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Technical Note

Postoperative single-dose interstitial high−dose-rate brachytherapy in therapy-resistant keloids

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ABSTRACT

PURPOSE: Patients with keloids complain of the cosmetic aspect, pain, and pruritus. Many different therapies are being used for keloids. The aim of this study was to evaluate the recurrence rate and outcome after resection followed by a single-dose brachytherapy.

METHODS AND MATERIALS: Patients treated by resection of the keloid plus a single dose of 13 Gy high−dose-rate brachytherapy were evaluated at least 1 year after treatment. Clinical response and cosmesis were assessed by a plastic surgeon and by the patients using the Patient and Observer Scar Assessment Scale.

RESULTS: Only 24 of the 61 invited patients responded to participate with the study; 29 keloids were evaluated. The recurrence rate was 24.1% after a median followup of 53 months (19−95 months). Patients scored on average 24.3 for their total Patient and Observer Scar Assessment Scale score (range 6−52), whereas the observer scored on average 14.6 (range 6−42).

CONCLUSIONS: This treatment has a higher recurrence rate than that reported in most other studies. This may be explained by differences in recurrence definition, differences in followup time among studies, and selection bias because of not contributing to the study. The cosmetic outcome for evaluated patients is relatively good. This treatment policy has the advantage that patients are treated in a single day.

Keywords: Keloid; Plastic surgery; Brachytherapy; Recurrence; Cosmetic outcome; Single radiation dose

Introduction

Keloids are benign fibrous dermal tumors characterized by excessive deposition of extracellular matrix due to excessive collagen synthesis and decreased collagen degradation (1, 2). The collagen is broad and irregular and has more capillaries and fibroblasts than usual in a scar of the same age (3). On inspection, keloids can be hard to distinguish from hypertrophic scars (4). By definition, keloids extend outside the initial wound area, have the tendency to recur after excision, and they do not regress without further treatment (3, 5). Patients seek treatment for keloids not only for the poor cosmesis but also for complaints of itching, burning, pain, and tightness, leading to a decreased quality of life (1,5−8). Although the etiology is not fully understood, most theories consider some form of skin trauma a requisite for forming keloids (6). Keloids can form even years after the inciting trauma (6). A maturation block in the healing process of the skin and an overexpression of fibronectin seem to be involved in its pathophysiology (3). Genetic predisposition, ethnicity, skin pigmentation, and age are also risk factors for the development of keloids (6). The incidence of keloids is hard to determine, although it is known that in Black and Hispanic people it lies between 4.5% and 16% with peaks during puberty and pregnancy (4, 7, 9). There also is a higher incidence in people with blood type A (7, 10).

Many therapies have been investigated in the treatment of keloids. Surgery, brachytherapy, external beam radiotherapy, cryotherapy, laser therapy, pressure therapy, 5-fluorouracil injections, bleomycin injections, botulinum toxin A, corticosteroid injections, interferon injections, topical tacrolimus, topical imiquimod, calcium channel blockers,

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retinoids, mitomycin C, and silicone products have all been used to treat keloids (6,11−16). Resection alone results in a 50−80% risk of recurrence (10). Therefore, surgery is usually combined with other treatments, of which a combination with immediate postoperative radiotherapy is considered the most effective treatment for severe therapy-resistant keloids (17). Although this combination has been used for nearly a century, it is not yet clear which radiation scheme yields the best results both to prevent recurrence and to get the best cosmesis (2, 18). The way of applying this radiation, either external beam radiotherapy or brachytherapy (which is perioperatively applied), is also debated (18). Kal *et al.* (18) investigated a possible dose−effect relationship for keloids treated with radiotherapy by calculation of the biologically effective dose assuming a linear-quadratic dose−response model. A biologically effective dose of at least 30 Gy (equal to 25 Gy equivalent dose in 2 Gy fractions) for an α/β ratio of 10 Gy is probably the optimal treatment, which should be administered within 2 days after resection (17). Furthermore, there are several advantages of using high−dose-rate (HDR) brachytherapy compared with external beam radiotherapy, such as more focused radiation delivery with consequently a lower dose to surrounding tissues (1).

Since 2007, patients with therapy-resistant keloids are treated in the Academic Medical Center in Amsterdam (AMC) by adjuvant HDR brachytherapy immediately after excision. The dose prescribed is a single dose of 13 Gy on the skin within 2 hours after resection. Guix *et al.* (13) found in 2001 good results with HDR brachytherapy, and several others have since confirmed this. However, to our best knowledge, no other hospital treats patients with one dose of 13 Gy HDR brachytherapy immediately after surgery. We describe our results in terms of both local control and cosmesis.

Methods and materials

Patients

Sixty-one patients with 72 keloids were treated between 2007 and 2015 at the AMC. All were asked to participate in this study. The median age at treatment was 27 years (15−67 years). There were 29 women and 32 men. Patient's skin type was categorized according to the Fitzpatrick scale (19).

Surgical technique

The keloid was marked preoperatively by the plastic surgeon together with the radiation oncologist to plan the incision, the position of the brachytherapy catheter(s), and how to close the skin. In six cases, keloid excision was performed in hospitals near the AMC.

The lesions were subcutaneously infiltrated with local anesthesia using lidocaine 2% with adrenaline 1:200,000. Excision was performed extralesionally. Hemostasis was achieved with electrocautery. Next, a flexible transparent double-leader catheter (6F) was positioned between the dermal edges of the wound, 5 mm below the surface of the skin and extending out of the skin beyond the wound at both sides. Extension was either through the wound margins or through separate stab wounds. More than one catheter was placed if necessary. Closure was performed in layers, and if necessary, the deep subcuticular sutures using polyglactin 910 were placed under the catheter to maintain the correct distance from the skin.

Postoperatively, the patient was transferred to the department of Radiation Oncology for dose delivery within 2 hours after excision. Sutures, if used, were according to the location removed 7−10 days after surgery.

Brachytherapy

After catheter placement and wound closure, the catheters were fixed with buttons on both sides. In case of a single catheter, the trajectory of the HDR source was just in between the buttons. In case of a volume implant according to the Paris system, the outer source positions were determined by Paris-system dosimetry. In certain cases for which multiple catheters were used, but not fulfilling the Paris-system implantation rules, a CT scan was done for catheter reconstruction and dosimetry on dose points.

For single-catheter implant, dose prescription was usually at 5 mm from the source axis but could vary between 4 and 7 mm according to measured depth of catheter placement. In case of Paris-system implant, dose prescription was according to Paris-system dosimetry for which the skin was encompassed by the reference isodose. In case of irregular multiple catheter implants, prescription was on dose point located on the skin.

The prescribed dose in all cases was 13 Gy as a single dose. Dose delivery was either with a microSelectron PDR or HDR afterloader (ELEKTA-Brachytherapy, Veenendaal, The Netherlands) containing an ^{192}Ir source with an initial activity of 74 or 370 MBq, respectively. Directly after dose delivery, the catheter(s) were removed without anesthesia. Patients were discharged on the same day.

Treatment evaluation

The study was approved by the hospital medical ethical committee (NL55213.018.15). The followup period after treatment was at least 1 year because if in that period no itching or burning sensations are reported, the chance of recurrence is minimal (2). All patients were invited to visit the Plastic and Reconstructive Surgery outpatient clinic. Patients not reacting initially were telephoned to ask them personally to participate in this study. All patients willing to participate in this cross-sectional observational study gave written informed consent. Traveling expenses for the participants were reimbursed by the hospital. Recurrence, as