

TREATMENT OF KELOIDS BY HIGH-DOSE-RATE BRACHYTHERAPY: A SEVEN-YEAR STUDY

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Purpose: To analyze the results obtained in a prospective group of patients with keloid scars treated by high-dose-rate (HDR) brachytherapy with or without surgery.

Methods and Materials: One hundred and sixty-nine patients with keloid scars were treated with HDR brachytherapy between December 1991 and December 1998. One hundred and thirty-four patients were females, and 35 were males. The distribution of keloid scars was as follows: face, 77; trunk, 73; and extremities, 19. The mean length was 4.2 cm (range 2–22 cm), and the mean width 1.8 cm (range 1.0–2.8 cm). In 147 patients keloid tissues were removed before HDR brachytherapy treatment, and in 22 HDR brachytherapy was used as definitive treatment. In patients who underwent prior surgery, a flexible plastic tube was put in place during the surgical procedure. Bottoms were used to fix the plastic tubes, and the surgical wound was repaired by absorbable suture. HDR brachytherapy was administered within 30–60 min of surgery. A total dose of 12 Gy (at 1 cm from the center of the catheter) was given in four fractions of 300 cGy in 24 h (at 09.00 am, 15.00 pm, 21.00 pm, and 09.00 am next day). Treatment was optimized using standard geometric optimization. In patients who did not undergo surgery, standard brachytherapy was performed, and plastic tubes were placed through the skin to cover the whole scar. Local anesthesia was used in all procedures. In these patients a total dose of 18 Gy was given in 6 fractions of 300 cGy in one and a half days (at 9.00 am, 3.00 pm, and 9.00 pm; and at 9.00 am, 3.00 pm, and 9.00 pm next day). No further treatment was given to any patient.

Patients were seen in follow-up visits every 3 months during the first year, every 6 months in the second year, and yearly thereafter. No patient was lost to follow-up. Particular attention was paid to keloid recurrence, late skin effects, and cosmetic results.

Results: All patients completed the treatment. After a follow-up of seven years, 8 patients (4.7%) had keloid recurrences. Five of these had undergone prior surgery (local failure rate 3.4%), and 3 had received only HDR brachytherapy (local persistence rate 13.6%). Cosmetic results were considered to be good or excellent in 130/147 patients treated with prior surgery and in 17/22 patients without surgery. Skin pigmentation changes were observed in 10 patients, and telangiectasias in 12 patients. No late effects such as skin atrophy or skin fibrosis were observed during the 7 years of follow-up.

Conclusions: HDR brachytherapy is an effective treatment for keloid scars. It is well tolerated and does not present significant side effects. The brachytherapy results were more successful in patients who underwent previous surgical excision of keloid scar than in patients without surgery. We favor HDR brachytherapy rather than superficial X-rays or low energy electron beams in keloid scars, because HDR provides a better selective deposit of radiation in tissues and a lower degree of normal tissue irradiation. Other advantages of high-dose-rate brachytherapy over low-dose-rate brachytherapy are its low cost, the fact that it can be performed on an outpatient basis, its excellent radiation protection, and the better dose distribution obtained. From the clinical perspective, the technique provides a high local control rate without significant sequelae or complications.
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INTRODUCTION

A keloid scar is an excessive proliferation of connective tissue of the skin that develops as a consequence of an insult to the skin, usually a wound. Clinically, it presents as a reddish tumor that extends beyond a surgical or traumatic scar. The scar does not improve with time and, besides its unattractive visual effect, it causes tingling, burning, and, above all, pruritus, which can lead to substantial functional impediments. The recurrence rate is high—as much as 80% after surgery alone (1).

The low local control rate achieved by surgery has led to the use of adjuvant treatments for keloid scars, with little success. Therapeutic techniques tested include continuous pressure after surgery (1), corticosteroid injections (2), carbon dioxide laser (3), NdYAG laser (4), silicone gel (5), retinoic acid (6), and Silastic sheet coverage (7). None of these methods have demonstrated real ability to prevent keloid recurrence; indeed, recurrence rates are above 50%.

Radiotherapy is the only treatment method that has demonstrated its effectiveness in preventing keloid scars, above all if they have been previously excised. The estimated recurrence rate is around 20% (8–11). Radiotherapy techniques used to date include external radiotherapy with superficial X-rays or electrons (8, 9) and low-dose-rate brachytherapy (10, 11). From a dosimetric (radiobiologic) point of view, brachytherapy involves less irradiation of normal tissue than external beam radiotherapy and so would be the treatment of choice if it provided equally good results. After loading, the radioprotection of the staff exposed is better with high-dose-rate (HDR) remote brachytherapy than with the low-dose-rate manual alternative (12). We therefore designed a pilot study using high-dose-rate brachytherapy to treat patients with keloid scars, comparing the results obtained with those published in the literature and with our previous experience (13).

This paper describes the radiation technique and presents the results obtained in a prospective group of patients with keloid scars treated with high-dose-rate brachytherapy. Tolerance, acute and late complications, and the local control rate were analyzed.

METHODS AND MATERIALS

Inclusion criteria

Diagnosis of keloid scar, caused by surgical procedure or trauma. Patients gave informed consent and agreed to radiation therapy treatment and follow-up.

Exclusion criteria

Pregnant or breastfeeding women were excluded, as were patients whose scars were caused by burns.

Patient characteristics

From December 1991 to December 1998, a total of 169 patients with keloid scars were enrolled in the study. One hundred and thirty-four patients were female (79%), and the

remaining 35 (21%) were male. The mean age of patients was 42 (range 16–78). One patient was Afro-American, and the remaining 168 Caucasian.

The distribution of keloid scars was as follows: face, 77; trunk, 73 (42 thorax, 31 abdomen); and extremities, 19 (12 legs, 7 arms). Before the start of treatment the length and width of the keloids were measured, and patients were asked about their signs and symptoms. Mean length was 4.2 cm (range 2–22 cm) and mean width 1.8 cm (range 1–2.8 cm).

The treatment and the study characteristics were clearly explained to all patients, and the importance of careful follow-up was stressed. Written informed consent was obtained from all patients.

After treatment, all patients were followed up at Day 10, one month later, every 3 months during the first year, every 6 months during the second year, and later on a yearly basis. At each visit the patient was given a date for the next appointment. Patients who missed their visit were contacted by telephone and given a new appointment. Up to the date of evaluation, none of the patients were lost to follow-up.

Treatment

All scars were treated by high-dose-rate brachytherapy after surgical excision of the keloid, except a group of 22 patients who were treated by HDR brachytherapy alone. These patients either refused surgery due to the large size of the keloid (7 patients) or due to multiple recurrences (15 patients).

Local anesthesia was administered in all surgical procedures. A complete, or almost complete, surgical excision of the keloid scar was performed. During the surgical intervention, one flexible 6-french plastic tube was inserted through the center of the wound, covering it fully, for use after loading HDR brachytherapy. The wound was then closed using a 4-0 silk continuous nonreabsorbable suture. In some cases, to avoid lateral movements of the plastic tube, a few additional subcutaneous sutured fixations were made. Bottoms were used to fix the plastic tubes without harming the skin. The length of the brachytherapy implant was the same as the surgical wound, to avoid new skin injuries. Finally, the wound was covered by an adhesive of Steri-strip (3M Health Care).

The protruding ends of the catheter were connected to the transfer tube, which was in turn connected to the afterloader. After the treatment, the source withdrew into the afterloader. HDR brachytherapy was administered within 30–90 min of surgery. Treatment was simulated, and its parameters were calculated. The length of the surgical wound was considered as the target volume. A 5-mm margin was left between the extremes of the source and the skin. The total dose administered was calculated taking as a reference a parallel line to all the active source points at 10 mm from the source axis. The treatment used standard geometric optimization to increase the weight of the dwell times in the edges of applicators.

The group of patients treated with surgical excision of the keloid scars received 4 fractions of 300 cGy within 24 h at

Table 1. Patient distribution according to signs and symptoms at the first visit and at 2 years follow-up

Sign and symptom	Before treatment		2 years after treatment	
	Frequency	%	Frequency	%
Tumor	169	100	8	4.7
Pruritus	147	86	8	4.7
Reddening	145	85	6	3.5
Burning sensation	126	74	0	0
Functional impotence	78	46	0	0
Telangiectasias	0	0	26	15.4

Note: Certain patients presented more than one symptom.

intervals of 4 h each (total dose 1,200 cGy). Treatment began between 30 and 90 min after surgery and was administered usually at 9.00 am, 3.00 pm, 9.00 pm, and 9.00 am the following day. Patients underwent brachytherapy; a total dose of 1,800 cGy in 6 fractions of 300 cGy was given over two days, at 9.00 am, 3.00 pm, and 9.00 pm; and at 9.00 am, 3.00 pm, and 9.00 pm the following day. Before any fractions were given, the distance between fixed bottoms (the total length to be treated) were carefully checked, as well as the relative position of the catheter and full contact between the fixed bottoms with skin. The accepted discrepancy of the initial measurements was ± 1 mm. In cases with higher discrepancies, a new dosimetry was introduced, and new treatment parameters were given.

As soon as the last brachytherapy fraction was administered, the plastic tube was withdrawn, and the wound was covered with a gauze pad, which the patient was instructed to remove two hours later. Ten days after surgery, patients were seen to evaluate the wound and to remove the suture. No other treatment was administered to patients.

Follow-up

In each follow-up, special attention was paid to the presence or absence of keloid recurrence, late effects, and cosmetic results. Recurrence was defined as the presence of a new keloid scar in the same location. To evaluate late skin effects, we considered pigmentation changes (hypo or hyperpigmentation), skin fibrosis, alopecia, telangiectasias, or skin atrophy in the treated area or just around it. Patients were evaluated according to the SOMA-LENT (Somatic Late Effects on Normal Tissues) scale of the EORTC (14). Cosmetic results were evaluated on a scale from 1 (poor) to 3 (excellent).

RESULTS

All patients completed the scheduled treatment. During the 7-year follow-up period (median 37.3 months, range 13–85 months), 8 patients (4.7%) presented with recurrence. Recurrences were seen in 5/147 patients treated with surgery (3.4%) and in 3/22 (13.6%) patients treated exclusively with HDR brachytherapy.



(a)



(b)

Fig. 1. Image of a patient before (a) and after (b) treatment with surgery and high-dose-rate brachytherapy; 4 fractions of 300 cGy were given in 24 h. After 7.5 years of follow-up, an excellent cosmetic result was observed without recurrence of the keloid.

Cosmetic results were considered to be excellent or good in 130/135 patients treated with previous surgical excision and in 17/22 patients without prior surgery.

The initial signs and symptoms, as well as their responses to brachytherapy treatment, are shown in Table 1. Tumor, followed by pruritus and skin reddening, were the most common symptoms observed. All signs and symptoms improved with treatment. Burning sensation and functional impotence completely disappeared. Telangiectasia was observed in 26 cases, 15.4% of patients.

Skin pigmentation changes were observed in 10 patients



(a)



(b)

Fig. 2. Patient previously treated with a mastectomy after a recurrence of a conservatively treated breast cancer, who presented a long presternal keloid scar as a consequence of cardiac surgery for

and classified as Grade 1 or 2. In 12 patients Grade 1 skin telangiectasias were noted. No patient experienced Grade 3 or 4 toxicity or other side effects such as skin atrophy, alopecia, or fibrosis.

Figure 1 shows a patient with a keloid scar before (a) and 2 years after (b) treatment with surgery and brachytherapy. The keloid disappeared completely, and no late effects were observed. Figure 2 shows a case treated exclusively by high-dose-rate brachytherapy, before (a) and after (b) treatment. In this case there was a notable cosmetic improvement, though it was classified as Grade 1 toxicity, as the surgical scar was still visible. Nevertheless, the patient was satisfied with the result and declined further treatment.

DISCUSSION

The value of radiotherapy as a complementary treatment to surgery in keloids was convincingly demonstrated by Borok *et al.* (8). Recurrence was observed in 23.5% of patients with keloids treated by excision, radiotherapy, and steroids (15). Ollstein *et al.* (16) reported a recurrence rate of 21% in a group of 68 keloids treated with excision followed by radiotherapy. Kovalic and Perez (9) found recurrences after a minimum 2-year follow-up in 27% of 113 keloids treated with surgery and radiotherapy. Bertiere *et al.* (17) found a rate of 13% in 46 keloids after surgery followed by low-dose-rate brachytherapy with 192 Iridium, in 10 months of follow-up. Clavere *et al.* (10) found recurrences in 12% of 27 keloids treated with surgery and low dose rate and implant of 192 Iridium. The study with the largest sample was by Escarmant *et al.* (11), who treated 855 keloids with surgical excision followed by immediate interstitial implantation of 192 Iridium, with a recurrence rate of 21%. All these studies offered much better local control rates than did those with other types of techniques, so today surgical excision followed by radiotherapy is considered the treatment of choice for keloid scars.

None of the authors mentioned above reported any significant differences in local control rate between external beam radiotherapy and low-dose-rate brachytherapy. The choice of one technique or the other (external beam radiotherapy or low-dose-rate brachytherapy) should be based on its availability, patient comfort, and cost.

In our series we found local recurrence rates of 3.5% if the keloid was excised before HDR brachytherapy and 13.6% if it was not. This higher local control rate compares favorably with the series mentioned above. The group of

a double mitral and aortic valve prosthesis replacement (a). The patient refused further surgery. She was treated with 6 fractions of 300 cGy high-dose-rate brachytherapy in 36 h. The entire scar could not be implanted due to its geometry. After 5 years of follow-up, despite the substantial decrease in the size of the scar, the cosmetic result was considered to be poor, as signs of the keloid persisted (b). The patient was satisfied with the result and declined further treatment.

excised patients was very selective, most of them coming from plastic surgeons, with a small scar; they could be defined as a favorable group, and therefore it may not be possible to extrapolate their results to other series. However, high-dose-rate brachytherapy proved to be highly effective for prevention of keloid recurrence in patients whose keloids had been excised, and its effectiveness for treating keloids in those patients who refused surgery was acceptable. These data suggest that it is better to excise the keloid scar before offering brachytherapy, even though the technique is still indicated when the patient refuses further surgery or if further surgery is contraindicated.

To our knowledge, this is the first time that results obtained from treating keloids with interstitial high-dose-rate brachytherapy have been reported. Brachytherapy was given in all cases on an outpatient basis. No patients had to be hospitalized. The greatest inconvenience for patients was that they had to come to the radiotherapy department for 4 or 6 fractions of radiotherapy within 24 to 36 h. This situation was not difficult for those who lived in Barcelona, but those who lived elsewhere were obliged to stay in a hotel or at the hospital.

High-dose-rate brachytherapy was very well tolerated. None of the 169 patients treated complained of pain or experienced any unpleasant sensation when the catheter was put in place. It was not necessary to remove the catheter in any patient before the end of treatment.

No patient experienced Grade 3 or 4 toxicity. In the least successful cases, limited areas of telangiectasias were observed, mostly in areas slightly closer to the catheter that received a higher dose of radiation treatment.

High-dose-rate brachytherapy allows both a very accurate dosimetry and geometric treatment optimization for proper treatment of the edges of the surgical wound, increasing the dose with geometrical optimization and avoiding introduction of the plastic tube a few millimeters beyond the wound to include the whole scar in the volume of prescribed therapeutic dose. The techniques present major advantages in terms of excellent cosmetic results, low recurrence rate, low complications, and late effects. In our experience, the use of plastic tubes requires a strict control of quality of the applicator before each fraction. A total of 720 fractions of high-dose-rate brachytherapy were given to these groups of patients (4 fractions to 147 patients and 6 fractions to 22

patients). In 554 fractions (76.9%), a new dosimetry was required, and new treatment parameters had to be calculated. This was accomplished in a few minutes and did not cause inconvenience, but it was nonetheless an added complication. Perhaps the efforts made in the quality assurance program (18) had an important influence on the results (19), forcing us to be more rigorous throughout the treatment.

High-dose-rate brachytherapy involves less normal tissue in the treated volume than external radiotherapy (superficial X-rays and electrons), as dose distribution curves demonstrate. For this reason the probability of late effects, such as fibrosis, skin pigmentation changes, alopecia, or skin atrophy, is very low. In the 7.5 years of follow-up, none of these alterations were observed in our patients.

The cost of any treatment is a question of major concern today. The expense of high-dose-rate brachytherapy for keloids compares favorably with that of external beam radiotherapy either with a superficial X-ray in a specialized unit or with electron beam from a linear accelerator. It also compares favorably with low-dose-rate brachytherapy, precluding the need for 2 to 3 days of hospitalization in a shielded room. If we consider patients' quality of life and the optimal radioprotection offered to the radiation therapy staff, there is no doubt that high-dose-rate brachytherapy is currently the most cost-effective treatment of keloids.

We treat all our keloid patients with high-dose-rate brachytherapy, given its ease of performance, excellent tolerance, good dose distribution, low level of normal tissue irradiation, high local control rates, low level of complication, better quality of life, excellent radioprotection, and low economic cost.

CONCLUSIONS

The results of this study prove the efficacy and efficiency of excision and high-dose-rate brachytherapy in the treatment of keloid scars. The advantages of this method are as follows: It is painless, easy to perform, and economical; it does not require hospitalization or general anesthesia; there are no contraindications; and it offers high local control and only a negligible risk of late sequelae. For all these reasons, high-dose-rate brachytherapy should be considered the treatment of choice for keloid scars and the gold standard against which other possible treatments should be compared.

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