

## **USE OF BETATHERAPY IN THE TREATMENT OF KELOIDS**

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**Abstract: Introduction:** The healing mechanisms occur in multiple, simultaneous and coordinated ways. When there is an imbalance between the synthesis of the new matrix and the lysis of the old matrix, there is the possibility of keloid formation. Because it is a genetically based disease with diverse pathophysiology, treatment is complex and challenging for medicine. The options currently available range from surgical to topical treatments. However, elucidating the factors involved in the pathology to improve individual therapy is still necessary. Therefore, the objective is to develop an integrative review of the scientific production on the effectiveness of using betatherapy in the treatment of keloids. **Methodology:** The selection of articles was carried out through several databases, namely: Scielo, Google Scholar, PubMed and Lilacs. The inclusion criteria for the defined articles were: articles published in Portuguese, English and Spanish, with abstracts available in the selected databases, in the period between 2008-2021. Articles whose approach did not present the use of betatherapy or only mentioned it were excluded. The keywords used were betatherapy, keloid and treatment. The search was carried out through online access, with a total of 41 non-repeated articles and, using the inclusion criteria, the final sample of this integrative review consisted of 7 articles, in addition to those that supported the theoretical foundation and discussion. **Results:** When analyzing the articles found, 7 met the previously established inclusion criteria. As for the type of research design of the articles evaluated, the following were evident in the sample: two systematic reviews, an epidemiological study and other case reports. Regarding the objective of this review, it was observed in the articles: 4 positive results, 1 result of sub-referral for betatherapy, 1 did not demonstrate superiority

between the modalities that use radiotherapy and 1 showed greater effectiveness in the use of beam therapy. electrons. **Conclusions:** In this integrative review, the literature converges in encouraging the combination of methods. Regarding the use of betatherapy, 4 of the 7 articles included in the integration concluded, positively, good long-term results, when started in the immediate postoperative period. As for the difficulties pointed out, these were related to cost, application of the method and its adverse effects. Finally, there is still no defined treatment protocol, which points to the need to develop more studies on the subject in question.

**Keywords:** Betatherapy, Keloid, Treatment.

## INTRODUCTION

Despite being classified as a hyperproliferative scarring dysfunction, keloid is characterized by the hyperproduction of collagen, and secondarily by a hyperproliferation of fibroblasts in the dermis. The fibroblast, secreting collagenase, would maintain the synthesis/degradation balance of the scar by regulating its size, since the collagen neoformation can normally be maintained for up to 12 months. The critical period of the healing process, when the balance between collagen synthesis and lysis breaks down, usually occurs in the 3rd or 4th week after injury. At that moment, for reasons not yet clarified, in cases of keloid synthesis, the synthesis becomes greater than the lysis, or the latter is less than the synthesis, for an indefinite period.

As for the clinical picture, the main involvement is related to aesthetics and quality of life. The lesion has continuous or intermittent growth, with no significant regression, and with a tendency to relapse after resection. It can develop in partial segments of the same scar, appear in a wound or incision and not in other wounds

or incisions caused in the same accident or operative act, in neighboring or distant body regions; and also if it develops in a certain place of the body, from a surgical incision and, in the future, a new incision in the same place, or immediately neighboring, may not develop this scar disorder.

Because it is a genetically based disease with diverse pathophysiology, treatment is complex and challenging for medicine. Surgery alone has a recurrence rate of 50-80%, which has allowed the use of a wide variety of adjuvant therapies. The treatment modality that achieved the lowest recurrence rates was postoperative percutaneous radiotherapy, with rates of 2-36%.

Betatherapy is a therapeutic modality in the arsenal of radiotherapy possibilities for benign diseases, with advantages and disadvantages in its use in keloids (Table 1). However, little is known about its practice in Brazil. This fact can be explained by the difficulty and high cost of acquiring the plates and by the availability of other modalities for the treatment of dermatological tumors such as 1-electron accelerators, high dose rate brachytherapy (HDR) and topical agents.

The interventionist proposal is to improve the symptoms and appearance of scars, relieving the physical and psychological damages of patients. However, elucidating the factors involved in the pathology to improve individual therapy is still necessary. Therefore, the objective is to develop an integrative review of the scientific production on the use of betatherapy in the treatment of keloids. Such investigation is justified for knowledge and interpretation of the production on the subject, in order to contribute to the development of future research.

## METHODOLOGY

This is an integrative literature review study on national and international scientific

Advantages	Disadvantages
Usually temporary side effects	Annoying hyperpigmentation in the irradiated area and carcinogenic potential of the procedure
Good long-term results when started in the immediate postoperative period	Worse tissue dose distribution compared to electron radiotherapy
More conservative approach than excision	Difficulty and high cost for the acquisition of plates
They do not have high radiation protection requirements.	Variable number of sessions
They show no damage to the tissues below the skin	Possibility of recurrence
It treats the entire length of the keloid	The active area of 1.0 cm <sup>2</sup> to 3.0 cm <sup>2</sup> of the applicator makes it difficult to use for large keloids

Table 1. Advantages and disadvantages of Betatherapy in the treatment of keloids.

production regarding the use of betatherapy in the treatment of keloids. This was guided by six steps: (1) choice of theme and research question; (2) establishment of criteria for inclusion, exclusion and search in databases; (3) definition of the information that will be extracted from the studies and categorization; (4) evaluation of studies included in the review; (5) interpretation of results and (6) synthesis/review.

To guide the integrative review, the following question was formulated: what is in the literature on the use of betatherapy in the treatment of keloids? The selection of articles was carried out through several databases, namely: Scielo, Google Scholar, PubMed and Lilacs. The inclusion criteria for the articles initially defined for this integrative review were: articles published in Portuguese, English and Spanish, with abstracts available in the selected databases, in the period between 2008-2021. This temporal cut was due to the recent reality of the publications that are part of the review. Articles whose approach did not present the use of betatherapy or only mentioned it were excluded.

The keywords used were betatherapy, keloid and treatment. The search was carried

out through online access, with a total of 41 non-repeated articles and, using the inclusion criteria, the final sample of this integrative review consisted of 7 articles, in addition to those that supported the theoretical foundation and discussion.

For the analysis and subsequent synthesis of the articles that met the inclusion criteria, a synoptic table specially built for this purpose was used, which included the following aspects, considered relevant: name of the research; authors' names; intervention studied; results; recommendations/conclusions. The presentation of the results and discussion of the data obtained was done in a descriptive way, allowing the reader to evaluate the applicability of the integrative review elaborated, in order to achieve the objective of this method, that is, to compendium the use of betatherapy in the treatment of keloids.

## RESULTS

(Table below).

In the present integrative review, 7 articles met the previously established inclusion criteria. Regarding the type of research design of the articles evaluated, the sample showed: two systematic reviews, an

Article name	Authors and year of publication	Intervention studied	Results	Recommendations/ Conclusions
Treatment of retroauricular keloid: Review of cases treated in the otorhinolaryngology service of HC/UFPR.	CARVALHO, Bettina et al. (2012).	To evaluate the results of patients undergoing treatment for retroauricular keloids after ENT surgeries in the service.	Nine patients were evaluated, of which 6 underwent resection and adjuvant beta-therapy, 2 underwent resection plus local corticosteroid application, 1 underwent resection only without adjuvant therapy. There was no recurrence in cases treated with betatherapy in the early postoperative period, 1 patient had a recurrence even with corticosteroid therapy and late betatherapy	While new techniques are not developed, resection followed by early betatherapy is still the best option.
Treatment of keloids in the auricular region with resection, steroids and betatherapy: case series.	JUNIOR, P. E. K. S. et al. (2015).	To report a case series of patients with keloids in the auricular region undergoing combined treatment with resection, corticotherapy and betatherapy.	The study included 11 patients with a previous diagnosis of keloids in the auricular region, who had already undergone previous treatment with exeresis. no recurrence of the lesions was observed in any case after beta-therapy.	In the analysis of 11 cases of recurrent keloids of the ears, treated with excision, intralesional corticosteroid infiltration and 10 sessions of betatherapy, with follow-ups ranging from 2 to 36 months, no new recurrence was observed.
Comparative study between electron radiotherapy and beta-therapy after keloid surgery	DE OLIVEIRA JÚNIOR, Batista et al. (2009).	To compare the results of betatherapy with the technique that uses electron beam in newly operated keloids.	Twenty-six patients participated in the study, 13 in each group. In G1, 54% presented unchanged and regular improvement criteria, and 46% presented good and excellent criteria. In G2, these results were, respectively, 23% and 77%.	Electron beam irradiation is superior to betatherapy for the treatment of operated keloids, due to better tissue distribution. No radio-induced tumors were observed.
Adjuvant electron beam radiotherapy to recalcitrant giant ear keloid surgery	FILHO, Francisco Ronaldo Moura et al. (2020).	The authors describe a patient who had a recalcitrant bulky keloid who had a good therapeutic result.	A 31-year-old male patient presented with a large keloid lesion, approximately 15 cm in the longest axis, originating in the lobe of the left ear pinna. He underwent a new surgical approach with total lesion excision. We opted for therapeutic c o m p l e m e n t a t i o n with electron beam radiotherapy, initiated in the immediate postoperative period.	Among the adjuvant treatments used, radiotherapy has been shown to be highly effective, with a lower probability of recurrence, and the main forms used are brachytherapy and electron beam therapy. There is no consensus on the best modality to be used or the total dose to be used.

<p>Betatherapy in Brazil: Practice Profile</p>	<p>HADLICH, Claudia Regina Scaramello et al. (2009).</p>	<p>To describe the patterns of betatherapy practice in radiotherapy services in the country.</p>	<p>Of the 175 institutions registered in the Brazilian Society of Radiotherapy, responses were obtained in 151 of them, which are the target of the study. Of these, 39 (25.82%) offer beta-therapy, distributed as follows: 27 in the Southeast region, 5 in the South region, 5 in the Northeast region and 1 in the Midwest region. Among them, 41% perform this service through the SUS.</p>	<p>It is suggested that there is a sub-referral to adjuvant and prophylaxis of relapse in pterygium and keloid and the need for greater dissemination of results compared to other medical specialties.</p>
<p>Keloid: factors of prognostic influence</p>	<p>FIGUEIREDO, Jason César de Abrantes et al. (2008).</p>	<p>To study variables that could be correlated with the recurrence of treated keloids.</p>	<p>Of the 48 lesions analyzed (45% male and 55% female), the mean age was 24 years (8-69 years), complete improvement, considering the different treatments adopted in the service, was achieved in 64.5% of keloids. The size of the lesion was significant (t-Student; <math>p &lt; 0.04</math> and ANOVA; <math>p = 0.042</math>) in recurrence for lesions <math>&gt; 40</math> mm and cure for the smallest than 20 mm. Therapy in lesions <math>&gt; 20</math> mm with excision associated with beta-therapy was significantly superior to the combination with injectable corticosteroids (chi-square; <math>p &lt; 0.04</math>).</p>	<p>The exeresis associated with betatherapy is significantly superior to the association with injectable steroids in lesions larger than 20 mm. Regarding the therapeutic response, the size of the lesion was the main prognostic factor.</p>
<p>Post-surgical radiotherapy in keloids. A meta-analysis and literature review.</p>	<p>OLIVEIRA, Ana Laura Paludetto (2019).</p>	<p>To verify the results of radiotherapy in patients with keloids, who underwent surgery to remove the lesion with subsequent irradiation of the scar bed</p>	<p>The scientific articles analyzed pointed to 1310 patients undergoing radiotherapy in keloid scars, in different anatomical regions, of which the average recurrence rate was 16.73%.</p>	<p>The studies conclude that the application of radiotherapy after keloid surgery helps to minimize the recurrence rates of the lesion, when compared to surgery alone.</p>

epidemiological study and other case reports. Regarding the objective of this review, it was observed in the articles: 4 positive results, 1 result of sub-referral for betatherapy, 1 did not demonstrate superiority between the modalities that use radiotherapy and 1 showed greater effectiveness in the use of beam therapy. electrons.

## DISCUSSION

The description in the literature of the use of betatherapy in the treatment of keloids is still incipient. Of the 41 results for the aforementioned descriptors, only 7 articles reported cases or described comparisons for the therapeutic method. Regarding the articles used in this study, 4 presented positive results regarding the use of betatherapy in the treatment of keloids, 1 demonstrated sub-referral for the performance of this procedure, 1 did not demonstrate superiority between the modalities that use radiotherapy and 1 demonstrated greater efficacy with the use of therapy with an electron beam.

The study carried out by Carvalho et al. aimed to evaluate the results of patients who underwent betatherapy for the treatment of retroauricular keloids. Of the 9 patients evaluated, 6 had a combination of resection with beta-therapy, 2 combined resection with the application of local corticosteroids and 1 had resection as the only method performed. As a result, patients who were treated with betatherapy in the early postoperative period did not have a recurrence, however, recurrence was observed in a patient who underwent late betatherapy, as well as a recurrence in the patient who underwent corticosteroid application. Their conclusion points out that while new techniques are not developed, the combination of resection with early betatherapy represents the best option.

In the study by Junior et al. there was a combination of three methods: resection,

corticotherapy and betatherapy. In this study, 11 cases of patients with recurrent keloids who underwent previous treatment with excision were analyzed. For the new evaluation, they were treated with excision, intralesional corticosteroid infiltration and 10 sessions of beta-therapy, with no further recurrences.

The systematic review by Oliveira, A. L. P. aimed to analyze the results of radiotherapy in patients with keloids, who underwent excision with subsequent irradiation of the scar bed. The result of this analysis showed that of the 1310 patients who underwent radiotherapy, the average recurrence rate was 16.73%, reaching the conclusion that the application of radiotherapy after surgery to remove the keloid helps to reduce the recurrence of the lesion, when compared to surgery as monotherapy.

Still on the studies that had positive results for the use of betatherapy in the treatment of keloids, we have the study by Figueiredo et al. which analyzed the variables that could possibly be related to the recurrence of treated keloids. Of the 48 lesions analyzed, complete improvement was achieved in 64.5% of keloids. The size of the lesion proved to be an important point for recurrence in lesions larger than 40 mm and for healing in lesions smaller than 20 mm. Furthermore, in this study, it was observed that excision associated with betatherapy was superior to the association with injectable corticosteroids for lesions larger than 20 mm.

The work by Filho et al. this was a case report of a patient with a voluminous keloid lesion, submitted to total lesion excision, associated with electron beam radiotherapy. In his conclusion, he pointed out that radiotherapy has shown high efficacy, with no consensus on the best modality or total dose to be used.

Hadlich et al. carried out an epidemiological study that described the practice of betatherapy in the country's services. Of the 151 institutions targeted by the study, 39 (25.82%) offer beta-therapy, being more concentrated in the Southeast region, totaling 27, and less in the North region, with 0 institutions. Thus, it was suggested that there is still a sub-referral for the treatment of keloid recurrences, requiring greater dissemination in relation to other medical specialties.

Finally, we have the study that showed greater effectiveness of another modality of radiotherapy used in the treatment of keloids. De Oliveira Júnior, et al. compared the results of using beta therapy with electron beam therapy, and in both situations, exeresis was performed together. There were 26 patients evaluated, divided into two groups with the same number of patients. As a result, electron beam irradiation was superior to beta therapy due to better tissue distribution.

## **CONCLUSIONS**

The treatment of keloids is still a challenge for medicine, a fact proven by the lack of defined protocols. Although several therapeutic modalities exist, most still have a high recurrence rate and some adverse effects.

In this integrative review, the literature converges in encouraging the combination of methods. Regarding the use of betatherapy, 4 of the 7 articles included in the integration concluded, positively, good long-term results of betatherapy when started in the immediate postoperative period. 1 of the articles, however, pointed out the difficulty and high cost of acquiring the plates, limitation in large keloids, uncomfortable hyperpigmentation in the irradiated area and worse dose distribution in tissues compared to electron radiotherapy.

The incipience of studies on the use of betatherapy in the treatment of keloids makes it difficult to establish its effectiveness robustly. For more reliable results, new studies must be developed and published, especially as it is a promising therapeutic alternative in the list of options for the management of keloids.



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