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The Efficacy of CT-Based Conformal Electron Beam Radiation Therapy After Keloid Excision

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BACKGROUND Adjuvant computed tomography–based conformal electron beam radiation therapy (RT) for patients with keloids enables radiation oncologists to customize the target volume with precision and deliver the maximal prescription dose while sparing normal surrounding tissues.

OBJECTIVE To report treatment and cosmetic outcomes by the patient's self-assessment survey.

METHODS Medical records of patients with keloids, who were treated with postoperative electron beam RT between January 2015 and December 2020, were reviewed. A total of 85 consecutive patients with 136 keloids were included in this study. Subjective cosmetic outcomes were scored by each patient using a 5-point Likert scale survey.

RESULTS The median follow-up time was 29.0 months (range, 12.1–77.9 months), and local recurrence was observed in 10 lesions (7.4%). The recurrence rate of keloids occurring in the ear was 5.4%, whereas the recurrence rate of keloids occurring at other body sites was 11.4%. Among the patients who responded to the questionnaire about the cosmetic outcome, 70.2% of patients declared being either very satisfied (44.7%) or satisfied (25.5%).

CONCLUSION Surgical excision, followed by CT-based conformal electron beam RT, for patients with keloids ensures a high degree of local control resulting in good cosmetic outcomes.

As one of the postoperative treatment options for keloids, radiation therapy (RT) has been evaluated as an effective treatment option in reducing the local recurrence, and several studies have been conducted on the clinical benefits of postoperative RT for keloids.[1–3] To date, various RT modalities, such as electron beam RT, orthovoltage RT, and brachytherapy, were used for the treatment of keloids. More recently, in South Korea, megavoltage electron beams have all but replaced orthovoltage x-ray as the modality of choice to treat superficial lesions such as skin cancers and keloids.[4,5] Megavoltage x-rays may also be applied to cases where acceptable dose distribution to the target volume may not be achieved with an electron beam.

Keloids are overgrown areas of scar tissue included in the spectrum of fibroproliferative disorders. The most common areas on the body for keloids include the chest, skin overlying joints, shoulders, head and neck regions, and particularly the ears.[6,7] This abnormal healing response is difficult to treat and can occur anywhere in the body where trauma, surgery, vaccinations, blisters, acne, or body piercing have injured the skin.[8] When evaluating keloids on different parts of the body, specific morphological and anatomical characteristics should be considered. For example, the organization of various parts of the external ear presents with a highly irregular skin surface; thus, the dose distribution of electron beam RT is highly affected by its irregularity of the surface. Furthermore, owing to the damaging effects of radiation to the surrounding healthy organs, the beams are carefully manipulated to limit unwanted dose.[9] Target volumes are carefully mapped out using computed tomography (CT)–based RT planning systems to further customize and increase the homogeneity of dose distribution.[10] This advancement in medicine allows physicians to personalize treatments, thus enhancing the accurate delivery of radiation doses based on clinical parameters and anatomical features.

The purpose of this study was to report their institutional treatment protocol and describe the techniques that are deemed to be safe and effective as a method to enhance postsurgical outcomes in the treatment of keloids.

METHODS

Patients

A retrospective chart review was conducted between January 1, 2015, and July 31, 2020. Patients who underwent keloid excision followed by immediate RT with a minimum of 1-year follow-up were included in this study. A

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total of 85 consecutive patients with 136 keloid lesions were identified. This study was approved by the Institutional Review Board of the Korea University College of Medicine (Approval Number: 2021AN0226).

Surgical Treatment

Complete extralesional removal of the fibrous keloid was conducted under local anesthesia using 2% lidocaine and 1: 100,000 epinephrine. To maximize cosmetic outcomes, efforts were made to minimize tension on closure by undermining the subcutaneous tissue and raising the overlaying marginal skin. Based on the esthetic judgment, an intralesional removal was considered in areas where complete excision was not possible to eliminate physical tension during skin closure. Tension-free closure of the excision site was performed using dermal approximation and epidermal closure using absorbable Vicryl and non-absorbable nylon sutures. A thin layer of protective dressing consisting of sterile gauze and topical antibiotic ointment was performed.

Radiation Therapy

Patients were instructed to visit the Department of Radiation Oncology for 3 consecutive days of RT. The first RT was performed within the first 24 hours after surgery. All patients underwent CT-based simulation. CT simulation was performed on patients using an appropriate immobilization device, depending on the location of the lesion, with a Philips Brilliance 16-slice Big Bore CT scanner (Royal Philips Electronics, Amsterdam, the Netherlands). For head and neck keloids, the patient was immobilized with a thermoplastic mask (Civco Medical Solutions, Orange City, IA) and the treatment area was exposed for the use of a bolus (Figure 1). The Super-Flex bolus (Radiation Products Design Inc., Albertville, MN) was used to increase the surface dose and reduce the penetration of the electrons, and the thermoplastic bolus pellets (Orfit Industries NV Vosveld 9A 2110 Wijnegem Belgium) were used to minimize air gaps and interfraction variations by creating a bolus that filled the inward defect and uniform layers (Figure 2).

Axial images with a slice thickness of 1.0 mm were acquired for RT planning. Radiation therapy planning was performed using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA). Radiation therapy was administered using the linear accelerators (VitalBeam or Clinac iX; Varian Medical Systems). The RT field was determined by adding a 1.0- to 1.5-cm margin from the scar in all directions. Normal tissues were shielded with a customized lead block. For ear keloids, the parotid gland and hairs were shielded with a 4-mm lead sheet tailored for each patient. A hypofractionated regimen of 15 or 18 Gy in 3 fractions was prescribed. Electron beam RT was prescribed to 90% of the given dose using 6 to 12 MV electrons (Figure 3).

Follow-Up

All patients were advised to return to their outpatient clinic 1 to 2 months after surgery and 3 to 6 months thereafter.

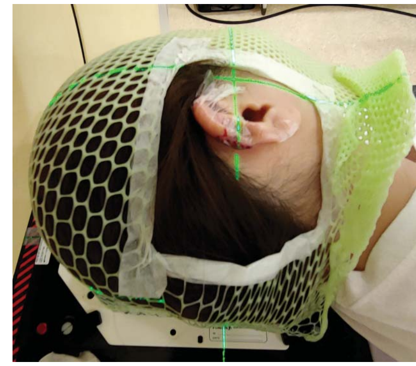

Figure 1. Computed tomography simulation for patient with ear helix keloid immobilized with a thermoplastic mask. The treatment area was opened for the use of a bolus.

Definition of local recurrence was any clinical evidence of a redeveloping keloid, regardless of the size, at the RT field. Slight hypertrophic scars were not classified as local recurrence. If recurrence was suspected, the patient was recommended to visit the Department of Plastic and Reconstructive Surgery, and the recurrence was judged by physicians. If the patient presented with a firm redness on the postoperative scar, steroid injection was considered. The intralesional steroid injection delivered 1 to 2 mL of triamcinolone acetonide (40 mg/mL) diluted 1:1 (vol/vol) with 2% lidocaine. The injection was repeated fortnightly, not exceeding more than 3 sessions. Subjective cosmetic outcomes were scored using a 5-point scale, where 0 = very satisfied, 1 = satisfied, 2 = neutral, 4 = dissatisfied, and 5 = very dissatisfied.

Statistical Analyses

Recurrence-free survival was measured from the date of surgery until the date of the first recurrence judged by physicians through physical examination and/or telephone survey. If no recurrence was observed, the local recurrence-free survival (LRFS) rate was measured from the date of surgery until the date of last follow-up. The survival function from time to event data was computed using a Kaplan–Meier estimator. Statistical differences between both groups were compared using the log-rank test. Statistical significance was set at $p < .05$. IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY), was used for statistical analyses.

RESULTS

Patients and Treatment

A total of 136 keloids from 85 patients were analyzed. Table 1 summarizes the likely cause of these keloids. The median age of the overall population at the time of surgery was 25 years (range, 15–77 years). Of the 85 patients, 22 patients (25.9%) were male and 63 patients (74.1%) were female. Three patients (3.5%) had a family history of keloid: 2 patients had a positive family history in a first-degree relative (mother and daughter) and 1 patient had a

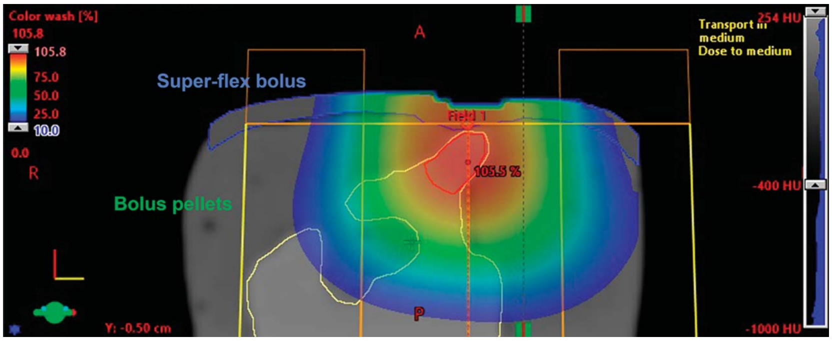

Figure 2. Dose wash of the electron beam radiation therapy plan for the treatment of the ear helix with the Super-Flex bolus and the thermoplastic bolus pellets.

positive family history in a second-degree relative (grandmother). Intralesional excision was performed on 10 lesions (7.35%): 2 lesions on the earlobe, 6 on the helix, and 2 on the scapha. Of the 136 lesions, 135 lesions (99.3%) were treated using an electron beam, and one patient (0.7%) with a long and curved keloid from the anterior chest wall to the right shoulder was treated with a 10 MV photon beam using the 15-mm Super-Flex bolus. Seventeen keloids (12.5%) received 15 Gy in 3 daily fractions, and 119 keloids (87.5%) received 18 Gy in 3 daily fractions. During the follow-up period, 48 patients with 82 lesions (60.3%) were treated with intralesional steroid injection and 37 patients with 54 lesions (39.7%) were not.

Local Control

The median follow-up time was 29.0 months (range, 12.1–77.9 months). During the follow-up period, local recurrence was observed in 10 lesions (7.4%): 3 recurrences on the ear helix, 2 recurrences on the earlobe, 2 recurrences on the upper trunk (chest wall), 2 recurrences on the head and neck (chin), and 1 recurrence on the extremities (upper arm). The recurrence rates by anatomic sites are summarized in Table 2. There was no recurrence during the follow-up in 10 lesions that underwent intralesional excision. The 5-year LRFS rate for all treated lesions was 84.9%. The 5-year LRFS rate was 88.0% for the ear keloids in contrast to 76.7% for other body sites (p = .183). Age, sex, size of keloid, surgical method, intralesional steroid injection, and subgroup analysis by site were not statistically significantly correlated with the LRFS rate.

Cosmetic Outcomes

The authors conducted a telephone 5-point Likert scale survey to evaluate patient satisfaction and cosmetic outcomes. Response rates were 55.3% (47 of 85 patients receiving the questionnaire). Among the patients who responded to the questionnaire, 70.2% of patients declared being either very satisfied (44.7%) or satisfied (25.5%) with the cosmetic outcome (Figures 4 and 5). Alternatively, 6.4% were neutral, 10.6% were dissatisfied, and 12.8% reported to be very dissatisfied with the cosmetic outcome. The reasons for the dissatisfaction were mainly because of local recurrence and skin tension scar widening after surgical excision.

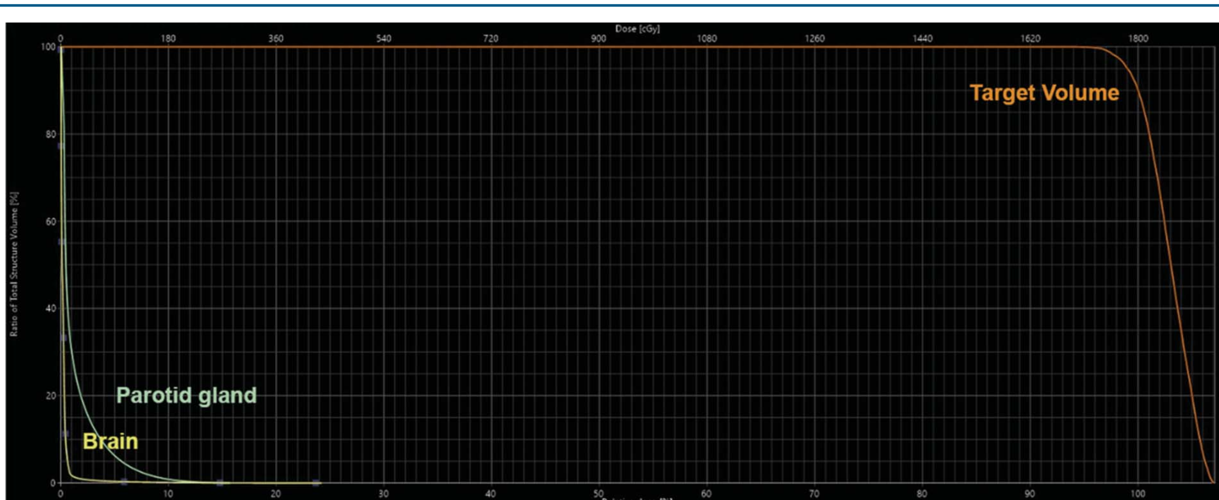

Figure 3. Dose–volume histogram of computed tomography–based conformal electron beam radiation therapy plan for ear helix keloid.

TABLE 1. Probable Cause of Keloids (n = 136)

Cause	No. of Keloids	Percentage (%)
Piercing	89	65.4
Surgical scar	26	19.1
Burn	2	1.5
Acne	1	0.7
Vaccination	1	0.7
Tattoo	1	0.7
Unknown	16	11.8

Acute and Late Complications of Radiation Therapy

The acute and late complications were scored according to the Radiation Therapy Oncology Group and European Organization for Research and Treatment of Cancer Radiation Morbidity Scoring Criteria.[11] Among the 85 patients, all patients experienced Grade 1 acute complications affecting the skin. Grade 1 acute skin complications included follicular or dull erythema and dry desquamation. Grade 2 or higher acute complications were not observed. For late complications, wound dehiscence was observed in 1 lesion (umbilicus, 0.7%) 9 months after RT. Hypopigmentation or hyperpigmentation was observed in 10 lesions (7.4%).

TABLE 2. Recurrence Rate of Keloids on Different Anatomical Sites

Site of Keloid	No. of Keloids	Recurrence	Recurrence Rate (%)
Ear	92 (67.6)	5	5.4
Earlobe	26 (19.1)	2	7.7
Ear helix, scapha, and conch	66 (48.5)	3	4.5
Head and neck	9 (6.6)	2	22.2
Trunk	26 (19.1)	2	7.7
Upper trunk	17 (12.5)	2	11.8
Mid and lower trunk	9 (6.6)	0	0.0
Extremities	9 (6.6)	1	11.1

Values are presented as No. (%).

Discussion

Keloids are considered a fibroproliferative disease, and the main target cells of RT are rapidly proliferating keloid fibroblasts. Postoperative RT has been proven to be the most effective treatment compared with other local treatments, and recurrence rates have been reported to vary from less than 10% to 20% or more.[3,12–14] There is a continued lack of consensus among physicians regarding the dose protocols in keloid treatment.[1,15,16] Furthermore, owing to the location propensity of these keloids, the recurrence rate may differ depending on the keloid's location, and the proportion of the sites in the previous studies may have also contributed to the overall recurrence rate.[17–20]

To date, there are no accepted guidelines for radiation dose fractionation schedules for postoperative RT for keloids. Because the radiation dose fractionation schedules are different for each study, it is necessary to compare the treatment outcome for biologically effective dose (BED). Regarding this, Kal and colleagues published the results of meta-analyses in 2005 and 2009.[15,16] They recommended an irradiation scheme resulting in a BED_{10} value of at least 30 to 40 Gy to prevent recurrence of keloids: for example, 13 to 15 Gy in a single fraction, 17 to 20 Gy in 2 fractions, or 18 to 22.5 Gy in 3 fractions. Typically, in radiobiology, late-responding tissues have a smaller α/β of 2 to 3 Gy while early responding tissues or rapidly proliferating cancer cells have an α/β of about 10 Gy. Kal and colleagues[15,16] assumed $\alpha/\beta = 10$, whereas Flickinger[17] reported that $\alpha/\beta = 2.08$ through a radiobiological analysis of multicenter data for postoperative RT for keloid. In the meta-analysis mentioned above, because several types of RT modality were mixed, and to reduce the confounding effect, it is necessary to evaluate the optimal dose by analyzing the results of only 1 treatment modality.

Electron beam RT is the most widely used RT modality for the treatment of keloid, and it is available in most linear accelerators. Electron beams are rapidly attenuated by soft tissue and thus can only treat to a depth of a few centimeters. This sudden drop-off of the percentage deep dose beyond the therapeutic field is one of the most useful features of electron beam disintegration in the clinical setting. In the past, electron beam RT was chosen using percent depth dose tables and the dose distribution was extrapolated using the

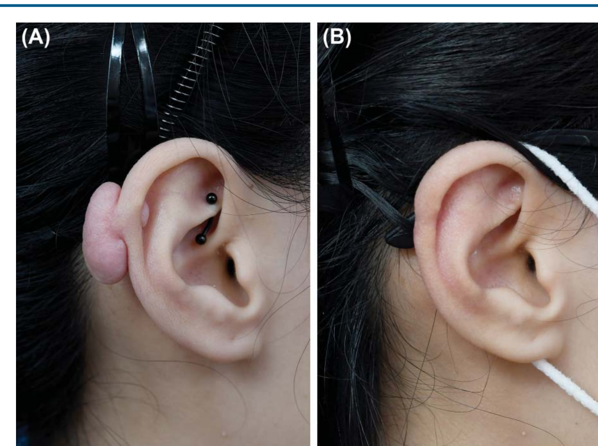

Figure 4. Ear helix keloid. (A) Before surgery and (B) 1-year after postoperative radiation therapy.

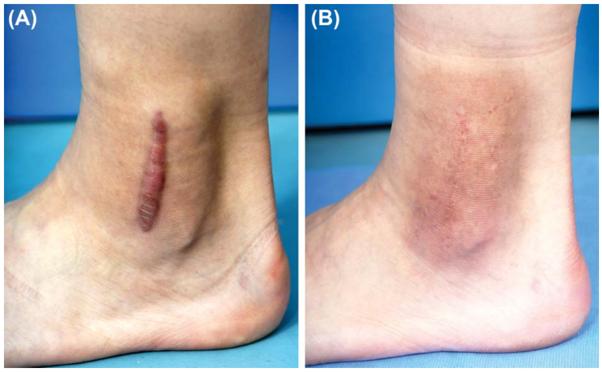

Figure 5. Lower extremity keloid. (A) Before surgery and (B) 1-year after postoperative radiation therapy.

standard isodose chart. The current CT-based RT planning system enables accurate calculation and 3-dimensional visualization of dose distribution. The authors were also able to create a conformal dose distribution to target volume by using the thermoplastic bolus pellets and Super-Flex bolus.

The recurrence rate of keloid varies by location.[1,17,19–21] This variation in recurrence rates based on the anatomical location is believed to be due in part to the difference in the tensile strength of the skin in each of those areas. It has been reported that the recurrence rates in the high-tension areas, such as chest and trunk (34%), are higher than other sites.[1] One study found recurrence rates of 30% for the abdomen, 13% for the upper extremities, and 21% for the head and neck.[19] The recurrence rate for the earlobe, which is considered to have a low tension, was 5.7%, while the auricle, which is considered to have a relatively higher tension, had a recurrence rate of 38.5%.[20] In the past, most patients presented with earlobe keloids, but recently, the authors encounter patients with keloids on various ear parts, including the helix, concha, and scapha. It can be assumed that the recurrence rate may vary depending on the keloid's location, and different parts of the same ear may experience varied degrees of physical tension compared with that of the earlobe. However, in this study, there was no significant difference in the recurrence rates of the earlobe versus ear helix, scapha, and concha. However, the recurrence rate at the other ear sites was 4.5%, which was lower than that of the earlobe (7.7%). Moreover, owing to the relatively small number of earlobe lesions compared with other sites on the ear, the recurrence rate may have been overestimated. Similarly, the number of lesions on the head and neck, trunk, and extremities was relatively low. Therefore, it is necessary that a larger number of lesions be evaluated in future studies.

There has been no consensus regarding the optimal timing of RT after keloid excision, and to the best of the authors' knowledge, no prospective randomized controlled trials investigating this issue have been conducted. However, RT is usually performed within 1 to 3 days after surgery.[2,4,5,12] Luo and colleagues[22] reported that cell lines of fibroblasts derived from keloid lesions showed distinct growth patterns and cell numbers increased sharply between the first and third days. Considering that RT affects rapidly proliferating fibroblasts, it is possible to infer the effective timing of RT based on this in vitro study. Recently, Hsieh and colleagues[23] presented the results of a meta-analysis regarding the timing of adjuvant RT by comparing the recurrence rates between the group treated within 24 hours and after 24 hours and concluded that delaying RT past 24 hours did not affect the recurrence of keloids. However, keloid recurrence is due to various factors and varies widely, making comparisons across studies difficult. Further study is needed to define the optimal timing of RT.

Tremendous efforts were made to contact all 85 patients to determine whether the authors' treatment protocol effectively prevented the recurrence of the keloids and to assess the overall patient satisfaction. This study provides further evidence that postoperative CT-based conformal electron beam RT within 24 hours, delivered over 3 consecutive days, resulted in good outcomes. The treatment protocol used 18 Gy in 3 fractions, which is within the range of other previous studies in effective cumulative dose. The authors agree that limited sample size about the different body locations and the lack of objective evaluation would be the limitation to this study. Another limitation is the short median follow-up period of 29 months. Treatment outcomes should be evaluated both objectively and subjectively at a regular follow-up by expert physicians. In patients with keloids, unlike those with malignant tumors, compliance to a regular follow-up was very low. Minor complications were tolerated, and most did not seek hospital treatment. Hence, acute and late complications may have been underestimated.

Conclusions

The authors have confirmed that postoperative CT-based conformal electron beam RT for patients with keloids ensures a favorable LRFS rate and produces a good cosmetic outcome. The authors used the RT planning system to create a 3-dimensional dose distribution to the target volume, customizing the target volume with precision and delivering the maximal prescription dose while sparing normal surrounding tissues.

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