Adjuvant intensity-modulated radiotherapy improves outcomes for resected complex keloids

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INTRODUCTION

Keloids are cutaneous lesions formed from abnormal wound healing secondary to excessive fibroblast function, resulting in excess tissue proliferation and disorganized collagen. Although benign, keloids may be physically disfiguring, symptomatic, debilitating, and have a significant psychologic impact, especially in the head and neck region.[1] Keloids differ from other scars in their propensity to extend beyond the borders of the initial injury. Although monotherapy, including surgical resection, laser ablation, intralesional injections, and pressure therapy can be effective, many patients experience local recurrence despite these interventions.[2,3]

For multiple recurrent keloids, the combination of resection/ablation and adjuvant radiotherapy (RT) can dramatically reduce recurrence rates from nearly 100% to as low as 15%.[2,4] Large and anatomically complex keloids present a technical challenge, with traditional superficial radiation techniques resulting in unfavorable radiation dose distribution, with resultant undercoverage of the target volume and/or excess dose to adjacent organs at risk.[5,6] For these patients, intensity-modulated radiation therapy (IMRT) can provide homogeneous conformal coverage of the target volume while maximally sparing normal tissue. Here we report our experience with IMRT in the treatment of complex keloids following resection or ablation.

Abbreviations used:

CT:	computed tomography
Gy:	Gray
IMRT:	intensity-modulated radiotherapy
RT:	radiotherapy

CASE REPORT

Four patients underwent treatment with IMRT for complex keloids at a tertiary institution between 2015 and 2021. All patients were African American and presented with large, symptomatic keloids. Keloid characteristics and treatment details are summarized in Table I. All were simulated (radiation planning session) the day of surgery and began adjuvant RT on postoperative day 1. Patients with head and neck keloids were immobilized with an aquaplast mask, and a vacuum-locked bag was utilized for patients with pelvic keloids. The clinical target volume was delineated to encompass the resection bed based on radio-opaque wires placed on the periphery of the resection bed at the time of computed tomography (CT) simulation. A planning target volume margin of 3 to 5 mm was added to the clinical target volume. IMRT prescriptions included 18 Gray (Gy) in 3 fractions (n = 1) and 21 Gy in 3 fractions (n = 3). The absence of recurrence after IMRT was defined as normal appearing skin and/or scarring without ongoing

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Table I. Case details

Case no.	1	2	3	4
Affected site	Head and neck	Head and neck	Suprapubic	Head and neck
Previous treatment	St+S+aRT	S+ILK	St	S+St
Treatment course	C+RT	C+RT	C+RT	C+RT
IMRT technique	Step and Shoot	Step and Shoot	VMAT	VMAT
PTV (cc)	122.7	46.4	183.2	102.9
Dose (Gy)	21	21	18	21
No. of fractions	3	3	3	3
Follow-up (months)	12	59	38	9
Outcome	NR	NR	NR	NR

aRT, Adjuvant radiotherapy; *C*, carbon dioxide (CO_2) laser; *ILK*, intralesional kenalog; *IMRT*, intensity-modulated radiation therapy; *NR*, no recurrence; *PTV*, planning target volume; *RT*, radiotherapy; *S*, surgical excision; *St*, steroids; *VMAT*, volumetric-modulated arc therapy.

keloid appearance or symptoms. This outcome was determined by the physician on physical examination. All toxicities were scored according to Common Terminology Criteria for Adverse Events (CTCAE) V4.0 grading system as determined by the treating radiation oncologist.

Case 1

A 56-year-old woman presented with a history of multiple recurrent keloids of the anterior aspect of the neck and bilateral jawlines. Ten years previously, the patient was treated with surgical resection and 12 Gy in 3 fractions using electron RT. The patient experienced 2 recurrences managed with resection and intralesional kenalog injection on both occasions. At the time of the third recurrence, the patient presented with a 10-cm keloid at the anterior aspect of the neck as well as bilateral 5-cm keloids of the left and right angle of the mandible, each (Fig 1, *A*). The keloids were painful and draining intermittently. The patient underwent CO_2 laser-based resection of all 3 lesions, and this procedure was followed by IMRT. All sites were treated with 21 Gy in 3 fractions using a single isocenter plan (Fig 2). The patient tolerated IMRT well with acute toxicity limited to a grade-1 taste change and dermatitis, which fully resolved within 2 months following IMRT. At 6 years post-IMRT, the patient has a favorable cosmetic outcome with only modest scarring (Fig 1, *B*).

Case 2

A 44-year-old woman presented with an 11-year history of painful and bothersome discontinuous keloids of bilateral jawlines that developed during pregnancy. The largest dimension of the left and right keloid was 7 and 9 cm, respectively. Previous management of the keloids included steroid injection that resulted in an increased size of the keloids and subsequent resection 2 years later. The keloids recurred and were managed with surgical excision followed by electron RT. The keloids recurred 6 months following electron RT with associated pain, swelling, and intermittent drainage. She underwent CO_2 laser resection with subsequent 21 Gy in 3 fractions using IMRT. The patient tolerated IMRT well with acute toxicity limited to grade-1 dermatitis, which fully resolved. As of 12-month follow-up, the patient has remained pain-free without keloid recurrence.

Case 3

A 77-year-old man presented with a complex suprapubic keloid conglomerate following CO_2 laser resection (Fig 3). The suprapubic wound was of variable depth, on a curved surface, and wrapped around the genitalia. IMRT was chosen to achieve comprehensive and homogeneous target coverage, while limiting the dose to the genitalia. The patient was simulated in a frog-leg position with the target wired, and water-filled condoms were placed in the skin folds extending inferiorly around the penis to bolus the skin and stabilize the penis. An additional 1 cm of bolus was applied to the entire area. A volumetric-modulated arc therapy plan was created using 2 anterior half-beam arcs treating the target to 21 Gy in 3 fractions. Figure 4 (*A* and *B*) includes CT simulation images with isodose lines demonstrating complete coverage of the target volume and aggressive sparing of the genitalia. IMRT was well tolerated with no reported toxicity. The patient remains without evidence of recurrence 38 months after IMRT.

Case 4

A 38 year old man presented with an 8-cm keloid on his left jawline. Six years prior to presentation, he underwent partial resection of the keloid followed by steroid injection. The keloid recurred 1 year later, and the patient decided simply to observe. The keloid became increasingly symptomatic, as it grew

Fig 1. A 56-year-old woman with a history of recurrent keloid of the anterior aspect of the neck and both keloids of the jawline**. A,** Pretreatment images of keloids. **B,** Images of the neck and both jawlines 27 months after treatment.

in size. The patient then pursued treatment with CO_2 laser excision followed by 21 Gy in 3 fractions. IMRT was tolerated well with no toxicities reported. Seven months after IMRT, the patient is pain-free with no evidence of keloid recurrence.

DISCUSSION

Keloids, although not malignant, can have a significant negative impact on the quality of life of patients and can be associated with significant psychologic implications. Large, complex keloids are often associated with high recurrence rates and can be challenging to treat. This report presents the treatment of 4 patients with large keloids treated with resection and adjuvant IMRT. IMRT is associated with limited toxicity, and in this limited series, IMRT was effective in preventing recurrence, even after prior electron RT.

RT for keloid prophylaxis after resection or ablation has historically used superficial x rays, surface brachytherapy, and electrons. Each form of RT has unique delivery and dose distribution advantages and disadvantages that impact the ability to treat complex keloids on irregular surfaces near critical organs adequately. Orthovoltage RT has very limited penetration (mm) which would provide inadequate dose coverage for deep keloids.[3] Brachytherapy is relatively inexpensive with short treatment duration; however, interstitial catheter placement in deeper resection cavities requires expertise. Electron RT is widely available across all centers; however, irregular surfaces, often associated with complex keloids, result in heterogeneous dose buildup and penetration that is difficult to account for during planning.[5] In addition, electron RT can be problematic when the target is in close proximity to an organ at risk, as a dose buildup region surrounding the target is required.

IMRT is an advanced form of conformal RT that provides precise target coverage while limiting the dose to organs at risk via nonuniform distribution of radiation beams of varying intensities.[7,8] IMRT can be optimized to provide homogeneous dose distribution to cover the entire target, and dose falloff can also be optimized to avoid nearby organs at risk. IMRT can be particularly useful for complex targets

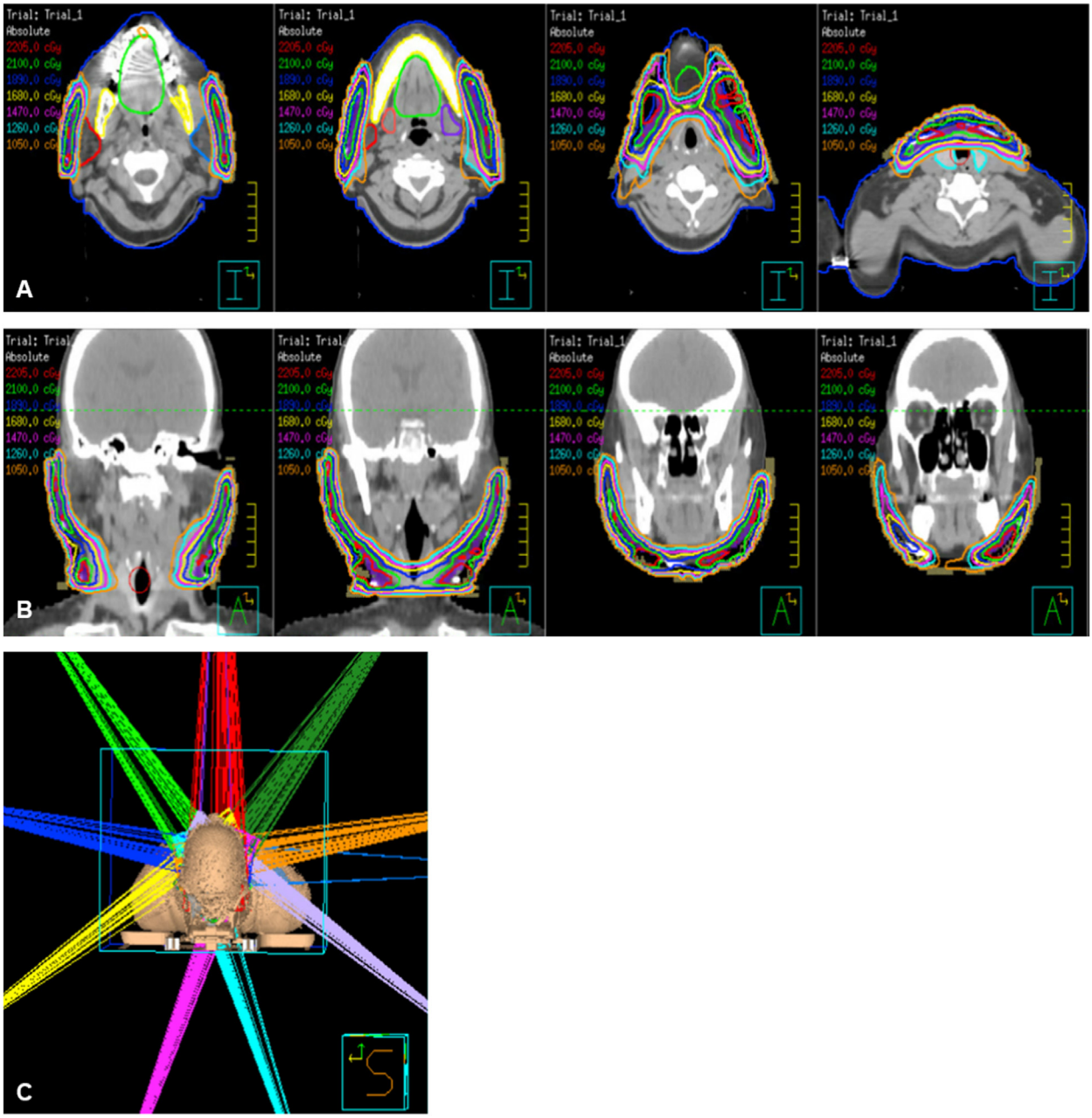

Fig 2. A 56-year-old woman with a history of recurrent keloid of the anterior aspect of the neck and both keloids of the jawline. Axial (**A**) and coronal (**B**) computed tomography images representing an intensity-modulated radiotherapy treatment plan using step-and-shoot to deliver 21 Gray in 3 fractions to the bilateral aspects of the head and neck. A 1-cm bolus was used over the entire treatment area. Excellent sparing of organs at risk is demonstrated, including the salivary glands, mandible, thyroid, oral cavity, and larynx. **C,** Three-dimensional rendition of the step-and-shoot fields delivered.

of irregular shape and surface contour.[9] As seen in the first case presented, IMRT is optimal for cases that involve multiple targets; however, it is limited by the increased planning time and expense as well as increased area receiving a low dose of radiation when compared with the previously discussed superficial techniques.[10] IMRT also requires targets that can be clearly delineated and targeted, which is why we recommend delineation of the target using a superficial radio-opaque marker, so the target can be accurately contoured on the simulation CT.[9]

In this series, we present 4 patients treated with resection or ablation, and postoperative IMRT for large, complex keloids. IMRT resulted in superior

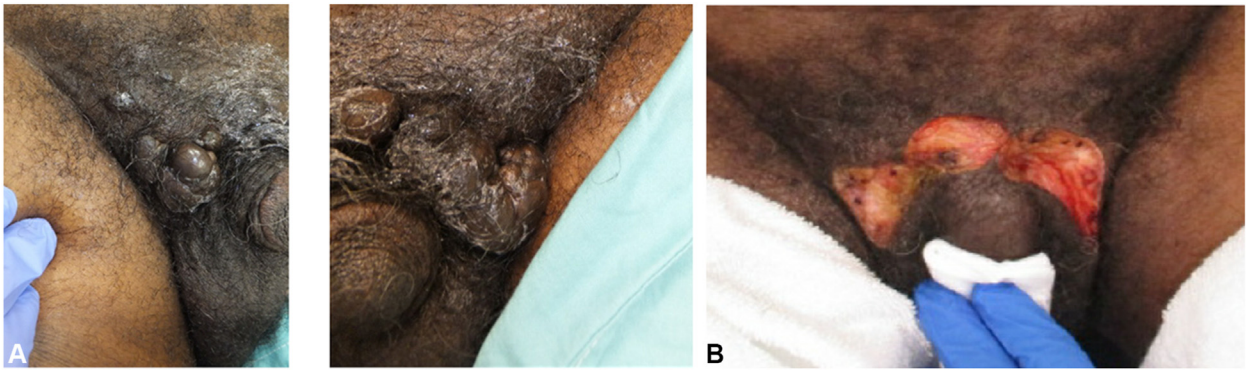

Fig 3. A 77-year-old man with keloid in the suprapubic region. **A,** Pretreatment images of the suprapubic keloids. **B,** Postsurgical image.

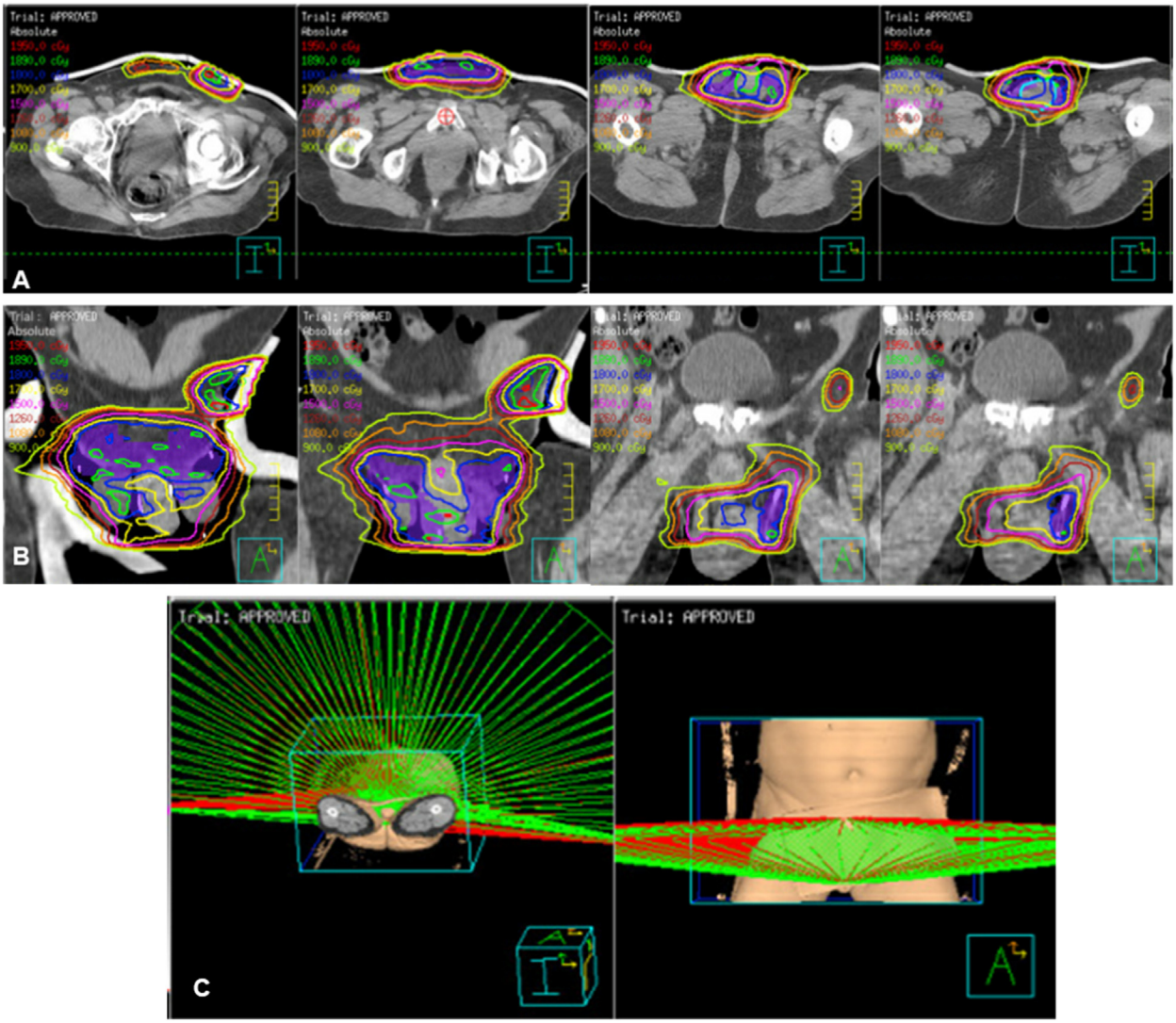

Fig 4. A 77-year-old man with keloid in the suprapubic region. Axial (**A**) and coronal (**B**) computed tomography simulation images representing an intensity-modulated radiotherapy treatment plan using volumetric-modulated arc therapy to deliver 18 Gray in 3 fractions to the suprapubic and both groins with good sparing of the penis, scrotum, and penile bulb.

dose distribution that was not achievable with traditional techniques, such as brachytherapy and electron RT. Although IMRT should not be used for all keloids, it can be particularly useful for large targets with irregular surface contours in close proximity to organs at risk.

Conflicts of interest

Dr Koyfman receives research support from Merck and Bristol-Myers Squibb, consults for Merck and Regeneron, and receives honoraria from Uptodate. Drs Ilori, Campbell, Smile, Keller, Joshi, and Woody have no conflicts of interest to declare.

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