid injections.[10] In the only randomized trial of any treatment for keloids, surgery and radiotherapy combined appeared to be more effective than surgery and corticosteroid injections (12.5 percent versus 33 percent relapse at 12 months after treatment), but patient numbers failed to reach significance.[11]

At our institution, for the past 10 years, high-risk keloids have been treated by a single protocol of extralesional excision followed by postoperative single-fraction radiotherapy the following day. Patients were also followed using a formal protocol within a single clinic. The purpose of this study was to review the results of the Marsden protocol and to highlight certain aspects of the protocol that contribute to its outcome and cost effectiveness.

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Patients and Methods

Notes of patients who were treated at St. George's Hospital and the Royal Marsden Hospital from 1987 were obtained. A standard form was used to collect and record information from the notes. All cases of keloid were diagnosed clinically using the criteria of Cosman et al.[12] The patients represented a high-risk group. For these patients, all other forms of treatment had failed, including prior excision surgery with silicone gel, intralesional steroids, and a combination of these treatments. Keloids that are excised and irradiated as first treatment show less than half the relapse rate of those that have failed prior treatments.[13] There were 80 keloids treated in 80 patients. There were many initiating events for the keloid scars: injury, infection, burns, iatrogenic response, and spontaneous occurrence. The youngest patient was a 12-year-old boy who developed keloids after severe burns.

Surgical Method

Keloids on the body were excised extralesionally and closed primarily with a single subcuticular 4-0 Prolene suture (Ethicon, Johnson & Johnson, United Kingdom). On the ear, the keloids were excised extralesionally and closed with interrupted 5-0 Prolene sutures. The operative scar was covered with topical lignocaine hydrochloride 2% and chlorhexidine 0.25% in a sterile lubricant gel (Instillagel; Farco-Pharma GmbH, Cologne, Germany), and the whole site was covered with a nonopaque, semiocclusive polyurethane dressing (OpSite; Smith+Nephew, Hull, United Kingdom). This enabled the radiotherapists to see the target area without disturbing the wound. Wound infection reduces the chance of keloid control.[14] This surgical technique has already been published by our team.[15]

Radiotherapy Method

Adjuvant postoperative radiotherapy was given at the Royal Marsden Hospital within 24 hours of surgery. For all skin sites except the earlobe, superficial 60-kV photon irradiation at a 25-cm source-to-skin distance using a 2-mm aluminum filter was used to give a half-value thickness of 1.7-mm aluminum. Because the earlobe keloid scars frequently involve both the medial and lateral surfaces of the earlobe, 100-kV photon irradiation was given at a 25-cm source-to-skin distance using a 4-mm aluminum filter to give a greater half-value thickness of 4-mm aluminum. For a typical 4-cm equivalent diameter field, this gives 90, 80, and 70 percent isodoses at 3.5-mm, 7.5-mm, and 12-mm depths for 60 kV, and 5-mm, 10-mm, and 16-mm depths for 100 kV. The dose was 10.0 Gy applied in a single fraction. The applied dose point is 100 percent at the Dmax, which is at the skin surface for this superficial therapy. The 90 percent isodose target area was the operative scar and any suture puncture holes. Allowance was made in field size for both the penumbra of low-voltage beams and the linear nature of the target. Nontarget areas were shielded with 2-mm plastic-coated lead. To reduce risk where possible, beams of radiotherapy were angled to avoid underlying tissue. The earlobes were taped back and shielded underneath to avoid irradiation to the skull and brain beneath and were treated with a single field.

Follow-up was formalized. Patients were seen at 4 weeks, 3 months, 6 months, and then annually within one clinic. Recurrence was defined as pain, itch from the scar, clinical evidence of a mass, or obvious return of lesion. Patients were asked to return earlier if any of these clinical features occurred. The follow-up data were recorded using a clinical life table and analyzed using the technique of Kaplan and Meier.[16] This expresses the probability of the treated keloid remaining controlled against the length of time since the operation.

Results

Eighty keloid scars were treated between 1987 and 1997. Patient characteristics are listed in Table I. All keloid scars were controlled at 4 weeks of follow-up. Patients were lost to follow-up as follows: 16 of 80 patients at 1 year (20 percent) and 20 of 80 patients by 5 years (25 percent). Analysis was by actuarial analysis for incomplete data sets. At 1 year, six of 64 patients had experienced treatment failure (probability of control at 1 year, 91 percent). At 5 years, an additional four of 54 patients followed had relapsed (cumulative probability of control at 5 years, 84 percent) (Table II).

Keloids at earlobe and anterior chest sites showed no greater chance of relapse than keloids at other sites on the body. Probability of control of ear keloids was 91 percent at 1 year and 79 percent by 5 years. Probability of control of chest keloids was 86 percent at 1 year and 86 percent by 5 years (Table III).

TABLE I
Patient Characteristics, 80 Keloids

	No.	%
Sex		
Male	33	41
Female	47	59
Age (years)		
Mean	25	
Range	12–53	
Race		
Nonwhite	61	76
White	19	24
Site		
Earlobes	35	44
Neck	9	11
Anterior chest	8	10
Arms	7	9
Abdomen and pelvis	7	9
Back	6	8
Face	5	6
Legs	2	3
Not specified	1	1

There were no cases of serious toxicity, defined as World Health Organization grade 3 or higher. Side effects included transient mild erythema, and hyperpigmentation was seen in many nonwhites. The hyperpigmentation could last for many months or years before fading.

Discussion

This study shows that in the majority of patients keloids can be controlled by a single operation with immediate adjuvant single-fraction radiotherapy. In this retrospective study, losses to follow-up may be important. Local control of keloids is usually defined by control at 24 months.[17] We have noted relapses after 2 years of follow-up. In this study of a young, mixed-race, inner-city population, 25 percent of patients had been lost to follow-up by 5 years from treatment. Results are therefore expressed as the probability of control by actuarial analysis.

No cases of serious late toxicity were reported (defined using the Radiation Therapy Oncology Group scale as grade 3 or greater). No case of malignancy has been observed. Black patients noted hyperpigmentation in the treated area that could last many months or years.

The preoperative diagnosis of keloid and the definition of keloid relapse were based on the clinical criteria of Cosman et al.[12] Not all cases were confirmed histopathologically, as in a previous study.[18]

From a review of the previous studies, reported recurrence rates at 1 year or more vary from 53 percent[17] to 2 percent.[19] It is difficult to make meaningful comparisons among treatment schedules because in many of these studies there was no standardization of diagnosis, surgical technique, radiotherapy technique, timing, or dose. Many reports included patients who had received no prior treatment for their keloids. Keloids in such patients are more than twice as likely to remain controlled after combined surgery and radiotherapy as compared with keloids that have failed prior treatments.[13]

Reports have included patients who did not have keloids but who were treated prophylactically for a surgical scar and thought to be at risk for subsequent keloid development and who had hypertrophic scars only.[19]

In many reports, recurrence was not clearly defined.[17] In many reports, patients were lost to follow-up but were not censored as lost.[13] In these reports, keloids in the patients who were lost were assumed to have remained controlled, although relapses after several years have been recorded in both this study and others.[13] This emphasizes the need for treatment results to be expressed as actuarial probability of control at given times after treatment, as well as the need for a significant proportion of cases to be followed for several years.

This study used strictly defined criteria for failure. Many cases of relapse were defined at an early stage by itching or scar pain rather than the actual reappearance of a keloid scar. At this point, other treatments were introduced, such as topical silicone gel or intralesional steroid. For several patients with these

TABLE II
Follow-Up Data Expressed as a Clinical Life Table

	Time (months)								
	0	1	3	6	12	24	36	48	60
Relapsed	0	0	0	0	6	0	0	0	4
Lost	0	0	6	0	10	0	0	2	2
Probability of control	1	1	1	1	0.906	0.906	0.906	0.906	0.839

TABLE III
Results: Probability of Control of Keloids at Different Sites

	Earlobe (%)	Anterior Chest (%)	All Sites (%)
At 4 weeks	100	100	100
At 1 year	91	86	91
At 5 years	79	86	84

relapses, salvage therapy without reexcision was successful and a visible recurrent keloid scar had never developed at up to 5 years of follow-up. Other reports have been less rigid in reporting relapse rates, as patients were reported as controlled who received subsequent salvage therapy. In one study, relapse rates at 1 year were reported as 9 percent, but 55 percent of patients studied did require postoperative intralesional steroid injections for recurrent nodules or itching. In our data, this would have been reported as local treatment failure, giving a relapse rate of 64 percent.[20,21]

Some patients in this study showed good early control of keloids treated at the earlobe but went on to have repeat cosmetic ear piercing for earrings followed by subsequent keloid appearance. Other studies have deleted these cases from the sum of treatment failures, blaming recurrence of keloid on repeat ear piercing.[19] All of these cases have been included in our data as local treatment failures. This may explain the higher rate of relapse seen at the earlobe compared with other skin sites in many reported series, but we have observed earlobe relapses without repiercing and repiercing without subsequent relapse. All but one of our 35 cases of earlobe keloid have been followed for 5 years.

In the literature, there is no agreement on optimal dosage, fractionation, or timing with respect to surgical procedures. Radiotherapy doses have been given over the range of 2 to 62 Gy.[22] Because so few reports used unified criteria for diagnosis or indications for treatment, surgical or radiotherapy technique, radiotherapy dose and energy, timing, or definitions of treatment failure, we believe that it is impossible to compare most studies or make conclusions about the effects of different treatments.

This single protocol was used by the Royal Marsden Hospital and St. George's Hospital team since 1987. Because radiotherapy is potentially carcinogenic, it was designed to gain the most effect for a given total dose of radiation. The effectiveness of the treatment protocol in this series may be related to the effective radiotherapy dose given and to the fact that all treatment was completed within 24 hours. Because it uses only one operation and one outpatient radiotherapy exposure, it is also the most cost-effective combined therapy.

A systematic literature review of keloid treatment with radiotherapy was performed. Articles and book chapters were identified by means of a MEDLINE search using the key terms "keloid" and "radiotherapy." Additional articles were identified from the references quoted in these publications. Great effort was made to review the literature. We acknowledge the help of the Library of the Royal Society of Medicine in retrieving original articles from as early as 1929 and from Africa, India, and Eastern Europe. We have reviewed data from 6656 cases of keloid treated with radiotherapy, involving 4263 keloids in articles published from 1961 onward. We have identified abstract or referenced data for keloid treatment by radiotherapy in 2393 additional keloids, but we have been unable to access the raw data in peer-reviewed publications.[11–14,17–63]

Physicians may hesitate to recommend radiotherapy for keloid treatment because of the risk of radiation-induced malignancy. Radiation-induced malignancies are rare, but sarcomas occur with a median latent period of more than a decade.[64] Radiation-induced malignancy seems to be a greater risk for patients irradiated at a younger age.[65,66] The total-body radiation dose from a superficial low-voltage radiotherapy technique is low, so the main excess risk would be expected to occur close to the treated site. Because there is no central record of patients treated with radiotherapy for keloids in one population to link with a cancer registry covering that same population, risk cannot be quantified with accuracy.

In reviewing the text of published articles and in MEDLINE searches for radiation-induced cancers, only five cases of possible radiation-induced cancers after keloid treatment have been documented. Our literature review has shown that radiotherapy has been used frequently. One series has followed patients for up to 20 years from treatment and has found no cancer induction.[13] One case of a thyroid carcinoma occurring in a potential exit dose site was reported 8 years after the treatment of a keloid on the chin of an 11-year-old child,[67] but subsequent investigations raise some doubts about causation.[68] A second case

involves bilateral breast cancer developing 29 years after radiotherapy for chest wall keloid treatments given at age 26 years.[68] In a third case, a basal cell carcinoma developed 10 years after operation and radiotherapy.[69] A fourth case is of a parathyroid adenoma occurring 38 years after radiotherapy to the neck for keloids when the patient was 10 years old.[70] A fifth case is of a 36-year-old woman who had a localized fibrous mesothelioma of the pleura and an ipsilateral breast carcinoma 23 years after receiving external radiation therapy at age 13 years for treatment of a chest wall keloid.[71] The risk cannot be quantified because it cannot be assumed that all radiation-induced cancers are reported in the scientific literature, nor is the number of patients alive following radiotherapy treatment for keloids known. With the cases from our literature review, our 80 cases, and these five case reports, we have documented that 6741 keloids have been treated with radiotherapy. The crude risk from the published data that we have accessed is therefore five reported cancer cases in 6741 reported treatments (one in 1348). It can be difficult to correlate cancer risk and environmental exposure with accuracy without a defined population of exposed cases and matched controls to compare and without long-term follow-up. Cancer is a common disease and so may be observed as a comorbid condition by chance without any specific association. Cancer is diagnosed each year in one in every 250 men and one in every 300 women.[72]

Because the risks are not known reliably, the radiotherapist must explain this to the patient as part of the consent procedure. In the reported cases of cancer induction, patients were all treated at a young age. This has been noted in other radiotherapy series, such as treatment for Hodgkin's lymphoma.[65] For these reasons, our treatment policy has been to treat only those patients for whom prior excision treatment has failed and who are therefore at significant risk of subsequent failure with reoperation.[13] Our policy is to recommend that treatment be deferred in young people until after 21 years of age and never offered to those who might be pregnant. Despite this, the demand for effective treatment is greatest in the young. The mean age of our patients is 25 years. We have treated a 12-year-old child with a very large and resistant keloid following burns, but only after significant demand from the patient and parents and a full discussion of both the known and unknown risks.

Conclusions

Our study has shown that extralesional excision of keloid followed by early, postoperative, single-fraction radiotherapy is both simple and effective in preventing recurrence at excision sites in high-risk keloids that have failed prior treatment. To enable true risks to be estimated, we encourage other centers to report any cases of potential radiation-induced cancers and to publish their overall experience of different modalities of treatment.

To enable meaningful comparisons between studies, we suggest that in reporting the outcomes of keloid treatments, the following criteria might be observed: for diagnosis, strict clinical criteria should be used to differentiate between hypertrophic and true keloid scars. Surgical and radiotherapy techniques should be defined strictly. Definitions of treatment failure should be clear, being defined as the reappearance of activity in the site of the keloid scar prompting salvage treatment and the clinical recurrence of a visible and palpable mass. It is recognized that some patients will fail to attend long-term follow-up. Where follow-up is incomplete, the outcome data should be reported as the probability of control at a given time using actuarial analysis. Control rates need to be reported at 5 years from the time of treatment because of the tendency for late relapses. The keloids may be stratified into those at high or low risk for relapse following surgical excision, high risk being defined as those keloids that occur in patients with keloids that have recurred despite prior optimal surgical resection.

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