Postoperative Electron-Beam Irradiation Therapy for Keloids and Hypertrophic Scars: Retrospective Study of 147 Cases Followed for More Than 18 Months

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Between 1988 and 2000, 378 cases of keloids were treated in the authors' department, and 147 keloids in 129 patients were selected for this study. Keloids that occurred at a different site in the same patient and keloids that recurred later at the same site were deemed to be different keloids. Those keloids were surgically removed, and the patients were treated postoperatively with 15-Gy electron-beam irradiation and followed for more than 18 months. The therapeutic outcomes were evaluated. Statistical analysis was performed using Fisher's exact probability test or chi-square test. Recurrence occurred in two sites on 14 earlobes (14.3 percent), in two sites on 12 necks (16.7 percent), in 22 sites on 51 anterior chest walls (43.1 percent), in 13 sites in 33 scapular regions (39.4 percent), in four sites on 15 upper limbs (26.7 percent), in four sites in 11 suprapubic regions (36.4 percent), and in one site on 11 lower limbs (9.1 percent). The overall recurrence rate was 32.7 percent. Analysis of the therapeutic outcomes showed that the recurrence rates in the sites with high stretch tension, such as the chest wall, and the scapular and suprapubic regions were statistically higher than in sites without high tension, such as the neck, earlobes, and lower limbs (41.1 percent versus 13.5 percent, $p = 0.0017$). The results suggested that keloid sites with a high risk of recurrence should be treated with escalated radiation doses and posttreatment self-management. (*Plast. Reconstr. Surg.* 111: 547, 2003.)

Keloids and hypertrophic scars are commonly encountered in plastic and aesthetic surgery departments, but they often present difficulties in treatment. Affected patients experience itching, aches, and cosmetic discomfort.

Various treatments of keloids and hypertrophic scars have been reported by many authors. As conservative therapies, the following have been tried: local injection and occlusive dressing therapy of steroids, tranilast medication, and pressure treatment with silicon gel sheets. After keloidectomy, simple suture, skin grafting, and flap transfer have been performed as surgical therapies, and electron-beam irradiation has been tried as a radiation therapy. In addition, cryotherapy and laser therapy with argon and dyes have been tried.

In our department, keloids and hypertrophic scars have been treated with multimodal therapy since 1988. In addition to surgical treatment and postoperative electron-beam irradiation, occlusive dressing therapy of steroids, tranilast medication, and pressure treatment with bandages have been tried. The purpose of this study was to evaluate the efficacy of this multimodal therapy. In this report, the cases that were followed for more than 18 months were selected and their therapeutic outcomes were evaluated. Statistical analysis was performed using Fisher's exact probability test or chi-square test.

Although keloids are generally classified as tumors that grow past the range of the wound scar and hypertrophic scars are classified as tumors that grow within the length of the wound scar, it is difficult to distinguish keloids from hypertrophic scars pathologically. There is a report that keloids and hypertrophic scars are distinguishable pathologically.[1] However,

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both keloids and hypertrophic scars are benign tumors originating from fibroblasts, and pathological discrimination of hypertrophic scars from keloids is difficult except for typical keloids.

In our department, we have encountered some cases in which keloids and hypertrophic scars seemed to be combined, and in some cases it was difficult to distinguish macroscopically between keloids and hypertrophic scars. Accord-

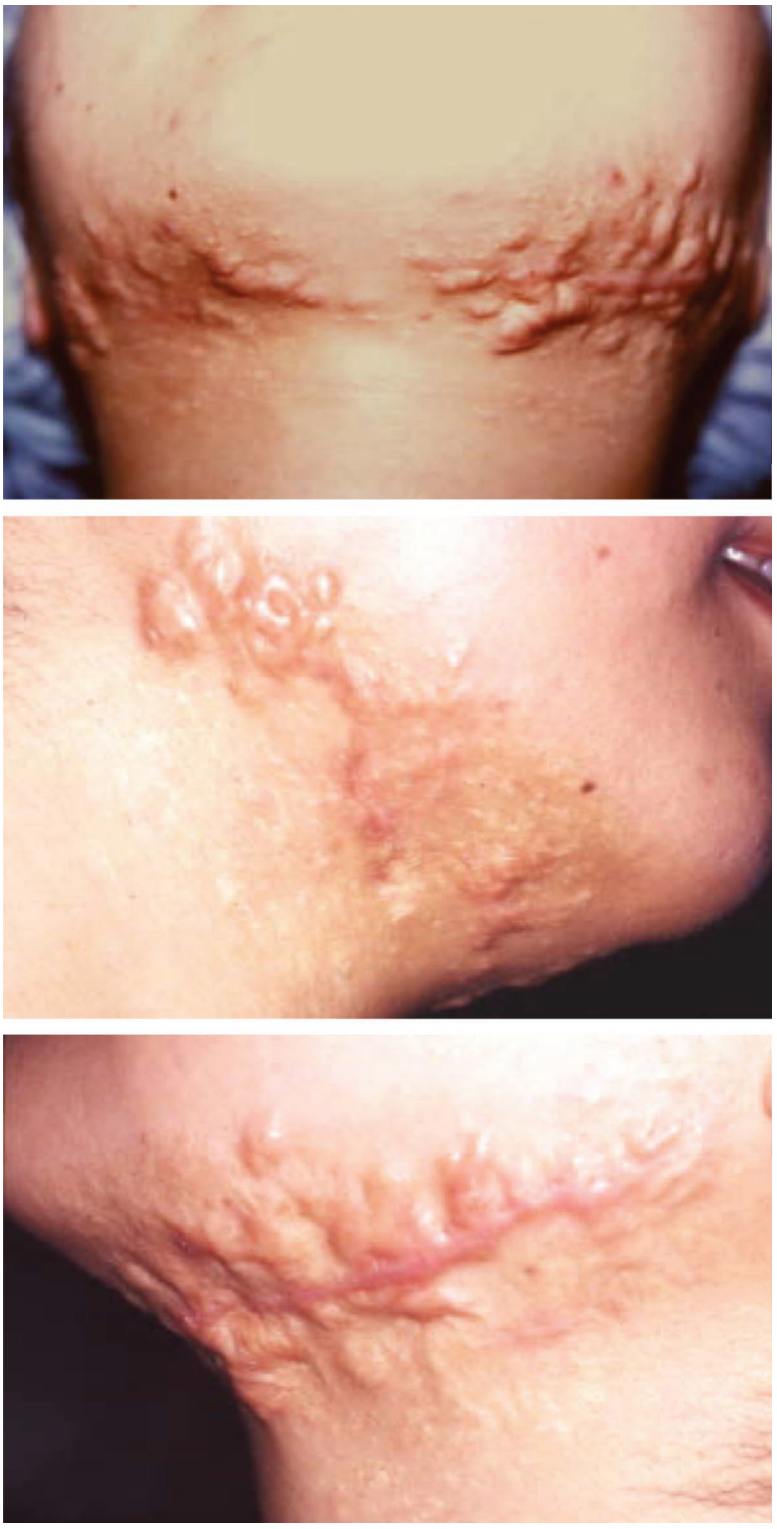

FIG. 1. Preoperative views.

ingly, we have treated these keloids and hypertrophic scars by the same method. In this report, we have made the decision not to distinguish between keloids and hypertrophic scars, and both are referred to hereinafter as keloids. Now we are studying the differences between keloids and hypertrophic scars at both the molecular level (polymorphism of the *p53* gene) and the metabolic level (hydrogen-1–nuclear magnetic resonance analysis of lactic acid).

MATERIALS AND METHODS

Three hundred seventy-eight cases of keloids were treated from 1988 to 2000 in our department. The cases that were followed for more than 18 months and that were treated with postoperative irradiation (total of 15 Gy of electron-beam irradiation) were selected for this study, and statistical analysis was performed on the outcomes. Thus, this study involved 147 regions in 129 cases (49 male cases and 80 female cases). Electron-beam irradiation was limited to the cases in which conservative therapy was ineffective and in which keloids recurred after surgical therapy.

In this study, keloids that occurred at a different site in the same patient and keloids that recurred later at the same site were deemed to be different keloids. A recurring keloid was considered to be different, therefore, from the original keloid, because the original was extirpated completely at operation and we believed that recurring keloids were caused by the operation.

Large keloids that we were unable to extirpate in one operation were excluded from the statistics presented here. All selected keloids were round, elliptic, and linear in shape and could be extirpated and sutured primarily.

The keloids were classified according to their site: earlobe, neck (including jaw), anterior chest wall, scapular region, upper limbs, suprapubic region, and lower limbs. We also treated keloids in other sites, such as the upper auricle, postauricle, penis, and inguinal region, but these were eliminated from the study for lack of sufficient examples.

Our surgical procedure was as follows. First, the keloid was extirpated completely and the wound was closed primarily. On closing the wound with a three-layer suture, subcutaneous tissue was exfoliated to decrease the tension. For subcutaneous sutures, Vicryl (Ethicon, Somerville, N.J.) was used; for dermal sutures, Maxon (Davis & Geck, Wayne, N.J.) or PDSII (Ethicon) was used. However, there were some cases in which, according to the judgment of the surgeon, monofilament nylon sutures were used instead of absorbable sutures. The wounds were elevated and fixed with dermal sutures. Skin sutures using Prolene (Ethicon) were not made any tighter than absolutely necessary to avoid suture marks. There were occasions when Z-plasty was performed. After removal of the sutures, surgical tape [Proxi-strip (Ethicon) or Steri-strip (3M Corp., St. Paul, Minn.)] was used.

Next, irradiation with a 4-MeV electron-beam administered by a linear accelerator was performed, totaling 15 Gy over the 3 days after the operation. Pressure treatment and tranilast medication were given for more than 3 months, but in a few cases, medication was stopped because of side effects such as nausea (Figs. 1 through 3).

The median follow-up period was 24 months (range, 18 to 128 months). The therapeutic outcome was judged as nonrecurrence (no recurrence was recognized) or recurrence (elevation of the lesion was recognized; the outcome was judged as recurrence no matter how small the elevation was, even if the patient was satisfied with the result). In many studies, therapeutic outcome is classified as partial response (recurrence was recognized but improvement over the preoperative state was noted), complete response (no recurrence was recognized), and no response (recurrence was clearly recognized). However, we considered the difference between partial response and no response to be imprecise: judgment is not always made by the same doctor, and the subjective element is too large, apart from which, in all our cases the keloids were improved from the initial state.

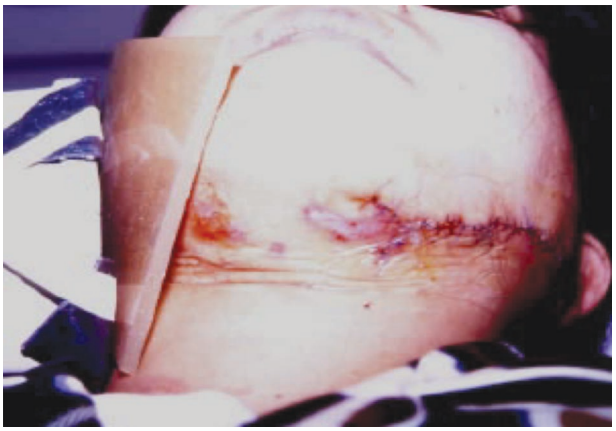

FIG. 2. Postoperative irradiation was performed.

FIG. 3. Eighteen months after operation.

RESULTS

Recurrence was noted in two sites on 14 earlobes (14.3 percent), in two sites on 12 necks (16.7 percent), in 22 sites on 51 anterior chest walls (43.1 percent), in 13 sites in 33 scapular regions (39.4 percent), in four sites on 15 upper limbs (26.7 percent), in four sites in 11 suprapubic regions (36.4 percent), and in one site on 11 lower limbs (9.1 percent). The overall recurrence rate was 32.7 percent.

TABLE I
Therapeutic Outcome by Keloid Site

Keloid Site	No. of Keloids	Recurrence (%)
Earlobe	14	2 (14.3)
Neck	12	2 (16.7)
Anterior chest wall	51	22 (43.1)
Scapular region	33	13 (39.4)
Upper limb	15	4 (26.7)
Suprapubic region	11	4 (36.4)
Lower limb	11	1 (9.1)
Total	147	48 (32.7)

Analysis of the therapeutic outcomes showed that the recurrence rates in the sites with high stretch tension, such as the chest wall, and the scapular and suprapubic regions were statistically higher than in sites without high tension, such as the neck, earlobes, and lower limbs (41.1 percent versus 13.5 percent, $p = 0.0017$) (Table I). No differences in recurrence rate according to keloid length, sex, or age were recognized (Table II). The causes of the keloids are shown in Table III; the average dimension of the extirpated keloids was 1.54 to 5.58 cm.

The therapy caused various side effects: pigmentation [45.6 percent (67 of 147 cases)] and hypopigmentation [2.0 percent (three of 147 cases)] because of electron-beam irradiation. Erythema occurred in almost all of the patients 2 or 3 weeks after irradiation, but it was temporary. Pigmentation and hypopigmentation occurred approximately 6 months after irradiation, but again the effects were temporary and mild. There were no cases of dysraphia or wound infection, but in some cases the dermal suture threads were exposed on the skin [6.1 percent (nine of 147 cases)]. There were no cases of malignant tumors being generated in the keloid site. Tranilast caused nausea in 13.2 percent of the patients (17 of 129 patients), and the medication was stopped when this happened.

DISCUSSION

The recurrence rate of keloids in our department was similar to that in previous reports[2–10] (Table IV), although exact comparisons are difficult because of racial differences and irradiation dosage. There is now a consensus that ionizing irradiation is an effective way to treat keloids. The mechanism of its effect is the control of collagen synthesis to strike the abnormal activated fibroblast and the promotion of the existing normal fibroblast.[11] In many institutions, electron-beam irradiation is started 24 to 48 hours after the operation, and the total dose is limited to 40 Gy over several administrations. It is said that electron beams are capable of more selectively reaching the area related to keloid generation than soft x-rays.[12] This area is the border of the papillary layer and the reticular layer in the dermis.

In our department, the recurrence rate in the anterior chest wall, the scapular region, and the suprapubic region was greater than 30 percent, because these three keloid sites are in areas where stretch tension occurs easily, and the total dose of irradiation seems to be lower

TABLE II
Recurrence Rate

	Nonrecurrence	Recurrence	Total	Recurrence Rate (%)
Keloid site*				
High-tension site	56	39	95	41.1
Low-tension site	32	5	37	13.5
Total	88	44	132	$p = 0.0017$†
Keloid length				
5 cm or less	58	33	91	36.3
More than 5 cm	40	16	56	28.6
Total	98	49	147	$p = 0.3367$‡
Sex				
Male	36	18	54	33.3
Female	62	31	93	33.3
Total	98	49	147	$p = 0.8560$‡
Age				
20 years or less	19	11	30	36.7
More than 20 years	79	38	117	32.5
Total	98	49	147	$p = 0.6642$‡

* The keloids in the upper limb were not included in this analysis.
† Fisher's exact probability test was performed because recurrence of "low-tension site" was a small number.
‡ Chi-square test was performed.

TABLE III
Cause of Keloid in Our Department

Keloid Site	Cause of Keloids	No. of Patients (%)
Earlobe	Piercing	5 (38.5)
	Surgery	3 (23.1)
	Trauma	2 (15.4)
	Other	3 (23.1)
Neck	Surgery	3 (30.0)
	Trauma	2 (20.0)
	Acne	2 (20.0)
	Other	3 (30.0)
Anterior chest wall	Acne	15 (34.1)
	Surgery	11 (25.0)
	Burn	3 (6.8)
	Other	15 (34.1)
Scapular region	Acne	11 (36.7)
	Herpes zoster	4 (13.3)
	Surgery	2 (6.7)
	Other	13 (43.3)
Upper limb	Trauma	7 (53.8)
	Folliculitis	1 (7.7)
	Surgery	1 (7.7)
	Other	4 (30.8)
Suprapubic region	Surgery	9 (100)
Lower limb	Trauma	5 (50.0)
	Surgery	3 (30.0)
	Burn	1 (10.0)
	Other	1 (10.0)

than required. In our department, we consider 15 Gy to be the optimum dose (i.e., the dose at which side effects such as pigmentation and malignant tumor generation are minimal but beneficial effects are recognized). There are actually no reports of malignant tumors being induced by electron-beam irradiation, although the risk of malignant change has always been exaggerated. We have encountered no cases among our patients, some of whom have been followed for as long as 128 months.

Therefore, keloid sites with a high risk of recurrence should be treated with an escalated radiation dose. In our experience, pigmentation increases when the radiation dose is increased to 21 Gy. However, we think that this dose should be used if it decreases the recurrence rate. Even if pigmentation occurs, if pain and itching are improved, there will be some patients who choose 21 Gy. In addition, it is considered that the possibility of carcinogenesis is very low.[2] Another possibility is to use 15 Gy only for primary irradiation and 21 Gy for recurring keloids. In addition, pigmentation can be suppressed by the following methods: (1) reducing the one-time dose of irradiation while keeping the total dose unchanged; and (2) lengthening the irradiation interval. These methods should be decided on after due consultation with the patient.

In sites without stretch tension, such as the neck, earlobes, and lower limbs, the recurrence rate was lower, and this fact indicates either that less than 15 Gy is sufficient or that no irradiation at all is necessary for these sites. Investigations into the possibility of reducing the total dose or of doing without electron-beam irradiation in these sites are needed. There have been reports that earlobe keloids should be treated with tape compression and without electron-beam irradiation.[13,14] If these reports are valid, keloids in these sites can be treated at hospitals that have no electron-beam equipment.

In surgical treatment, we perform three-layer suturing after keloidectomy. For subcutaneous sutures, Vicryl is used; for dermal sutures, Maxon or PDSII is used. However, there are some cases in which, according to the judgment of the surgeon, monofilament nylon sutures are used instead of absorbable sutures. It is said that absorbable sutures do not have

TABLE IV
Therapeutic Outcome in Earlier Reports and Our Results

First Author (ref)	Ethnicity	Irradiation Dose (Gy)	Object	Classification of Most Favorable Outcome	Rate of Most Favorable Outcome (%)
Enhamre[3]	Caucasian	10–15	56 sites	Sampling only excellent	29.0–35.0
Sallstrom[9]	Caucasian	18	124 sites	Sampling only great improvement	64.0
Norris[7]	Black	8–12	56 sites	Sampling only CR	47.1
Ollstein[8]	Caucasian	15	17 sites	Sampling only CR	75.0
	Noncaucasian	15	51 sites	Sampling only CR	81.0
Kovalic[5]	White	3–20	10 cases	Sampling only no evidence of recurrence	60.0
	Black	3–20	65 cases	Sampling only no evidence of recurrence	75.0
Borok[2]	No description	12–16	393 sites	Sampling only excellent	92.0
Takahashi[10]	Japanese	20	25 sites	Sampling only CR	48.0
Mitsuhashi[6]	Japanese	14–21	139 sites	Sampling only CR	63.3
Ogawa (this study)	Japanese	15	147 sites	Sampling nonrecurrence	66.0

CR, complete response (no recurrence was recognized).

sufficient tensile strength and generate greater tissue response compared with nylon sutures. However, if absorbable sutures are exposed on the surface of the wound, they are much easier to remove than nylon sutures and do not cause new wounds. For skin sutures, we use Prolene and avoid fastening it so tightly as to make suture marks. In the future, we intend to use Dermabond (Ethicon) to protect the skin surface as much as possible.

CONCLUSIONS

Between 1988 and 2000, 147 keloids in 129 patients were surgically removed. The patients were treated postoperatively with 15-Gy electron-beam irradiation, and the therapeutic outcomes were evaluated. Analysis of the therapeutic outcomes showed that the recurrence rates in the sites with high stretch tension, such as the chest wall and the scapular and suprapubic regions, were statistically higher than in sites without high tension, such as the neck, earlobes, and lower limbs. The results suggested that keloid sites with a high risk of recurrence should be treated with escalated radiation doses and posttreatment self-management.

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