







# Postoperative radiotherapy with an electron beam on keloid scar: epidemiological evaluation in a teaching hospital

## *Radioterapia pós-operatória com feixe de elétrons sobre cicatriz quelóideana: avaliação epidemiológica em hospital de ensino*

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### ■ ABSTRACT

**Introduction:** Keloids are one of the most aggressive spectrums of healing disorders. They have a unique pathophysiology and multiple specific genetic and cellular factors, which have not yet been fully elucidated. So far, literature reviews have found the influence of genetics, injury site, and ethnicity on the incidence and rate of recurrence. Furthermore, the need to associate an adjuvant method with surgical excision has already been verified, but the best therapy has yet to be defined. **Method:** A retrospective analysis of medical records was carried out to assess the profile of patients who underwent postoperative radiotherapy with an electron beam to treat keloids at the Hospital das Clínicas da Faculdade de Medicina de Botucatu between 2015 and 2019. **Results:** Data from 131 patients were evaluated, with 269 keloid scars treated. The average duration of treatment was 51 days, and the number of sessions was 17. White patients were predominant (78%) and women (70%), with surgical incision being the main cause of formation (49%) and ear the most identified location (33%). Women were more likely to complete the proposed treatment ( $p=0.04$ ), while non-literates completed less than those who had at least completed primary or secondary education ( $p<0.0001$ ). **Conclusion:** Postoperative radiotherapy for keloid scars is a well-established treatment in the literature and an important tool for plastic surgeons. Knowing the profile of patients who need this therapy is essential to create methods that improve adherence and results. **Keywords:** Keloid; Scar; Radiotherapy, adjuvant; Reconstructive surgical procedures; Medical records.

### ■ RESUMO

**Introdução:** Os queloides correspondem a um dos espectros mais agressivos dos distúrbios da cicatrização. Possuem fisiopatologia ímpar e múltiplos fatores genéticos e celulares específicos, ainda não totalmente elucidados. Até o momento, revisões literárias encontraram influência da genética, local da lesão e etnia sobre a incidência e taxa de recorrência. Ademais, já foi constatada a necessidade de associação de um método adjuvante com a excisão cirúrgica, mas ainda sem definição da melhor terapia. **Método:** Realizada uma análise retrospectiva de prontuários para avaliação do perfil dos pacientes submetidos a radioterapia pós-operatória com feixe de elétrons para o tratamento de queloides no Hospital das Clínicas da Faculdade de Medicina de Botucatu, entre 2015 e 2019. **Resultados:** Foram avaliados os dados de 131 pacientes, com um total de 269 cicatrizes quelóideanas tratadas. A média da duração do tratamento foi de 51 dias e do número de

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sessões, de 17. Houve predominância de pacientes brancos (78%) e de mulheres (70%), sendo incisão cirúrgica a principal causa de formação (49%) e a orelha a localização mais identificada (33%). As mulheres tiveram mais chance de completar o tratamento proposto ( $p=0,04$ ), enquanto os não alfabetizados completaram menos do que aqueles que tinham pelo menos ensino fundamental ou médio completo ( $p<0,0001$ ). **Conclusão:** A radioterapia pós-operatória em cicatrizes queloidianas é um tratamento consagrado na literatura e uma importante ferramenta do cirurgião plástico. Conhecer o perfil dos pacientes que necessitam desta terapia é fundamental para criar métodos que melhorem a adesão e o resultado da mesma.

**Descritores:** Queloides; Cicatriz; Radioterapia adjuvante; Procedimentos cirúrgicos reconstrutivos; Registros médicos.

## INTRODUCTION

Healing, a dynamic and multifactorial process divided into three phases – inflammatory, proliferative, and remodeling – is one of the most important defense mechanisms of the human body by preventing blood loss and ensuring tissue repair. However, as it is a dynamic process, several known and unknown factors can positively affect it, resulting in an adequate recovery of the injured tissue.

Thus, when the site is the skin, the aim is to return to the state as close as possible to the previous one, which, depending on the mechanism and type of trauma, is not achieved<sup>1</sup>. Despite all the efforts of the cellular recovery mechanism, many cases do not reach the desired aesthetic or functional appearance<sup>2</sup>.

From the classification of scars, it was possible to elaborate protocols for their treatment, which differ in light or more invasive therapies, depending on the severity of the case. Thus, because they are considered more severe, scars classified as keloids require different therapeutic strategies<sup>3,4</sup>.

Keloids, first described and named by Alibert in 1806<sup>5</sup>, were presented as a growth similar to the projection of branches or the claws of a crab, which from the Greek *khele* derived the English word keloid, being translated into Portuguese as *queloide*.

Considered a benign tumor, it is characterized by the expansion of the limits of the initial lesion with a prolonged course of activity, in addition to having a unique pathophysiology and multiple specific genetic and cellular factors, with many of its variables not yet fully understood<sup>6</sup>. At the histological level, there is a chronic inflammation of the reticular dermis, with increased fibroblasts and collagen, specifically type I, eosinophilic and hyalinized.

So far, it is known that there is a greater development and growth of keloids during puberty, in addition to an increase during pregnancy and a decrease after menopause<sup>7</sup>. Among the factors that promote its emergence, we can highlight genetics, the site of the initial lesion, and ethnicity<sup>8</sup>.

Although not yet fully elucidated, several findings suggest genetic influence as a predisposing factor to the formation of keloids. For example, some families have multiple members affected, and the prevalence in twins is more frequent. When evaluating such families, possible patterns of autosomal dominant heterogeneity are observed, but cases suggesting recessive or X6-linked inheritance have also been described.

In addition to being associated with the genetic component, ethnicity has special emphasis when evaluated along with the phototypes of patients according to the Fitzpatrick scale<sup>9</sup>. As it is more frequent in blacks, Hispanics, and Asians, a possible relationship with the activity of melanocytes during the healing process can be traced.

Furthermore, the location of the keloid can directly affect its recurrence rate. Based on the current literature, systematic reviews and meta-analyses have shown high recurrence rates in the trunk region, up to three times higher than in the head and neck region, including ears, or even when compared to the limbs. Therefore, it is believed that the variation of skin tension forces in different body regions possibly generates these statistically significant differences<sup>10</sup>.

Despite its non-lethality, keloids impair mental and emotional quality of life, as demonstrated in recent studies, which is recovered after treatment<sup>11</sup>.

For its treatment, it is important to point out that exclusive excision, without association with an adjuvant method, has high recurrence rates, close to 50%, with an increase with each new attempt, especially in the first four years<sup>12</sup>.

Several studies have been trying to demonstrate the great importance of combining therapies, but still without a definitive result for this problem. New technologies are being associated with classic treatments, but also without showing maximum effectiveness<sup>13,14</sup>.

Among the classic treatments, we can highlight the intralesional infiltration of drugs, such as corticosteroids and 5-fluoracil, in addition to the various adjuvant radiotherapy (RT) modalities: conventional RT, RT with an electron beam, RT in a single dose, and conventional X-ray<sup>15,16</sup>.

Radiotherapy interferes with the formation of keloids by inhibiting the release of histamine by mast cells, reducing the proliferation of fibroblasts, and inhibiting TGF- $\beta$ 1, which suppresses collagen production<sup>17</sup>. External radiotherapy after surgical excision of keloids, proposed in the 1960s<sup>18</sup>, showed that alone it could alleviate the symptoms but failed to resolve the lesion when not associated with surgical excision. Furthermore, delay in performing radiotherapy after excision has been shown to result in higher recurrence rates.

However, radiotherapy with adjuvant in treating keloids raises great concern due to its carcinogenic potential. In 2009, a literature review found 5 cases that reported this occurrence. However, it was impossible to define whether adequate doses had been used in the reported cases and whether there was effective protection around the adjacent tissues<sup>19</sup>. Therefore, the conclusion is that the risk of carcinogenesis does not prevent the procedure from being performed, as long as care measures are taken for the surrounding tissues, which includes protection of the thyroid and mammary glands, especially in children and adolescents<sup>19</sup>.

Later, the possibility of treatment with internal or interstitial radiotherapy, known as brachytherapy, was introduced<sup>20</sup>. In this modality, there is a great capacity to focus the radiation on the target area, requiring a smaller dose and being more efficient, with less local radionecrosis and adverse effects on healthy tissues close to the keloid. However, there is still a higher hospital cost due to prolonged hospitalization and the use of specific and poorly available materials<sup>19</sup>.

A work carried out in Brazil highlighted the importance of RT with an electron beam; therefore, this possibility of treatment is maintained in the current approach routine for these lesions in our institution<sup>21,22</sup>.

The keloid scar remains a medical challenge, both because of the difficult definition of the physiological factors that influence its formation and because of the need to associate therapies that, in some cases, do not cure or prevent the appearance of new lesions and recurrences.

## OBJECTIVE

Therefore, this study aims to present a retrospective analysis of patients undergoing postoperative radiotherapy at the Hospital das Clínicas da Faculdade de Medicina de Botucatu over a four-year period to outline their epidemiological profile.

## METHOD

### Postoperative radiotherapy treatment protocol

Patients are referred to the Radiotherapy sector for clinical evaluation and scheduling the first photoelectron

radiotherapy session using the Clinac 2100-C linear accelerator device (Varian-USA), with an energy of 4 million electron volts (MeV). 32Gray schemes divided into 16 sessions are programmed, 5 days a week. At the end of the 16 sessions, patients are reassessed for the need for booster doses of 8Gray in 4 sessions.

Radiotherapy was indicated for all referred patients who had undergone some previous therapy without success for treating keloids or recurrences and who were going to undergo keloid resection surgery.

The first session is always scheduled within 24 to 48 hours after keloid resection surgery in adults and children.

### Analysis of medical records

Retrospective analysis of medical records to assess the profile of patients who underwent postoperative radiotherapy for the treatment of keloids at Hospital das Clínicas da Faculdade de Medicina de Botucatu (HC-FMB) from January 2015 to January 2019, whose data from the medical record allowed the inclusion in the study.

All female and male patients, adults, and children who underwent the treatment protocol of the Radiotherapy service at HC-FMB UNESP were included.

Patients whose medical records did not have confirmatory data on keloid scar treatment with surgery performed at the same hospital or an outpatient service and radiotherapy were excluded.

As it is a cross-sectional study, it was possible to apply the STROBE initiative partially (Strengthening the Reporting of Observational Studies in Epidemiology)<sup>23</sup> to guide the review.

### Researched variables - Epidemiological data

While analyzing medical records, we sought to determine the following variables: age, sex, education level, city of origin, race, cause of the scar, previous treatments, keloid site, treatment time, dose, and number of applications of radiotherapy.

### Data collect

The data collection methodology used a form developed especially for this study (Appendix I), filled out by the researcher in the Department of Plastic Surgery, while evaluating the medical records of the patients included in the study. Data collection was carried out after approval by the Research Ethics Committee.

### Analysis of data from medical records

These data were tabulated using Microsoft Excel® software to perform descriptive statistical analysis.

For qualitative variables, Pearson's non-parametric chi-square test was performed, while, for the quantitative variables, analysis of variance was used to compare the different means and standard deviations related to the year of attendance and Student's t-test to compare the means and standard deviations according to the patient's gender.

The Kaplan-Meier estimator was also used to study the duration of treatment and its conclusion according to several variables (gender, specialty that made the referral for radiotherapy, city of origin, education, previous treatments, race, keloid etiology, and location).

The software used for statistical analysis was SAS version 9.2. The confidence interval was 95%, considering the p-value statistically significant when less than 0.05.

### CEP evaluation

The work complies with the recommendations of the Research Ethics Committee (CEP) of the HC-FMB UNESP, being approved under opinion number 4,399,507.

## RESULTS

After reviewing medical records, we identified 27 people treated in 2015, 43 in 2016, 21 in 2017, and 40 in 2018, totaling 131 patients. Some had more than one irradiated lesion, with a total of 269 treated keloid scars.

Treatment duration ranged from 1 to 92 days after the first irradiation, averaging 51 days. The number of sessions was between 1 and 25, with a mean of 17. Table 1 shows the mean and standard deviation for the variables age, dose, number of applications, and treatment time in days according to the years evaluated, being that in 2018 and 2017, there were a greater number of sessions than in previous years.

The majority of patients were white (78.8%), followed by black (10%), brown (3.7%), and yellow (1.1%). There was no distinction of race described in the medical records in 6.3% of the cases, in addition to not being possible to classify the patients according to the Fitzpatrick scale (Table 2).

According to the Kaplan-Meier estimator, there was no difference between races in terms of whether or not they completed treatment with radiotherapy (Figure 1).

As causes of keloid formation, a surgical incision was described in 49% of the lesions, followed by earrings in 11%. There was no adequate information about the etiology of the lesion in 30% of the cases. Other causes with an incidence of less than 2% were, in descending order: trauma (blunt-cut injuries), acne, tumors, spontaneous appearance, bites, and folliculitis (Table 3). According to the Kaplan-Meier estimator (Figure 2), those patients with keloid scars secondary

to acne or of undetermined cause tended to complete the treatment more than those caused by earrings and surgical incisions ( $p < 0.0001$ ).

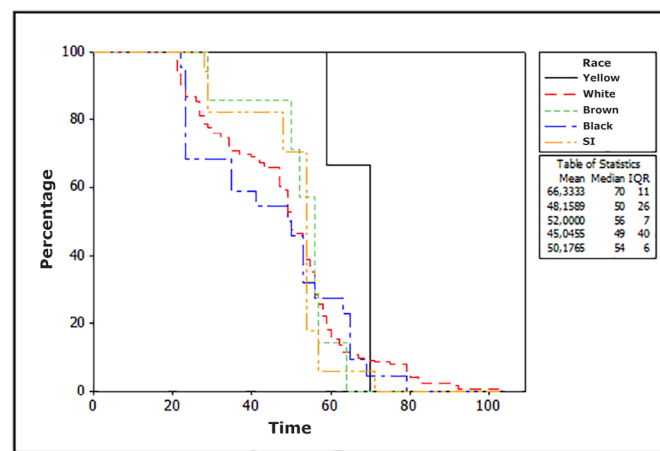
**Table 1.** Mean, and standard deviation refer to age, dose, number of applications, and treatment time according to years.

	Year				P
	2015	2016	2017	2018	
<b>Age (in years)</b>	31.5	29.2	33.5	31.9	0.17
	12.9	10.7	11.8	10.9	
<b>Doses</b>	3164.0	3394.7	3668.2	3994.8	<0.001
	991.1	834.6	835.4	574.0	
<b>Number of applications</b>	15.7	17.0	18.5	19.9	<0.001
	5.0	4.2	4.3	2.9	
<b>Time (in days)</b>	36.1	37.4	46.1	56.2	<0.001
	19.6	17.7	16.2	17.7	

**Table 2.** Frequency distribution of patients according to race and year.

Year	Race					Total
	Yellow	White	Brown	Black	N/D	
2015	-	37	6	two	5	50
	0.0	74%	12%	4%	10%	100 (%)
2016	-	70	-	6	-	76
	0.0	92.1%	0.0	7.9%	0.0	100 (%)
2017	-	39	3	15	9	66
	0.0	59.1%	4.6%	22.7%	13.6%	100 (%)
2018	3	66	1	4	3	77
	3.9%	85.7%	1.3%	5.2%	3.9%	100 (%)
<b>Total</b>	3	212	10	27	17	269
	1.1%	78.8%	3.7%	10%	6.3%	100 (%)

P < 0.001; N/D: no data



**Figure 1.** Kaplan-Meier estimator for total treatment time according to race and whether or not treatment was completed ( $p = 0.66$ ). Time in days; SI: no data; Mean; Median; IQR: interquartile range

Several locations were identified, the most prevalent being the ears – including the lobe (33%), breasts (23%), and abdomen (22%). The other locations described were, in descending order: thorax, neck, inguinal region, sternum, arm, armpit, hand, thigh, leg, and lip (Table 4). Using the Kaplan-Meier estimator (Figure 3), we observed a greater chance of completing the treatment for those with injuries to the neck, back, and chest (including sternum) than those with injuries to the abdomen and earlobe ( $p < 0.0001$ ).

Most injuries referred came from male and female plastic surgeons (63%), followed by Dermatology (12%), Head and Neck Surgery (3%), and Mastology (0.4%). In 20% of cases, there was no information on the specialty that referred the patient to the Radiotherapy sector.

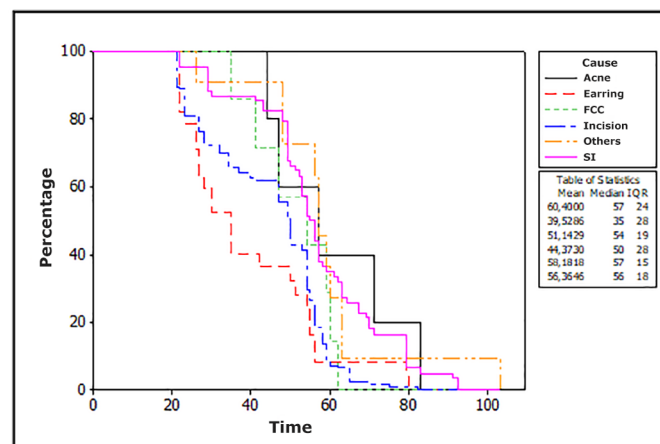
Regarding education, 38% completed or attended high school, 29% completed or were attending higher education, and 15% and 2% completed or attended elementary school II and I, respectively. In all, 3% of the patients were illiterate and in 11% of the cases this

information was not available (Table 5). According to the Kaplan-Meier estimator (Figure 4), illiterate patients

**Table 3.** Distribution of patient frequencies according to cause and year.

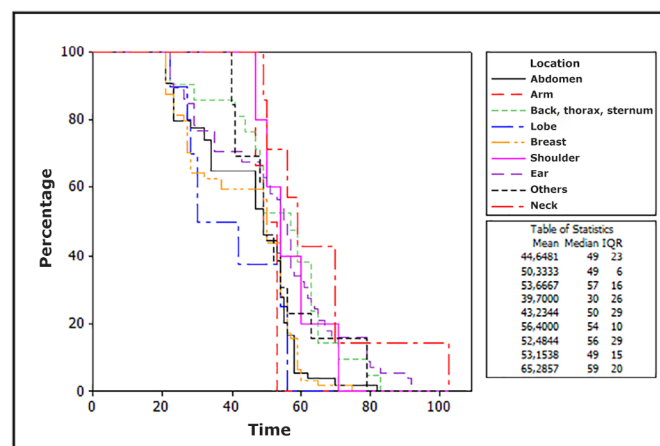
Cause	Year				Total
	2015	2016	2017	2018	
<b>Acne</b>	-	1	2	2	5
	0.0	1.3%	3%	2.6%	1.9%
<b>Earring</b>	18	14	-	-	32
	36%	18.4%	0.0	0.0	11.9%
<b>Spontaneous</b>	-	-	-	1	1
	0.0	0.0	0.0	1.3%	0.4%
<b>CBW</b>	2	4	-	1	7
	4.0%	5.3%	0.0	1.3%	2.6%
<b>Folliculitis</b>	0	1	1	-	2
	0.0	1.3%	1.5%	0.0	0.7%
<b>Incision</b>	19	37	34	42	132
	38%	48.7%	51.5%	54.5%	49.1%
<b>Bite</b>	2	-	-	-	2
	4%	0.0	0.0	0.0	0.7%
<b>Burn</b>	1	2	-	-	3
	2%	2.6%	0.0	0.0	1.1%
<b>N/D</b>	6	17	27	31	81
	12%	22.4%	40.9%	40.3%	30.1%
<b>Tumor</b>	1	-	2	-	3
	2%	0.0	3%	0.0	1.1%
<b>Wart</b>	1	-	-	-	1
	2%	0.0	0.0	0.0	0.4%
<b>Total</b>	50	76	66	77	269

$P < 0.001$ ; N/D: No Data; CBW: Cut-Bruiise Wound



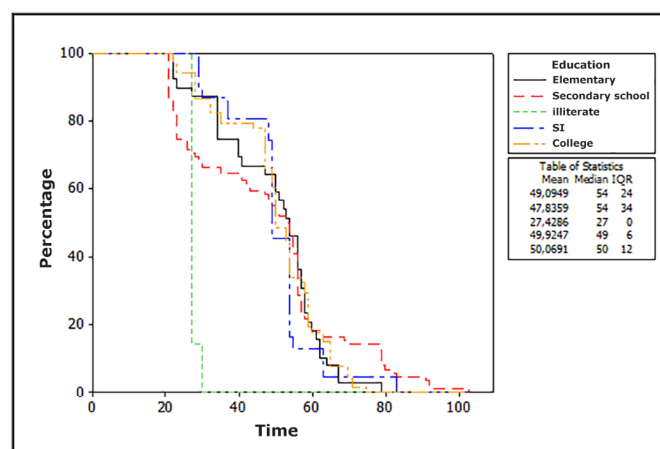
**Figure 2.** Kaplan-Meier estimator for total treatment time by cause and whether or not treatment was completed ( $p < 0.0001$ ).

Time in days; FCC: Cut-Bruiise Wound; SI: no information; Mean; Median; IQR: interquartile range



**Figure 3.** Kaplan-Meier estimator for total treatment time according to location and whether or not treatment was completed ( $p < 0.0001$ ).

Time in days; Mean; Median; IQR: interquartile range



**Figure 4.** Kaplan-Meier estimator for total treatment time according to schooling and whether or not treatment was completed ( $p < 0.0001$ ).

Time in days; SI: no information; Mean; Median; IQR: interquartile range

**Table 4.** Frequency distribution of patients according to location and year.

Location	Year				Total
	2015	2016	2017	2018	
<b>Abdomen</b>	11 22%	14 18.4%	21 31.8%	15 19.5%	61 22.7%
<b>Armpit</b>	- 0.0	- 0.0	- 0.0	2 2.6%	2 0.7%
<b>Hip</b>	- 0.0	- 0.0	- 0.0	2 2.6%	2 0.7%
<b>Arm</b>	- 0.0	5 6.6%	- 0.0	1 1.3%	6 2.2%
<b>Thigh</b>	1 2%	- 0.0	- 0.0	- 0.0	1 0.4%
<b>Back</b>	1 2%	- 0.0	2 3%	2 2.6%	5 1.9%
<b>Sternum</b>	2 4%	1 1.3%	2 3%	1 1.3%	6 2.2%
<b>Face</b>	- 0.0	- 0.0	3 4.5%	- 0.0	3 1.1%
<b>Inguinal</b>	3 6%	- 0.0	- 0.0	- 0.0	3 1.1%
<b>Lip</b>	1 2%	- 0.0	- 0.0	- 0.0	1 0.4%
<b>Lobe</b>	12 24%	- 0.0	- 0.0	- 0.0	12 4.5%
<b>Breast</b>	6 12%	23 30.3%	10 15.2%	25 32.5%	64 23.8%
<b>Hand</b>	- 0.0	1 1.3%	- 0.0	- 0.0	1 0.4%
<b>Shoulder</b>	2 4%	2 2.6%	- 0.0	1 1.3%	5 1.9%
<b>Ear</b>	10 20%	24 31.6%	20 30.3%	22 28.6%	76 28.3%
<b>Leg</b>	- 0.0	1 1.3%	- 0.0	- 0.0	1 0.4%
<b>Neck</b>	1 2%	2 2.6%	3 4.5%	3 3.9%	9 3.3%
<b>Fist</b>	- 0.0	- 0.0	1 1.5%	- 0.0	1 0.4%
<b>Chest</b>	- 0.0	3 3.9%	4 6.1%	3 3.9%	10 3.7%
<b>Total</b>	50	76	66	77	269

P<0.001

**Table 5.** Distribution of frequency of patients according to schooling and year.

Education	Year				Total
	2015	2016	2017	2018	
<b>Elementary 1</b>	1 2%	1 1.3%	3 4.6%	1 1.3%	6 2.2%
<b>Elementary 2</b>	15 30%	11 14.5%	8 12.1%	6 7.8%	40 14.9%
<b>Average</b>	16 32%	34 44.7%	25 37.9%	28 36.4%	103 38.3%
<b>Illiterate</b>	1 2%	- 0.0	2 3%	6 7.8%	9 3.4%
<b>N/D</b>	5 10%	1 1.3%	19 28.8%	7 9.1%	32 11.9%
<b>Higher</b>	12 24%	29 38.2%	9 13.6%	29 37.7%	79 29.4%
<b>Total</b>	50	76	66	77	269

p<0.0001; N/D: No Data

completed less treatment than those with complete elementary and middle classes (p<0.0001).

There was a predominance of women undergoing this treatment, corresponding to 70% of the treated lesions. Furthermore, we observed that women tend to complete more treatment than men (Table 6) in a statistically significant way (p=0.04). This finding is also confirmed when evaluating the number and volume of larger doses in women, with p-values of 0.03 and 0.02. The average age of women was also higher, being 34 years for women and 24 years for men. Using the Kaplan-Meier estimator to assess the relationship between sex and treatment time as factors for completing or not completing radiotherapy sessions, there was no statistically significant difference (Figure 5).

Another interesting assessment was that female patients had a higher mean age than men, with more radiation doses received and, therefore, a greater number of applications, but in a total treatment time similar to that of men (Table 7).

In 43% of the lesions, some previous treatment had already been tried without success; in 41% of the cases, this was impossible to determine. Using the Kaplan-Meier estimator, no statistical difference was observed for completing the radiotherapy scheme in those who had or had not previously undergone other treatments. (Figure 6).

According to the Kaplan-Meier estimator (Figure 7), patients referred by the Dermatology and Head and Neck Surgery specialties tended to complete more treatment than those referred by Plastic Surgery (p=0.002).

**Table 6.** Frequency distribution of patients according to gender and if treatment was completed.

Completed	Sex		Total
	Feminine	Masculine	
No	15	13	28
	7.9%	16.2%	10.4%
Yes	174	67	241
	92.1%	83.8%	89.6%
<b>Total</b>	<b>189</b>	<b>80</b>	<b>269</b>

P=0.04

**Table 7.** Mean, and standard deviation refer to age, dose, number of applications, and treatment time according to gender.

	Sex		P
	Masculine	Feminine	
Age (in years)	24.9	34.2	<0.0001
	10.5	10.7	
Doses	3417.5	3664.0	0.03
	1030.8	759.4	
Number of applications	17.0	18.3	0.02
	5.2	3.9	
Time (in days)	43.6	45.2	0.56
	22.3	18.1	

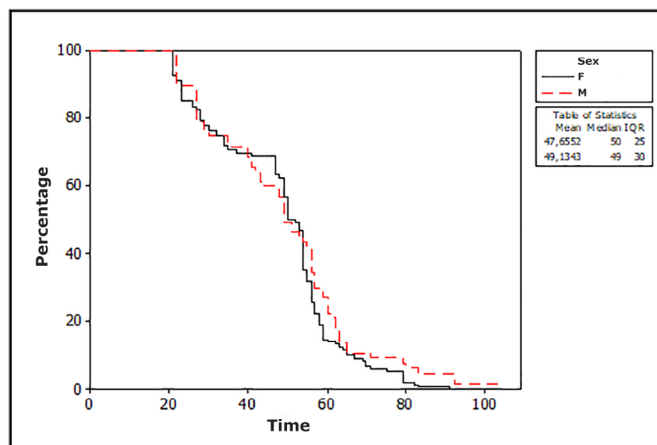
## DISCUSSION

Keloids, being benign alteration, can easily have their treatment neglected for several reasons. Therefore, we consider it essential that the doctor who conducts this type of treatment, in addition to knowing the available techniques, also knows how to identify and guide their patients about the evolution of the treatment and the importance of completing it, especially because it has high rates of relapse when not done properly.

From the analysis of the medical records, we observed some findings that can guide our attention during the consultations to achieve better results for the patients.

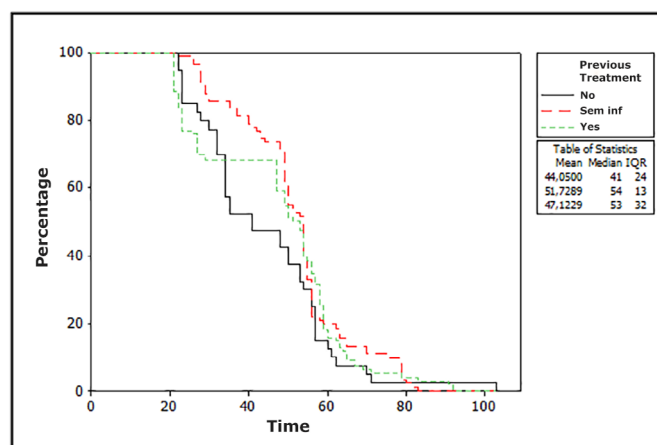
Some studies demonstrate a higher prevalence and incidence of keloids in the black population of African origin<sup>24</sup>; however, in our review, we observed a greater predominance of patients declared to be white. This may be related to the historical and social fact that in Brazil, blacks have their health neglected, not seeking health services to treat benign conditions.

It is also necessary to consider the great miscegenation of the Brazilian population, which means that many declared white patients have African roots. The Botucatu region is predominantly colonized



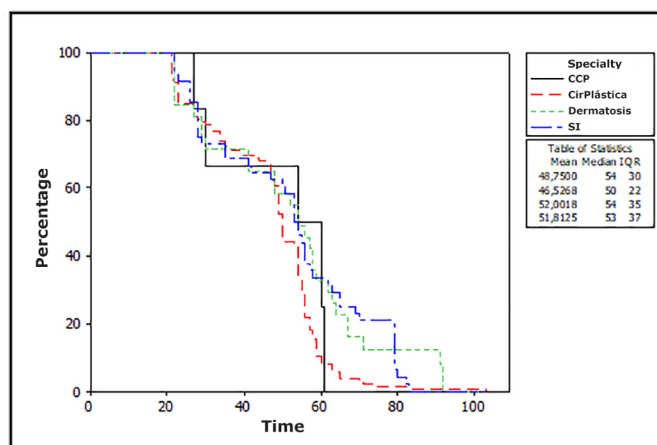
**Figure 5.** Kaplan-Meier estimator for total treatment time according to gender and whether or not treatment was completed (p=0.18).

Time in days; F: female; M: male; Mean; Median; IQR: interquartile range



**Figure 6.** Kaplan-Meier estimator for total treatment time according to previous treatment and whether or not treatment was completed (p=0.34).

Time in days; Sem Inf: no information; Mean; Median; IQR: interquartile range



**Figure 7.** Kaplan-Meier estimator for total treatment time by specialty and whether or not treatment was completed (p=0.002).

Time in days; CCP: Head and Neck Surgery; CirPlástica: Plastic Surgery; SI: no information; Mean; Median; IQR: interquartile range

by Europeans, which may also interfere with these data. Fortunately, the racial factor was not decisive for the patient to complete or not the treatment.

The scar's location suggests that it is related to the formation of keloids since the areas that suffer the most stretching or elongation have a higher frequency of pathological scars<sup>25</sup>. Our study observed their higher prevalence in the ears, breasts, and abdomen. Other body regions, such as the face and scalp, were less frequent or absent. These data are similar to the literature<sup>26</sup>. Furthermore, there was a greater chance of completing the treatment for neck, back and chest injuries than for abdomen and earlobe injuries. Thus, it was unclear whether exposed areas influenced prolonged treatment commitment.

We noted that the causes of keloid formation were predominantly from surgical incisions, with almost half of the cases followed by earrings. Such patients tended to complete less treatment compared to those with keloid scars secondary to acne or of undetermined cause, with statistical significance.

Another interesting fact was that illiterate patients completed less treatment than those with complete primary and secondary education, which indicates an influence of schooling on adherence to complete treatment.

We observed that the average age of the patients was between 24 and 34 years old, characterizing a young and economically active population, that is, people who are inserted in the labor market and will miss many working days of service during treatment, which has an average of 43 to 45 days. This can have a major negative impact on the completion of treatment, favoring relapses over time.

Some studies show a predominance of keloids in women, with a possible relationship with estrogen levels<sup>27</sup>. There are many reports of worsening symptoms during pregnancy, for example. In our analysis, women sought the health service more than men, which justifies their great predominance, more than two-thirds, in the total number of cases; in addition, female patients tended to complete more treatment than males.

Furthermore, women were older on average than men, receiving higher numbers of radiation doses performed in more applications; however, the total treatment time was similar, which may suggest that male patients are attending on dates outside the deadline, lengthening the time, but without completing it properly. These data align with what we know about men seeking fewer health services<sup>28</sup> and being less adherent to the proposed treatments.

When reviewing the medical literature, we observed that there are many ways described for treating keloid scars. Due to the great challenge of the definitive and effective treatment of this pathological scar, new therapeutic modalities and combinations of previous treatments are constantly emerging.

Radiotherapy reduces the action of fibroblasts on keloids in a dose-dependent manner<sup>29</sup>. Currently, after its great evolution in the 20th century, it presents itself in two main forms: internal and external. Brachytherapy is studied as an internal option, while electron beams and X-rays are the most common external application forms. Although some studies indicate the superiority of brachytherapy in preventing keloid recurrence<sup>30</sup>, many meta-analyses have not been able to confirm this in a statistically significant way<sup>13</sup>.

By associating surgical excision with early radiotherapy, superior results were found<sup>11</sup>.

It is important to emphasize that the adverse signs and symptoms of radiotherapy are similar to those of corticoids, involving erythema, desquamation, and depigmentation; however, the complaint of pain is not frequent<sup>19</sup>. In our review, we could not properly identify these complaints due to the descriptions not clearly reporting whether or not there were such complaints.

As a limitation of this study, it was impossible to assess the current rate of HC-FMB recurrence with the proposed therapies and clinically reassess the patients who had their data reviewed in the medical records.

## CONCLUSION

Postoperative radiotherapy on keloids is a treatment enshrined in the medical literature and an important tool for plastic surgeons who manage these pathological scars. Treatment is usually long-term and should be started early after surgery, requiring patient commitment to achieve the best results.

There was a predominance of women and white patients seeking and receiving the complete treatment, while people with low education could not adequately complete the treatment, and may have lower therapeutic success rates.

Therefore, changing the approach to patients with less education and those who are male will help improve adherence and short- and long-term outcomes for these patients.

## COLLABORATIONS

- BFMN** Analysis and/or data interpretation, Conceptualization, Data Curation, Investigation, Project Administration, Visualization, Writing - Original Draft Preparation, Writing - Review & Editing.
- LVM** Data Curation, Realization of operations and/or trials, Writing - Review & Editing.
- BOJ** Conceptualization.
- AAP** Supervision, Validation, Visualization.



## REFERENCES

1. Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. Growth factors and cytokines in wound healing. *Wound Repair Regen.* 2008;16(5):585-601.
2. Wang PH, Huang BS, Horng HC, Yeh CC, Chen YJ. Wound healing. *J Chin Med Assoc.* 2018;81(2):94-101.
3. Gold MH, Berman B, Clementoni MT, Gauglitz GG, Nahai F, Murcia C. Updated international clinical recommendations on scar management: part 1--evaluating the evidence. *Dermatol Surg.* 2014;40(8):817-24.
4. Gold MH, McGuire M, Mustoe TA, Pusic A, Sachdev M, Waibel J, et al; International Advisory Panel on Scar Management. Updated international clinical recommendations on scar management: part 2--algorithms for scar prevention and treatment. *Dermatol Surg.* 2014;40(8):825-31.
5. Addison T. On the Keloid of Alibert, and on True Keloid. *Med Chir Trans.* 1854;37:27-47.
6. Glass DA 2nd. Current Understanding of the Genetic Causes of Keloid Formation. *J Invest Dermatol Symp Proc.* 2017;18(2):S50-3.
7. Wolfram D, Tzankov A, Püzl P, Piza-Katzer H. Hypertrophic scars and keloids--a review of their pathophysiology, risk factors, and therapeutic management. *Dermatol Surg.* 2009;35(2):171-81.
8. Son D, Harijan A. Overview of surgical scar prevention and management. *J Korean Med Sci.* 2014;29(6):751-7.
9. Hochman B, Farkas CB, Isoldi FC, Ferrara SF, Furtado F, Ferreira LM. Distribuição de queloides e cicatriz hipertrófica segundo fototipos de pele de Fitzpatrick. *Rev Bras Cir Plást.* 2012;27(2):185-9.
10. Ogawa R, Okai K, Tokumura F, Mori K, Ohmori Y, Huang C, et al. The relationship between skin stretching/contraction and pathologic scarring: the important role of mechanical forces in keloid generation. *Wound Repair Regen.* 2012;20(2):149-57.
11. Siotos C, Uzosike AC, Hong H, Seal SM, Rosson GD, Cooney CM, et al. Keloid Excision and Adjuvant Treatments: A Network Meta-analysis. *Ann Plast Surg.* 2019;83(2):154-62.
12. Ogawa R. The most current algorithms for the treatment and prevention of hypertrophic scars and keloids. *Plast Reconstr Surg.* 2010;125(2):557-68.
13. van Leeuwen MC, Stokmans SC, Bulstra AE, Meijer OW, Heymans MW, Ket JC, et al. Surgical Excision with Adjuvant Irradiation for Treatment of Keloid Scars: A Systematic Review. *Plast Reconstr Surg Glob Open.* 2015;3(7):e440.
14. Shin JY, Lee JW, Roh SG, Lee NH, Yang KM. A Comparison of the Effectiveness of Triamcinolone and Radiation Therapy for Ear Keloids after Surgical Excision: A Systematic Review and Meta-Analysis. *Plast Reconstr Surg.* 2016;137(6):1718-25.
15. Kim JH, Koo JM, Park TH. Optimizing Radiotherapy for Keloids: A Meta-Analysis Systematic Review Comparing Recurrence Rates Between Different Radiation Modalities. *Ann Plast Surg.* 2018;80(1):91-2.
16. Xu J, Yang E, Yu NZ, Long X. Radiation Therapy in Keloids Treatment: History, Strategy, Effectiveness, and Complication. *Chin Med J (Engl).* 2017;130(14):1715-21.
17. Lee SY, Park J. Postoperative electron beam radiotherapy for keloids: treatment outcome and factors associated with occurrence and recurrence. *Ann Dermatol.* 2015;27(1):53-8.
18. van den Brenk HA, Minty CC. Radiation in the management of keloids and hypertrophic scars. *Br J Surg.* 1960;47:595-605.
19. Ogawa R, Yoshitatsu S, Yoshida K, Miyashita T. Is radiation therapy for keloids acceptable? The risk of radiation-induced carcinogenesis. *Plast Reconstr Surg.* 2009;124(4):1196-201.
20. Nicoletis C, Chassagne D. Interstitial irradiation by iridium 192 in the prevention of recurrence after surgical excision of keloid cicatrices. *Ann Chir Plast.* 1967;12(3):237-42.
21. Oliveira Júnior B, Lastória JC, Pereira HR, Silveira L, Oliveira LVA, Stolf HO. Estudo comparativo entre o tratamento radioterápico com elétrons e betaterapia, após cirurgia de queloides. *Surg Cosmet Dermatol.* 2009;1(2):53-7.
22. Oliveira Júnior B, Schellini SA, Lastória JC, Carvalho LR, Stolf HO, Oliveira ALP. Tratamento de queloides usando radioterapia pós-operatória com elétrons: Estudo comparativo e randomizado com dois esquemas. *Surg Cosmet Dermatol.* 2013;5(1):16-26.
23. Malta M, Cardoso LO, Bastos FI, Magnanini MM, Silva CM. STROBE initiative: guidelines on reporting observational studies. *Rev Saúde Pública.* 2010;44(3):559-65.
24. Kiprono SK, Chaula BM, Masenga JE, Muchunu JW, Mavura DR, Moehrl M. Epidemiology of keloids in normally pigmented Africans and African people with albinism: population-based cross-sectional survey. *Br J Dermatol.* 2015;173(3):852-4.
25. Dohi T, Padmanabhan J, Akaishi S, Than PA, Terashima M, Matsumoto NN, et al. The Interplay of Mechanical Stress, Strain, and Stiffness at the Keloid Periphery Correlates with Increased Caveolin-1/ROCK Signaling and Scar Progression. *Plast Reconstr Surg.* 2019;144(1):58e-67e.
26. Wang JC, Fort CL, Hom DB. Location Propensity for Keloids in the Head and Neck. *Facial Plast Surg Aesthet Med.* 2021;23(1):59-64.
27. Noishiki C, Hayasaka Y, Ogawa R. Sex Differences in Keloidogenesis: An Analysis of 1659 Keloid Patients in Japan. *Dermatol Ther (Heidelb).* 2019;9(4):747-54.
28. Gomes R, Nascimento EF, Araújo FC. Why do men use health services less than women? Explanations by men with low versus higher education. *Cad Saúde Pública.* 2007;23(3):565-74.
29. Ji J, Tian Y, Zhu YQ, Zhang LY, Ji SJ, Huan J, et al. Zhou XZ, Cao JP. Ionizing irradiation inhibits keloid fibroblast cell proliferation and induces premature cellular senescence. *J Dermatol.* 2015;42(1):56-63.
30. Mankowski P, Kanevsky J, Tomlinson J, Dyachenko A, Luc M. Optimizing Radiotherapy for Keloids: A Meta-Analysis Systematic Review Comparing Recurrence Rates Between Different Radiation Modalities. *Ann Plast Surg.* 2017;78(4):403-11.

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