Postoperative Radiation Protocol for Keloids and Hypertrophic Scars

Statistical Analysis of 370 Sites Followed for Over 18 Months

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Background: Before 2002, keloids and intractable hypertrophic scars were treated at our facility with postoperative irradiation of 15 Gy (the traditional protocol). Analysis of the therapeutic outcomes of patients treated with this protocol showed that the recurrence rates of keloids and intractable hypertrophic scars in the anterior chest wall, as well as the scapular and suprapubic regions, were statistically higher than at other sites, while the recurrence rates in earlobes were lower. Thus, we customized doses for various sites. This report describes our trial of postoperative radiation therapy.

Methods: Between January 2002 and September 2004, 109 patients with 121 keloid and intractable hypertrophic scar sites were treated with surgical excision following the new protocol: electron-beam irradiation at total doses of 10, 15, or 20 Gy, depending on the site. The recurrence rates and toxicities were historically followed in 218 patients with 249 keloid and intractable hypertrophic scar sites treated with the old protocol of surgical removal followed by irradiation at 15 Gy (without variation by site). The minimal follow-up time was 18 months. Statistical analysis was performed using Fisher exact probability test.

Results: Total recurrence rates were 29.3% before 2002 and 14.0% after 2003. The recurrence rate in the anterior chest wall was statistically reduced. Outcomes of earlobe did not differ between irradiation with 15 Gy or 10 Gy.

Conclusions: Keloids and intractable hypertrophic scars should be treated with dose protocols customized by site. Our results suggest that keloid and intractable hypertrophic scar sites with a high risk of recurrence should be treated with 20 Gy in 4 fractions over 4 days and that earlobe should be treated with 10 Gy in 2 fractions over 2 days.

Key Words: keloid, radiation, electron beam, hypertrophic scar

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PATIENTS AND METHODS

Before 2002, 218 patients with 249 keloid sites, who received 15 Gy in 3 fractions over 3 days of postoperative 4-MeV electron-beam irradiation, were extracted for this study; recurrence rates were analyzed by site. The keloids were also classified by site: auricle, earlobe, anterior chest wall, scapular region, suprapubic region, and other (upper limb, lower limb, and back). After 2003, 109 patients with 121 regions (2003) were also classified by site: auricle excluding earlobe, anterior chest wall, scapular region, and suprapubic region, 10 Gy in 2 fractions over 2 days (earlobe), and 15 Gy in 3 fractions over 3 days (other regions), were extracted for this study. The keloids included 35 sites in the anterior chest wall, 13 sites in the scapular region, and 10 sites in the suprapubic region, which were irradiated by electron beam at 4 MeV energy, 5 Gy daily, for a total dose of 20 Gy over 4 days immediately after excision. Twenty-eight sites in the earlobe received 10 Gy in 2 fractions over 2 days. Other areas were treated with 15 Gy (the traditional protocol). Differences in recurrence rates were analyzed by region.

All keloids selected for this study were round, elliptical, or linear in shape and could be extirpated and sutured. Large keloids that could not be extirpated in a single operation were excluded. All keloids were treated using the same methods, with the exception of irradiation dose. Our surgical procedure has previously been documented.2 Postoperative irradiation was started on postoperative day 1 or 2. Pressure treatment and tranilast medication1 were administered over 6 months, with the exception of a few cases in which medication was stopped because of side effects such as nausea and frequent urination.

The median ages were 29 years old (ranging from 18 to 65) and 26 years old (ranging from 19 to 62) for patients treated before 2002 and after 2003, respectively. The median follow-up periods were 26 months (ranging from 18 to 148 months) and 23 months (ranging from 18 to 30 months) for patients treated before 2002 and after 2003, respectively. The therapeutic outcomes were judged as recurrent or controlled. Even very small elevations in patients satisfied with results were considered cases of recurrence. The statistical analysis was performed using Fisher exact probability test.

RESULTS

Table 1 shows that before 2002, recurrence occurred in 5 sites on 13 auricles, excluding earlobes (38.5%), 2 sites on 35 earlobes (5.7%), 32 sites on 82 anterior chest wall regions (39.0%), 17 sites on 45 scapular regions (37.8%), 8 sites on 22 suprapubic regions (36.4%), and 9 sites on 52 other regions (17.3%). The overall recurrence rate was 29.3%.

After 2003, recurrence occurred in 3 sites on 11 auricles (27.3%), no sites on 28 earlobes (0%), 5 sites on 35 anterior chest wall regions (14.3%), and 3 sites on 13 scapular regions (20.0%), one site on 3 suprapubic regions (33.3%), and 2 sites on 10 other regions (20.0%). The overall recurrence rate was 14.0%.

Recurrence rates on the anterior chest wall sites treated with escalated doses were statistically improved (before 2002, 39.0%, versus after 2003, 14.3%; P = 0.006). Recurrence rates were decreased, but not statistically, in the scapular and suprapubic regions and auricle excluding the earlobe. Moreover, no statistical differences (before 2002, 5.7%, versus after 2003, 0.0%; P = 0.305) were observed in the earlobe following treatment with decreased doses. Similarly, recurrence rates (before 2002, 17.3%, versus after 2003, 16.7%; P = 0.611) did not differ statistically between the sites treated with the same dose.

The electron-beam irradiation therapy caused various side effects: hyperpigmentation (before 2002, 34.9%, 87/249; after 2003, 37.2%, 45/121; P = 0.672), hypopigmentation (before 2002, 1.2%, 3/249; after 2003, 0.0%, P = 0.225), and transient erythema in almost all of the patients 2 or 3 weeks after irradiation. Hyperpigmentation and hypopigmentation were temporary and mild and occurred from 1 to 6 months after irradiation. There were no cases of dysphagia or wound infection, but dermal suture threads were exposed on the skin in some cases (before 2002, 4.8%, 12/249; after 2003, 1.7%, 2/121; P = 0.134). There were no cases in which malignant tumors appeared at the keloid sites treated with postoperative electron-beam irradiation.

### Table 1. Results of Our Study

<table>
<thead>
<tr>
<th>Region</th>
<th>Before 2002 (218 Patients)</th>
<th>Since 2003 (109 Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recurrence/Total</td>
<td>Rate (%)</td>
</tr>
<tr>
<td>Earlobe</td>
<td>2/35**</td>
<td>5.7</td>
</tr>
<tr>
<td>Auricle excluding earlobe</td>
<td>5/13**</td>
<td>38.5</td>
</tr>
<tr>
<td>Anterior chest wall</td>
<td>32/82**</td>
<td>39.0</td>
</tr>
<tr>
<td>Scapular region</td>
<td>17/45**</td>
<td>37.8</td>
</tr>
<tr>
<td>Suprapubic region</td>
<td>8/22**</td>
<td>36.4</td>
</tr>
<tr>
<td>Others</td>
<td>9/52**</td>
<td>17.3</td>
</tr>
<tr>
<td>Grand total</td>
<td>73/249</td>
<td>29.3</td>
</tr>
</tbody>
</table>

Cases followed over 18 months were selected. The therapeutic outcomes were analyzed statistically using Fisher exact probability test. A total of 218 patients with 249 regions (before 2002) and 109 patients with 121 regions (after 2003) were extracted for this study. The results suggest that keloid sites with a high risk of recurrence should be treated with 20 Gy/4 fractions/4 d. Moreover, earlobe keloids should be treated with 10 Gy/2 fractions/2 d. Total radiation dose: *10 Gy, **15 Gy, ***20 Gy.
DISCUSSION

Keloids can cause severe symptoms such as strong itching, pain, and a stretching sensation. Local steroid injections effectively reduce these symptoms but cannot be used in large doses, because of side effects such as capillary dilatation and menstrual disorder in female cases. Moreover, many patients refuse treatment with painful injections administered over an extended period, even when steroids are mixed with local anesthetics. Other conservative treatments are sometimes ineffective for the treatment of itchy, painful keloids. Surgical treatment may be the only effective therapy in patients with severe discomfort. Thus, we have strived to prevent the recurrence of keloids after surgery. In our experience, postoperative electron-beam irradiation is the most effective treatment of the prevention of recurrent keloids. Furthermore, this approach has been independently described as effective.3–11 Sclafani et al12 also reported that postoperative radiation therapy was much more effective than postoperative corticosteroid injections in a randomized study of earlobe keloids.

Postoperative electron-beam irradiation may control collagen synthesis by inhibiting the promotion of abnormal activated and normal fibroblasts.10 Electron-beam irradiation has been initiated immediately after surgery in many institutions, with the total dose limited to 40 Gy over several treatments. Electron beams are believed to more selectively reach the areas related to keloid generation—the border of the papillary layer and the reticular layer in the dermis—than are soft x-rays.11

In our experience, there are 2 types of recurrence. The first occurs immediately following or within 3 months of surgery. In this type, operative invasiveness activates fibroblasts, especially when postoperative inflammation continues for a month or more. The second type occurs more than 3 months after, and often about 6 months after, surgery. Here the postoperative inflammation resolves completely, but the associated stimulation activates fibroblasts. In the present study, therefore, we observed patients for more than 18 months after surgery to include both types of recurrence. Keloids have recurred after several years in some patients. However, we believe that recurrence after long intervals can be prevented.

Before 2002, we had considered 15 Gy the optimal dose, ie, the dose at which side effects (pigmentation, malignant tumor generation, etc) are minimal and beneficial effects are attained. However, we have since recognized that 15 Gy is not an optimal dose for all sites.2 Thus, since 2003, we have administered a new protocol of electron-beam irradiation. Sites with a high risk of recurrence, such as the anterior chest wall and the scapular and suprapubic regions, should be treated with an escalated radiation dose. We found that pigmentation increases as the radiation dose increases, but the benefit of decreased incidence of recurrence outweighs this negative side effect, in our opinion. We believe that many patients would choose the escalated dose to improve pain and itching, despite the increased pigmentation. Additionally, pigmentation can be suppressed by the following measures:

1. using steroid ointments to reduce radiation dermatitis immediately after irradiation

FIGURE 1. A case of chest keloid. A, Preoperative view. B, Postoperative view and delineation of the irradiation field. C, Two years after the operation and postoperative electron beam irradiation. A 61-year-old male suffered from keloids on the chest. Under local anesthesia, the chest keloid was excised. Starting from the day after the operation, postoperative electron-beam irradiation was performed (20 Gy/4 fractions/4 days). Pigmentation was reduced 2 years after the operation. The keloids have not recurred.
2. reducing the single dose of irradiation while keeping the total dose unchanged
3. lengthening the irradiation interval

Individual treatments should be established after due consultation with the patient concerned. Based on the above rationale, we administered 20 Gy in 4 fractions over 4 days to the anterior chest wall, scapular region, and suprapubic region. On the other hand, the radiation dose for sites with a low risk of recurrence, such as earlobes, should be decreased. Thus, since 2003, we have administered 10 Gy in 2 fractions over 2 days to earlobes. Other regions, such as limbs, are continually treated with 15 Gy in 3 fractions over 3 days.

We compared the results observed before 2002 with those observed after 2003. The present data suggest that keloids derived from the anterior chest should be treated postoperatively with 20 Gy in 4 fractions over 4 days (Figure 1). Moreover, postoperative irradiation of keloids on earlobes can be reduced from 15 Gy in 3 fractions over 3 days to 10 Gy in 2 fractions over 2 days. Thus, we believe that keloid treatment should be based on the unprecedented concept of customized, site-dependent doses of postoperative electron-beam irradiation.

An important concern associated with this protocol of escalated irradiation doses is the risk of inducing malignant tumors. Malignant tumors have reportedly been induced by electron-beam irradiation. Hoffman documented a case of carcinoma of the thyroid in a 19-year-old man 8 years after he had received x-ray treatment of 12 Gy to his chin. However, a subsequent written communication from this author suggests uncertainty about the causal relationship between the treatment and the carcinoma (S. Hoffman, personal communication, 1988). Botwood reported a case of breast cancer after superficial x-ray treatment of 13 Gy to the breast. However, this patient also took hormone replacement therapy and was 3 days.

In conclusion, our results suggest that 10 Gy is sufficient to prevent the recurrence of keloids on the earlobe and that 20 Gy is more effective than 15 Gy for preventing recurrence of keloids on the anterior chest wall. Of course, postoperative electron-beam irradiation should not be the sole therapy to prevent the recurrence of keloids. In addition to postoperative self-management, multimodal therapy, including tranilast medication and pressure treatment using silicon gel sheets or bandages, is also important.

We will continue to investigate optimal doses of radiation by site, but we currently propose the following new protocol of postoperative electron-beam irradiation to prevent recurrence of keloids:

1. 20 Gy in 4 fractions over 4 days: anterior chest wall, scapular region, and suprapubic region
2. 10 Gy in 2 fractions over 2 days: earlobes
3. 15 Gy in 3 fractions over 3 days: other sites

In the near future, we will begin a prospective study, as compared with this retrospective study, to determine the optimal radiation doses.

REFERENCES
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