ORIGINAL ARTICLE

Using adjuvant radiotherapy for keloid scars: a patient and observer assessment study

Uso de radioterapia adyuvante para cicatrices queloides: estudio de evaluación de paciente y observador

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Abstract

Objective: *The study presented in this article assesses the effectiveness of adjuvant electron beam radiotherapy (RT) in reducing keloid recurrence and improving scar-related outcomes.* **Methods:** *The retrospective study included 32 patients with 36 keloid scars who underwent surgical excision and adjuvant electron beam RT. The patient and observer scar assessment scale patient and observer scar assessment scale was used for all patients after RT.* **Results:** *The results showed no major treatment-related adverse events, and significant correlations were observed between overall score and color, stiffness, thickness, and irregularity of keloid scars. The study highlights that electron beam RT is an effective adjuvant therapy in reducing keloid recurrence and improving scar-related outcomes.* **Conclusion:** *Surgical excision combined with adjuvant RT is an excellent treatment option for keloids, with high patient satisfaction and low recurrence rates.*

Keywords: *Keloid. Radiotherapy. Scar Assessment.*

Resumen

Objetivo: *Evaluar la efectividad de la radioterapia (RT) con electrones en la reducción de la recurrencia de queloides y la mejora de los resultados relacionados con la cicatriz.* **Métodos:** *Estudio retrospectivo con 32 pacientes y 36 queloides que se sometieron a escisión quirúrgica y RT adyuvante. En todos los pacientes se aplicó la Escala de Evaluación de Cicatrices por Paciente y Observador (POSAS, Patient and Observer Scar Assessment Scale) después de la radioterapia.* **Resultados:** *No hubo eventos adversos y se observaron correlaciones significativas entre la puntuación general y el color, la rigidez, el grosor y la irregularidad de las cicatrices queloides. El estudio destaca que la RT es una terapia eficaz para reducir la recurrencia y mejorar los resultados.* **Conclusiones:** *La escisión quirúrgica con RT adyuvante es una excelente opción de tratamiento para queloides, con alta satisfacción del paciente y bajas tasas de recurrencia.*

Palabras clave: *Queloide. Radioterapia. Evaluación de cicatrices.*

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Introduction

Keloid scars are a common benign condition that occurs due to a fibroblast proliferation disease. The primary cause of this disorder is chronic inflammation of the dermis during the wound-healing process, which leads to an abnormal accumulation of collagen[1]. Keloids differ from hypertrophic scars as they typically grow beyond the boundary of the original wound, continuously invading the neighboring healthy skin.

Patients with a higher Fitzpatrick phototype tend to show keloid scars more frequently. The incidence of keloid scars ranges from 4.5% to 16% in individuals with type VI Fitzpatrick skin type compared to only 0.09% in those with type I[2]. Furthermore, genetic conditions, such as Bethlem myopathy and Noonan syndrome can contribute to the development of this condition, as well as a family history of keloid scars[3].

Most studies report a similar distribution of keloid scar incidence between genders. However, Noishiki et al. concluded that before the normal onset age of 15, females have a two-fold incidence compared to men[4]. The pathophysiology of keloids is not yet fully understood. Some studies suggest that hormonal changes during puberty and pregnancy may exacerbate tissue inflammation due to the vasodilatory effect of estrogens on blood vessels. Local risk factors, such as delayed wound healing, depth, and skin tension, also contribute to keloid formation[5]. Inflammation plays a crucial role in the development of keloids by continuously activating fibroblasts. Therefore, any condition that activates these cells in a genetically predisposed individual can increase the probability of a keloid scar[6].

Keloid scars may be asymptomatic or cause itching, pain, erythema, and continuous lump growth, leading to malformations in function and esthetic appearance[7]. Histologically, keloids are characterized by the presence of disarrayed fibrous nodules and hyalinized thick collagen, with a unique appearance in size, pigmentation, and pattern[8].

Although keloid scars are a benign condition, they are often refractory to most treatments and have a high risk of recurrence. Combined treatments are currently used to manage them, aiming to relieve symptoms and improve the appearance of the scar without the risk of recurrence. Several treatments have been described, including the use of medical ointments, compression therapy, silicone gel pads, corticosteroid injections, topical administration of antineoplastic drugs (such as bleomycin, 5-fluorouracyl, and mitomycin), immunotherapy (such as tacrolimus, imiquimod, and interferons), surgical excision, laser treatment, intralesional cryotherapy, and post-operative radiotherapy (PORT)[8]. Radiotherapy (RT) protocol can vary widely, and studies have shown that a dose of 20 Gy in 5 fractions may be associated with a lower recurrence rate of keloid scars[9].

This study aims to assess the effectiveness of PORT in reducing keloid recurrence and improving scar-related outcomes, as evaluated both by patients and by clinicians.

Methods

Our retrospective study included all patients who underwent surgical excision and PORT using electron beams for keloid scars at our institution between May 2016 and September 2022. Demographic and clinical data were collected from the medical charts of the Plastic Surgery and RT Departments.

All patients undertook the patient and observer scar assessment scale (POSAS v 2.0/EN) to evaluate various scar-related parameters, with scores ranging from 1 to 10[10].

The POSAS is composed of two components: the patient scale and the observer scale. Each scale consists of six items that are rated on a numerical scale from 1 to 10, with 1 representing characteristics of normal skin and 10 representing the most severe and imaginable scar. A seventh item in each scale provides an overall assessment of the scar, offering a comprehensive evaluation of the treatment s outcome.

The POSAS observer scale was performed by the same investigator in all patients after RT. A prescription dose of 18 Gy/2 fractions (9 Gy/Fraction) was used, with 6MeV electrons and a 3D conformal technique. PORT treatment started within 24 h after surgery, and the fractions were administered 7 days apart.

Data were analyzed using IBM® SPSS® Statistics, version 28. Quantitative variables were reported either as mean ± standard deviation, when normally distributed, or as median and interquartile range (IQR), when normal distribution was not observed or when considering an ordinal scale variable. For qualitative variables, absolute and relative frequencies were reported for descriptive purposes. Spearman's correlation coefficient was used to determine correlations between POSAS scale parameters, and reliability was assessed through standardized Cronbach's alpha and

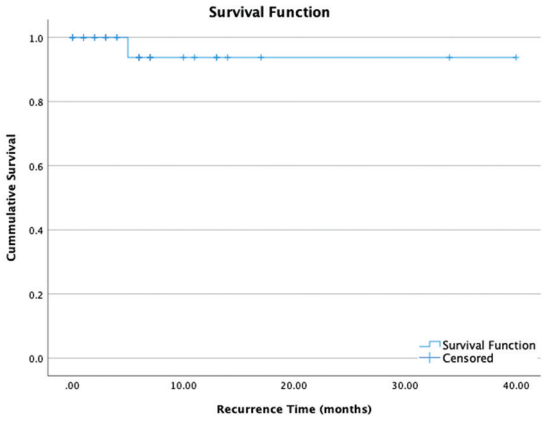

Figure 1. *Recurrence observed, with a 1-year progression-free survival of 93.8%.*

item-by-item sensitivity analysis. Survival was assessed using Kaplan-Meier's method. A type I error of 0.05 was considered for inferential analyses. This study was approved by the Institutional Ethics Board.

Results

Thirty-two patients (13 women and 19 men) with a total of 36 keloid scars were included, with an age at diagnosis of 29.3 ± 13.7 years, ranging from 12 to 69 years. Five patients were African descendants and 27 were Caucasians. The median follow-up period was 3.5 years (IQR: 8.25).

Among the 36 keloid scars, 21 (58.3%) were located in the ear, 5 (13.9%) in the trunk, 2 (7.7%) in the neck, 2 (7.7%) in the breast, and 6 (16.7%) in other locations. No major treatment-related adverse events were reported. Only one recurrence was observed, with a 1-year progression-free survival of 93.8% (Fig. 1). Table 1 summarizes demographic, clinical and treatment related data.

POSAS patient-reported parameters showed a median ranging between 1 and 3, with an overall classification of 2 (IQR of 3). The parameter with the highest score was 'color' (median of 3) and those with the lowest score were 'pain' and 'itching' (median of 1) (Table 2).

Significant correlations were observed between patient overall score and color ($\rho = 0.35$, $p = 0.042$), stiffness ($\rho = 0.75$, $p < 0.001$), thickness ($\rho = 0.74$, $p < 0.001$), and irregularity ($\rho = 0.71$, $p < 0.001$).

Reliability for patient-related items was $\alpha = 0.796$, with stiffness, thickness, and irregularity contributing most on the item-by-item removal sensitivity analysis.

Table 1. Patient, keloids and treatment related characteristics

Variable	p
Age (mean ± SD)	29.3 ± 13.7
Gender, n (%)	
Male	19 (59.4)
Female	13 (40.6)
Race, n (%)	
Black	5 (15.6)
Caucasian	27 (84.4)
Keloid-associated onset event, n (%)	
Iatrogenic/Surgery	21 (58.3)
Piercing	7 (19.4)
Accident	3 (8.3)
Others	5 (13.9)
Locations, n (%)	
Ear	21 (58.3)
Trunk	5 (13.9)
Cervical	2 (7.7)
Breast	2 (7.7)
Others	6 (16.7)
Previous treatments, n (%)	
No	17 (47.2)
Yes	19 (52.8)
POSAS Patient Scale, median (IQR)	
Pain	1 (1)
Itching	1 (1)
Color	3 (2)
Stiffness	2 (3)
Thickness	2 (3)
Irregularity	2 (2)
Overall opinion	2 (3)
POSAS Observer Evaluation Scale, median (IQR)	
Vascularization	1 (1)
Pigmentation	1 (1)
Thickness	1 (2)
Relief	1 (1)
Pliability	1 (1)
Surface Area	1 (1)
Overall opinion	2 (1)
Local recurrence, n (%)	
No	35 (97.2)
Yes	1 (2.8)

IQR: interquartile range; SD: standard deviation.

POSAS observer-reporter parameters showed a median ranging between 1 and 2, with an overall score of 2 (IQR of 1). The parameter with the highest score was color and all other parameters had a score of 1 (Table 2).

All individual observer-assessed parameters showed significant correlations with the observer's overall score ($\rho > 0.55$, $p < 0.001$). Reliability for observer-related items was $\alpha = 0.898$, with thickness, relief, pliability, and area contributing most on the sensitivity analysis. No significant correlation between

Table 2. Patient and observer scar assessment scale value

Parameter	Patient		Observer	
	Median	IQR	Median	IQR
Pain	1	1	1	1
Itching	1	1	1	1
Color	3	2	1	2
Stiffness	2	3	1	1
Thickness	2	3	1	1
Irregularity	2	2	1	1
Opinion	2	3	2	1

patient and observer overall score were observed ($\rho = 0.26$, $p = 0.14$).

Discussion

Keloid scars are a type of benign dermal condition that occurs due to excessive activation of fibroblasts, which leads to the deposition of collagen. This excessive expression of growth factors (such as TGF-ß, PDGF, and VEGF) and cytokines is responsible for the development of keloid scars[11]. Without treatment, the activation cycle progresses over time, leading to an increase in size associated with local symptoms. The definitive treatment for keloid scars involves removing the fibrotic tissue, while breaking the cytokine and collagen cycle.

Numerous treatment options for keloid scars have been proposed, but no treatment is yet defined as gold standard. These options include non-invasive treatments, such as silicone gel pads, medical ointments, and compression therapy, as well as invasive treatments, such as intralesional corticosteroid injections, topical administration of antineoplastic drugs, immunotherapy, cryotherapy, surgical excision, and PORT[8,11].

Surgical excision is a popular option for treating keloids, and it is the first-line treatment for a disabling scar. However, when not combined with other treatments, recurrence rates can range from 45% to 100%[12]. To prevent and treat keloids, present international guidelines recommend intralesional corticosteroid injections as first-line therapy[13]. Although injections can be painful, response rates range from 50% to 100%, and the recurrence rate varies between 9% and 50%[14]. Intralesional injections of 5-fluorouracil have also been found effective in treating hypertrophic, fibrous, and painful scars; however, its use in this setting remains controversial[15].

RT has been used as a treatment option for keloids, and can be an excellent choice when combined with surgical excision. PORT has been found to be the most effective treatment for severe keloid cases, reducing recurrence rates by 55% after 30 months of follow-up[13,15]. However, the mechanism by which RT exerts positive effects in the management of keloids is still uncertain. The possible mechanism is the induction of DNA damage on fibroblasts, preventing collagen synthesis and proliferation, which can inhibit keloid formation. Previous studies have reported good local control rates ranging from 67% to 98% and a recurrence rate of < 10-20% after PORT[16,17].

In our study, we investigated the effectiveness of PORT in the management of keloid scars. The rationale behind utilizing PORT in keloid scars is its potential to achieve better treatment outcomes compared to primary RT alone. This is primarily due to the fact that PORT is administered to a more radiosensitive immature target after surgical excision[18].

The timing of RT following surgical excision is a crucial factor in determining its efficacy, although it remains a topic of debate. Several studies have reported favorable disease control benefits ranging from 10% to 23% when RT is initiated within 24 h after surgery[16,19]. The rationale behind the efficacy of a short time interval is to prevent fibroblast proliferation, which is crucial in keloid formation and recurrence.

In our study, we adhered to the recommended practice of initiating PORT treatment within 24 h after surgery. The radiation fractions were administered at intervals of 7 days apart. Notably, our study observed only one recurrence, resulting in a 1-year progression-free survival rate of 93.8% (Fig. 1). These findings suggest that early initiation of PORT following surgical excision may contribute to improved treatment outcomes and reduced recurrence rates in keloid scars.

Renz et al. reported that lesions treated with 20 Gy had a recurrence rate of 1.6%, compared to 9.6% with < 20 Gy[9]. In this study, a RT protocol of 18 Gy in 2 fractions, 7 days apart was used for all keloids regardless of their location, and the results were considered optimal with only one recurrence observed. The recurrence may have been due to trauma with a ball after the patient's RT sessions, which could explain the final result.

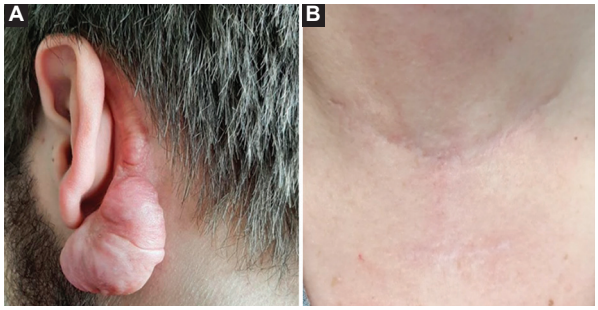

Figure 2. A: *post-auricular keloid before post-operative radiotherapy (PORT).* **B:** *after PORT, 24 months of follow-up.*

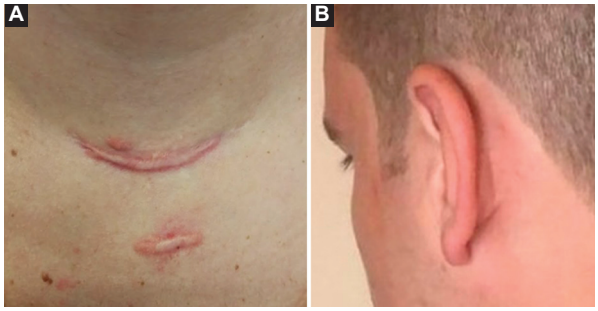

Figure 3. A: *keloid total thyroidectomy, located on the anterior neck keloid, before post-operative radiotherapy (PORT).* **B:** *after PORT, 5 years of follow-up.*

Overall, our study adds to the existing body of evidence supporting the use of PORT in keloid scar management. The favorable results observed (Figs. 2 and 3) in terms of disease control and progression-free survival; further emphasize the importance of timely intervention and adherence to recommended treatment protocols. However, additional research and larger-scale studies are required to confirm these findings and establish optimal guidelines for the timing and administration of PORT in the management of keloid scars. It is also important to consider the potential toxicity associated with PORT. The use of radiation therapy in the treatment of keloid scars can lead to adverse effects, including skin toxicity, such as erythema, desquamation, and hyperpigmentation[20].

Further studies are required to assess the long-term effects of PORT, such as cosmetic outcomes, quality of life, and patient satisfaction. It is also essential to assess the toxicity profile of PORT in keloid treatment and explore strategies to minimize adverse effects while maximizing treatment efficacy by establishing optimal dose schedules and fractionation protocols to balance the potential benefits of treatment with the risk of toxicity.

Conclusion

According to this study, the combination of surgical excision and PORT proves to be a highly effective treatment approach for keloids. It not only demonstrates remarkable patient satisfaction but also significantly reduces the likelihood of recurrence. Nevertheless, it is important to conduct longer-term patient follow-up to comprehensively assess the treatment's effectiveness.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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