American Journal of Ophthalmology Case Reports 36 (2024) 102157

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Yttrium-90 (^{90}Y) brachytherapy for squamous carcinoma: Treatment of the conjunctiva, cornea, and sclera

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ARTICLE INFO

Keywords:
Yttrium-90
HDR
Brachytherapy
Squamous
Carcinoma
Plaque

ABSTRACT

Purpose: Patients with conjunctival squamous cell carcinoma that present with persisting disease or recurrence following topical chemotherapy and/or surgery especially when invading the sclera are challenging to treat. Herein, we describe the use of high-dose-rate (HDR), FDA-cleared, yttrium-90 (^{90}Y) plaque brachytherapy for such lesions.

Observation: Three cases of invasive conjunctival squamous cell carcinoma that had exhibited a poor response or recurrence following topical chemotherapy and/or surgery are described. As treatment, HDR ^{90}Y beta-radiation was applied to the tumor and margins for a single, continuous duration. In contrast to low-dose-rate (LDR) plaque, HDR ^{90}Y brachytherapy did not require episcleral sutures, amniotic membrane buffering of the cornea, a Gunderson flap, outpatient dwell time, or second surgery. Radiation safety was improved by eliminating LDR-implant related post-operative radiation exposure to health care personnel, the community, family, and pets. Follow-up examination at one month revealed complete tumor resolution in all patients. At last follow-up (8, 11 and 18 months) all patients remained clinically tumor-free as confirmed by slit-lamp biomicroscopy, anterior segment optical coherence tomography, and high-frequency ultrasound imaging. There were no acute complications (e.g., corneal edema, iridocyclitis, scleropathy, keratopathy or cataract).

Conclusion and Importance: ^{90}Y brachytherapy demonstrated efficacy as a single-surgery, minimally invasive, outpatient irradiation for squamous carcinoma of the ocular surface. While short-term results were promising, long-term follow-up monitoring for side-effects and recurrence are essential.

1. Introduction

Squamous carcinoma is the most common malignant ocular surface cancer.[1] Due to high rates of recurrence after primary excision, adjuvant cryotherapy has been used to extend margins.[2–4] Recent publications suggest a shift toward primary topical chemotherapy.[4,5] Though episcleral plaque radiation therapy for conjunctival tumors and benign growths have been described in the late 1940s, it is currently used only for select conjunctival tumors.[6–10]

Two beta-radiation sources, ruthenium-106 (^{106}Ru/^{106}Rh) and strontium-90/yttrium-90 (^{90}Sr/^{90}Y) have been commercially available. But they differ in that the German ^{106}Ru/^{106}Rh plaques are low dose rate (LDR) and thus take days to deliver the prescribed dose. In contrast, the English ^{90}Sr/^{90}Y were high-dose-rate (HDR) applicators.[10] Of these, the HDR ^{90}Sr/^{90}Y device is the most radio-similar to the monoisotopic ^{90}Y disc described in this study. However, it differs in that the English ^{90}Sr/^{90}Y source was permanently embedded at the distal end of a steel shaft. Whereas, the stand-alone LV ^{90}Y Disc ® (Liberty Vision Corporation, Portsmouth, NH, USA) used in this study could be assembled into specialized clinical applicators with unique capabilities for radiation shielding and localization.[10] Another key difference is that the strontium-90 component takes 28.8 years to lose half of its activity, whereas the monoisotopic LV ^{90}Y Disc takes only 64.2-h.[10] This difference simplifies radiation calibration, device maintenance, and disposal safety.

The hand-held anterior segment applicator (iWand A®, Liberty Vision (LV), Portsmouth, NH, USA) allowed the LV ^{90}Y Disc ® to be affixed within a conformal receptacle located on its active surface.[10] The applicator's radiation-absorbant head-module envelopes all but the active surface of the source. Designed for radiation protection, the 2-mm

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https://doi.org/10.1016/j.ajoc.2024.102157
Received 12 January 2024; Received in revised form 23 May 2024; Accepted 29 August 2024
Available online 31 August 2024

plastic wide side walls and 12-mm overlying module thickness absorbs and thus shields beta ^{90}Y radiation emissions in the directions of normal patient tissues, the surgeon, and operating room personnel.[10] Head-module transparency allowed for direct viewing of the ^{90}Y Disc during episcleral application.

Beta radiation has long been used to treat eye cancers, benign tumors, and to inhibit fibrosis.[8–18] Specifically, beta radiation has been used to treat conjunctival cancers such as squamous carcinoma and melanoma as well as benign pterygium and fibrosis associated with trabeculectomy surgery.[10–23] Of those, the most common use of HDR ^{90}Sr/^{90}Y was to prevent pterygium-related episcleral fibrovascular growths, the most mature literature (including prospective randomized studies) describes HDR ^{90}Sr/^{90}Y treatment used to reduce fibrovascularization of trabeculectomy flaps when compared to 5-fluorouracil and mitomycin, as well as for poorer prognosis congenital glaucoma, and darkly pigmented eyes.[17–24]

While in 1980 Tarr and Constable reported scleromalacia after HDR ^{90}Sr/^{90}Y applied to bare sclera (with multiple overlapping spots, and poorly defined dosimetry); in 2023 Murdoch reported the Moorfield HDR ^{90}Sr/^{90}Y applications as both safe and efficacious for trabeculectomy with 20-years follow up.[25,26] Herein, we present a series of three patients with conjunctival squamous cell carcinoma treated with ^{90}Y plaque brachytherapy. The tumor dimensions and radiation parameters are summarized in Table 1.

2. Case presentations

2.1. Case 1

n 80-year-old patient presented with a white temporal epibulbar conjunctival tumor surrounded by intrinsic and recruited tumor blood vessels (Fig. 1A). High-frequency ultrasound imaging (UBM) revealed a dome-shaped epibulbar tumor with hypo-echoic invasion of the underlying sclera. There was no ultrasonographic ciliary body thickening or angle blunting, nor was gonioscopic evidence of intraocular invasion. The tumor was 1.7 mm in thickness and 4.0 × 3.5 mm in basal diameter (Fig. 1B). An exfoliative biopsy revealed dysplastic cells and the tumor was diagnosed as epibulbar conjunctival squamous carcinoma (SCC)[1]

After the tumor did not respond to a 6-week course of topical interferon alpha, followed by 2-weeks of 5-fluorouracil, informed consent led to a discussion of the potential risks and benefits of observation, excision with adjuvant cryotherapy, additional topical chemotherapy, or brachytherapy (e.g., ^{125}I, ^{103}Pd, ^{90}Y). Factoring in the patient's past medical history (i.e., cerebral vascular accident, cardiac pacemaker, coronary artery bypass graft x3, and bilateral renal cell carcinoma), the patient chose single session, minimally invasive, HDR ^{90}Y beta radiation.

Treatment was performed in the operating room (by P.T.F), under conscious sedation, peribulbar anesthesia, and sterile conditions. The ^{90}Y disc was affixed within a hand-held applicator whose translucent plastic head-module shielded the ^{90}Y beta radiation in all directions other than toward the targeted zone. The methods of assembly, calibration, safety testing, and LDR to HDR dose conversion methods have been described.[10] For this patient, ^{90}Y disc activity was 15.31 mCi, which allowed a HDR dose of 22 Gy to a depth of 2.5 mm [≈63.8 Gy LDR equivalent biologic effective dose (BED)].[7] To achieve that dose, the duration of continuous episcleral ^{90}Y application was 5 minutes 56 seconds.

Table 1
Tumor characteristics and radiation parameters.

Patient	*Tumor dimensions in mm(basal dimension x tumor height)*	^{90}Y disc activity (mCi)	*HDR*	*Duration*
1	4.0 × 3.5 x 1.7	15.31	22 Gy	5 min 56 s
2	5.0 × 5.0 x1.5	8.27	25 Gy	5 min 17 s
3	5.0 × 3.0 x 0.8	13.99	30 Gy	2 min 16 s

At day #26 the tumor resolved, leaving only traces of epibulbar pigmentation (Fig. 1C and D). This residual pigmentation was noted to progressively diminish until 18-months follow up, where there was no residual conjunctival pigmentation or evidence of tumor by clinical and/or ultrasonographic examination (Fig. 1E and F). There has been no acute or chronic radiation-associated keratopathy, scleropathy, conjunctivopathy, or sector cataract. The patient's visual acuity has remained stable at 20/32. The pre-treatment central scleral thickness underlying the lesion measured 0.45mm on UBM and the scleral thickness at the last visit measured 0.61mm. We attribute this slight increase in thickness to the scleral remodeling in the area while healing.

2.2. Case 2

A 69-year-old patient presented for management of right conjunctival squamous cell carcinoma. He had previously undergone two cycles of 5-Fluorouracil 1 % eye drops, which led to some reduction in the size of the lesion. The residual conjunctival tumor measured 15 × 15mm. It had feeder vessels, dense keratinization and involved the corneal limbus from 7:00 to 9:00 clock hours (Fig. 2A). UBM revealed a tumor height of 3.6 mm with no scleral invasion (Fig. 2B). Due to the size of the lesion and a partial response to prior treatment, surgical excision with cryotherapy was recommended. However, the surgery was delayed by two months due to changes in the patient's job and insurance. In the interim, the patient received two additional cycles of 5-fluorouracil 1 % (1 week on, 3 weeks off), with no improvement. Ultimately, surgical excision was performed with 4 mm conjunctival margins. However, we noted a small area at 8:00 clock, where the lesion was invading the sclera. Therefore, a lamellar sclerectomy excision was followed by double freeze-thaw cryotherapy to both the conjunctival margins and the scleral base, followed by repair with an amniotic membrane.

Histopathological examination confirmed scleral invasion. Then, 1 month after the surgery, there was a recurrent lesion measuring 6.0 × 5.0mm, and 2mm thick by UBM. Topical mitomycin 0.02 % treatment was initiated while awaiting brachytherapy (1 week on, 1 week off). After two cycles, the tumor size was only reduced to 5.0 × 5.0mm with 1.5mm thickness by UBM. (Fig. 2C). Given these findings, treatment options were discussed including additional topical chemotherapy with mitomycin, brachytherapy (e.g., ^{125}I vs ^{90}Y), external beam radiotherapy (EBRT), or enucleation. In consideration of prior failures of topical chemotherapy and the patient's desire to keep the eye, we recommended plaque brachytherapy. However, due to the extensive prior conjunctival resection, there was a lack of mobile conjunctiva needed to facilitate LDR plaque. In contrast, ^{90}Y brachytherapy offered a single session, relatively non-invasive method to deliver radiation to the recurrence. Treatment was carried out in the operating room by M.A.M as described in Case 1. For this patient, ^{90}Y disc activity was 8.27 mCi, allowing for a HDR dose of 25 Gy to a depth of 1.5 mm [≈72.5 Gy LDR equivalent biologic effective dose (BED)].[7] The duration of episcleral ^{90}Y application was 5 minutes 17 seconds.

One month after the procedure, the lesion had completely resolved. At −11-month follow-up, there has been no evidence of superficial or deep recurrence (Fig. 2D and E). There were no surgical or radiation complications related to application of HDR ^{90}Y treatment. In this case the pre-treatment central scleral thickness underlying the lesion and thickness at the last visit was equivalent at 0.75mm.

2.3. Case 3

A 59-year-old patient presented with pain and redness in the right eye. Prior history included an extensive conjunctival resection for SCC, which involved the lateral canthus, and inferior eyelid 2 years prior. Following that surgery, he was treated with 3 months of adjuvant topical

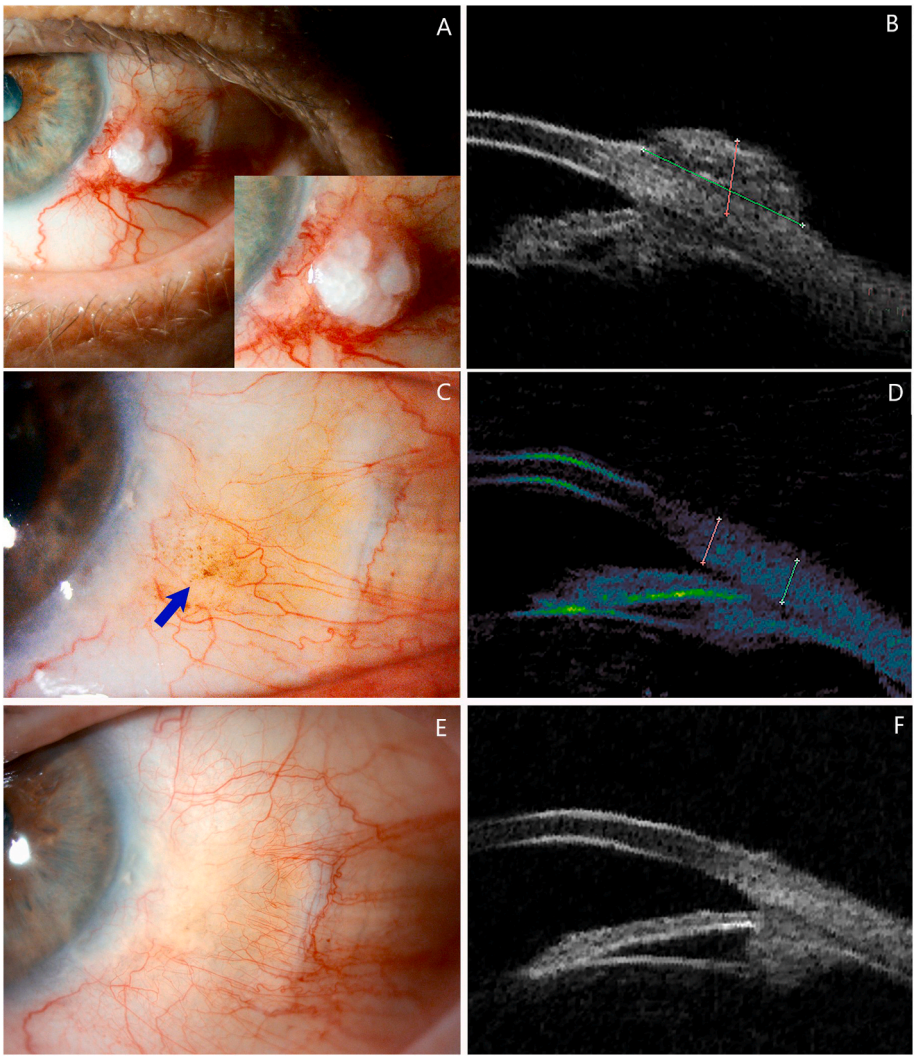

Fig. 1. A, Prior to treatment a slit lamp photograph reveals a nodular malignant ocular surface squamous carcinoma characterized by limbal conjunctival corkscrew-shaped blood vessels, and overlying hyperkeratosis. B, corresponding UBM demonstrates a nodular shape and low reflective microinvasion into the subjacent sclera. C, one-month after Y-90 plaque brachytherapy the tumor and its anomalous blood vessels have resolved, leaving normative appearing conjunctiva with slight hyperpigmentation (blue arrow). D, the one-month UBM shows resolution of the tumor. E, 18 months after Y-90 brachytherapy, a slit lamp photograph reveals resolution of the conjunctival pigment, no keratitis, conjunctivitis, or scleropathy. F, the corresponding UBM shows no evidence intraocular invasion or scleral degeneration. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

interferon alpha2b 1 million IU/ml due to positive margins. He was clinically free of tumor until his last follow-up, 1 year ago.

At presentation, examination of the right eye revealed a best corrected visual acuity of 20/30, and intraocular pressure of 13 mmHg, and a thickened, keratinized conjunctival lesion overlying the inferonasal cornea from the 3:00 to the 5:30 clock hour meridians (Fig. 3A). The tumors dimensions by UBM were 5.0 × 3.0 base x 0.8 mm height. Anterior segment Optical Coherence Tomography (AS OCT) revealed the thickened epithelium with abrupt transition from normal to abnormal epithelium on the cornea. (Fig. 3B).

Symblephara were present affecting both the nasal and lateral bulbar conjunctiva. Similarly, the inferior fornix was shortened. Informed consent involved a detailed discussion of the relative risks and benefits of topical chemotherapy, surgical excision, and brachytherapy. However, given the patient's history of extensive surgery and prior chemotherapy, we recommended HDR ^{90}Y brachytherapy.

The procedure was performed in the operating room by M.A.M in a similar manner as described in patient 1. The ^{90}Y disc activity was 13.99 mCi, allowing for a HDR dose of 30 Gy to a depth of 0.8 mm [≈87 Gy LDR equivalent biologic effective dose (BED)].[7] The duration of episcleral ^{90}Y application was 2 minutes 16 seconds.

At one-month post-radiation, the lesion had completely resolved. At 8 months, there was a complete tumor regression to underlying pannus (Fig. 3C) with corresponding ASOCT showing normal epithelial thickness and hypo-reflectivity (Fig. 3D). There have been no acute radiation complications and patient maintains a best corrected visual acuity of 20/32 in the right eye.

3. Discussion

Beta radiation has been used for over a century as an anti-neovascular and anti-fibrovascular tool in treatment of a variety of ocular tumors (benign and malignant) and growths.[6–24] However, it wasn't until the 1950s that an episcleral strontium-90 (^{90}Sr/^{90}Y) beta applicator became commercially available and thus widely used around the world. The literature contains multiple comparative, statistically significant, and randomized studies demonstrating its efficacy in prevention of pterygium recurrence, treatment of conjunctival and uveal melanoma and to reduce trabeculectomy failure in high-risk eyes (e.g., congenital glaucoma and darkly pigmented eyes).[17–26] In 2023,

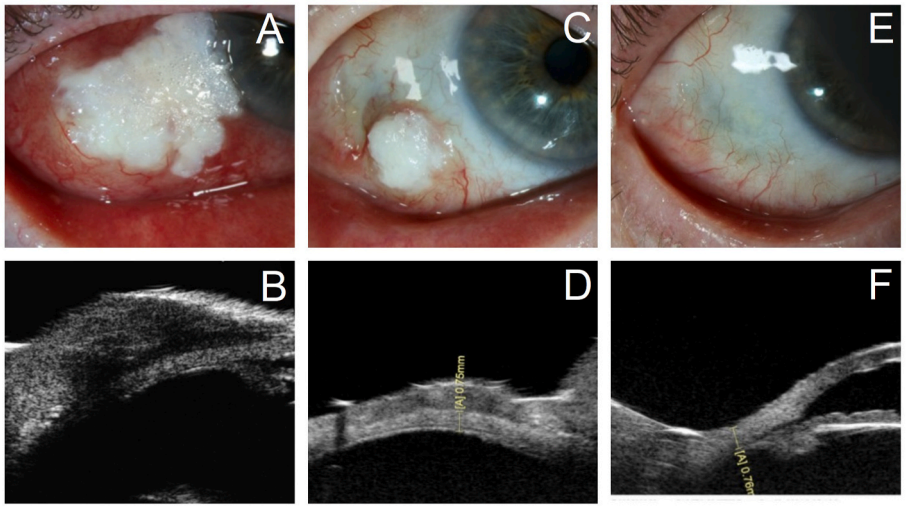

Fig. 2. A, Slit lamp photograph at presentation showing squamous cell carcinoma extending from 7:00 to 9:00 clock hour with dense keratinization. B, corresponding UBM with no evidence of scleral invasion. C, slit lamp photograph showing residual tumor invading the sclera prior to Y-90 treatment. D. corresponding UBM showing residual tumor along with the pre-treatment central scleral thickness underlying the lesion measuring 0.75mm E, slit lamp photograph showing complete tumor resolution at last visit. F, corresponding UBM confirming no superficial or deep recurrence with no evidence of scleral thinning (scleral thickness measures 0.76mm).

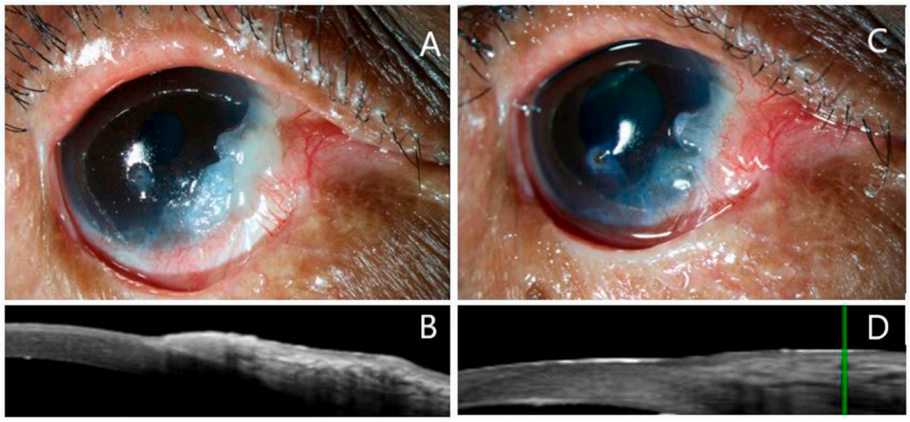

Fig. 3. A, slit lamp photograph at presentation showing squamous cell carcinoma from 3:00 to the 5:30 clock hour meridians over the corneal pannus. B, corresponding AS OCT revealed the thickened epithelium with abrupt transition from normal to abnormal epithelium on the cornea. C, slit lamp photography showing resolution of tumor with visualization of the pannus. D, corresponding ASOCT showing hypo-reflective epithelium with normal thickness.

Murdoch reported on its safety and efficacy for treatment of trabeculectomy after 20-years follow up.[26]

In 1988, Kearsly et al. reported adjunctive use of strontium-90 for conjunctival squamous cell cancer in 123 patients and showed a 97.5 % regression rate.[27] In recent times, Arepalli et al. described their experience in the use of gamma emitting iodine-125 (^{125}I) plaque brachytherapy for the treatment of sclero-invasive conjunctival squamous cell carcinoma.[28] They achieved 100 % local tumor regression in their cohort of 15 patients. Similarly, Rao et al. also achieved a 100 % tumor regression in 42 eyes treated with ^{106}Ru brachytherapy of corneo/sclero-invasive squamous cell carcinoma.[29]

In this study we used a new Food and Drug Administration (FDA) cleared and thus commercially available ^{90}Y beta-radiation disc that has been used to produce HDR ^{90}Y brachytherapy in treatment of 6 patients with iris and iridociliary melanomas with 100 % local regression at a mean 18 months follow up.[30,31] In our study, the same ^{90}Y beta-radiation system was used to treat 3 patients with malignant ocular surface squamous carcinoma that had invaded the sclera and/or cornea.[32] For treatment, the disc source was affixed within an iWand A hand-held applicator, whose function is to shield normal ocular tissues, the surgeon, and health care personnel. The applicators clear head-module provided a view of the disc source as it is placed on the ocular surface. Unlike LDR plaque therapy (e.g., ^{125}I, palladium-103 (^{103}Pd), ^{106}Ru), HDR ^{90}Y allowed for a single, incisionless treatment. For all treatments, the ^{90}Y disc was topically applied and removed in less than 6 minutes.

In contrast to low dose rate plaque therapy, HDR ^{90}Y plaque was a single fraction, outpatient surgery (Table 2). Therefore, it does not require episcleral sutures, amniotic membrane corneal buffering, a Gunderson flap, outpatient dwell time, second removal surgery with anesthesia. Thus, unlike LDR plaque (e.g., ^{125}I, ^{103}PD, ^{106}Ru), HDR ^{90}Y plaque does not require that the patient leave the hospital with a radioactive device sewn to the eye, thereby eliminating post-surgical hospital and community radiation exposure (Table 2). There were no significant surgical or radiation complications in any of the patients.

Risks of episcleral radiation include a small incidence of scleral thinning and cataract. Tarr and Constable noted that late scleropathy with and without secondary infection can occur when anti-vascular and anti-fibrovascular beta radiation was used on bare sclera and with variable dosimetry.[25] However, it is important to note that scleropathy has

Table 2
HDR Versus LDR Brachytherapy for Squamous Carcinoma.

Differences	***HDR***	***LDR***
Available Sources	^{90}Y	^{125}I, ^{103}Pd, ^{106}Ru
Treatment Time	Minutes	Days
Surgical Differences		
Plaque Sutures Needed	None	Yes
Surgery	1	2
Anesthesia(s)	1	2
Overnight Hospitalization	No	Possible
Outpatient Radiation Exposure		
Family / Pet* Exposure	None	^{125}I and ^{103}Pd
Community Exposure	None	Yes
Distancing Required	No	Yes
Environmental Impact		
	Half-life	Increasing Half-life Affects Disposal/Maintenance
^{90}Y	64 hours	
^{103}Pd	16.9 days	
^{125}I	59.5 days	
^{106}Ru	373.6 days	
^{90}Sr	29 years	

HDR = high-dose-rate, LDR = low-dose-rate, ^{90}Y = yttrium-90, ^{125}I = iodine-125.
^{103}Pd = palladium-103.
^{106}Ru = ruthenium-106.
^{90}Sr = strontium-90. Distancing rule = >3 feet away from others required in New York State, USA for.
^{125}I.
^{103}Pd. In patient hospitalization for.
^{106}Ru.
Pet* = Many patients inquire about radiation exposure to their pets.
Distance rule = distance patient required to stay away from others as outpatient.
Community = outpatient community radiation exposure.

also been reported after anti-vascular and anti-fibrovascular mitomycin treatment on bare sclera for pterygium, conjunctival malignancies, and for the cosmetic "brite-eyes" procedure.[33–36] The literature suggests that a variety of episcleral anti-vascular, antifibrotic treatments on bare sclera risk thinning, and poor wound healing.

Unlike the prior dual-isotopic Sr-90/Y-90 sources, the mono-isotopic LV Y-90-disc source used were individually calibrated to deliver a highly conformal dose to a specific intrascleral or intraocular depth. Unlike the prior relatively heavy steel-applicator viewed through a lucite radiation-blocking window, the LV iWand-A applicator light (8 ounce), ergonomic, and translucent allowing for visualization of the tumor target during treatment. These differences enhance both usability and reproducibility of radiation dose delivery.

The device is FDA-cleared and thereby available for clinical use in the United States. Beta-radiation has proved useful in the management of a variety of ocular conditions, such as pterygium, glaucoma (trabeculectomy, blebs), age related macular degeneration (AMD), as well as treatment of malignant tumors (conjunctival SCC and melanoma; uveal melanoma). Clearly, a cost -benefit analysis that includes: differences between health care systems, costs of the devices, number of surgeries required, surgical/radiation side-effects, loss of vision and loss of eye are beyond the scope of this case series. However, our clinical experience suggests this device can prove to be cost-effective at large academic medical centers as well as smaller multi-subspecialty ophthalmology practices.[6–24,37]

Herein, we describe the use of a new ^{90}Y HDR brachytherapy system for 3 patients with invasive epibulbar squamous carcinoma which completely and persistently resolved without significant evidence of intraocular invasion, scleropathy, keratopathy, or cataract. While short term results are excellent, long-term follow-up is required to establish the efficacy and side-effect profile in these cases. This series reveals that single-session HDR ^{90}Y radiation therapy is feasible for conjunctival squamous carcinoma.

Patient consent

The patients consented to publication of the case in writing. This report does not contain any personal information that could lead to the identification of the patient. Therefore, this study conformed to the Declaration of Helsinki and the U.S. Health Insurance Portability and Accountability Act (HIPAA) of 1996. All participants gave informed consent for treatment with HDR ^{90}Y brachytherapy after a discussion of the relative risks and benefits of observation, resection, and all available forms of radiation sources.

Research ethics

We further confirm that any aspects of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Funding

No funding.

CRediT authorship contribution statement

Arpita Maniar: Writing – review & editing, Writing – original draft, Visualization, Resources, Methodology, Data curation. **Junzo Chino:** Writing – review & editing, Validation, Supervision, Resources, Data curation. **Sheridan Meltsner:** Writing – review & editing, Supervision, Resources. **Paul T. Finger:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Formal analysis. **Miguel A. Materin:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

None.

References

1. Conway RM, Graue GF, Pelayes D, et al. In: Amin MB, Edge S, Greene F, et al., eds. *Chapter 65: Conjunctival Carcinoma Ophthalmic Sites: Part XV the AJCC Cancer Staging Manual*. 8h Ed. New York: Springer; 2017:787–794.
2. Finger PT. "Finger-tip" cryotherapy probes: treatment of squamous and melanocytic conjunctival neoplasia. *Br J Ophthalmol*. 2005;89:942–949.
3. Yousef YA, Finger PT. Squamous carcinoma and dysplasia of the conjunctiva and cornea: an analysis of 101 cases. *Ophthalmology*. 2012 Feb;119(2):233–240.
4. Chaugule SS, Park J, Finger PT. Topical chemotherapy for giant ocular surface squamous neoplasia of the conjunctiva and cornea: is surgery necessary? *Indian J Ophthalmol*. 2018;66(1):55–60.
5. Monroy D, Serrano A, Galor A, Karp CL. Medical treatment for ocular surface squamous neoplasia. *Eye (Lond)*. 2023 Apr;37(5):885–893. https://doi.org/10.1038/s41433-023-02434-x. Epub 2023 Feb 8. PMID: 36754986; PMCID: PMC10050251.
6. Iliff CE. Beta ray radium applicator for ocular use; preliminary report. *Arch Ophthalmol*. 1947 Dec;38(6):827–830. https://doi.org/10.1001/archopht.1947.00900010850008. PMID: 18919410.
7. Hughes Jr WF. Reevaluation of beta radiation therapy in ophthalmology: preliminary results with the Sr-90 applicator. *Arch Ophthalmol*. 1953 Aug;50(2):261–264. PMID: 13064906.
8. Lommatzsch PK. beta-Ray treatment of malignant epibulbar melanoma. *Albrecht Von Graefes Arch Klin Exp Ophthalmol*. 1978 Dec 15;209(2):111–124. https://doi.org/10.1007/BF00407844. PMID: 311166.
9. Cohen VM, Papastefanou VP, Liu S, Stoker I, Hungerford JL. The use of strontium-90 Beta radiotherapy as adjuvant treatment for conjunctival melanoma. *JAMA Oncol*. 2013;2013, 349162. https://doi.org/10.1155/2013/349162. Epub 2013 Jan 31. PMID: 23431299; PMCID: PMC3572694.
10. Finger PT, Stewart R, Rivard MJ, et al. First clinical implementation of yttrium-90 disc brachytherapy after FDA clearance. *Brachytherapy*. 2023 May-Jun;22(3):416–427. https://doi.org/10.1016/j.brachy.2023.02.004. Epub 2023 Mar 21. PMID: 36948988.
11. van Ginderdeuren R, van Limbergen E, Spileers W. 18-years' experience with high dose rate strontium-90 brachytherapy of small to medium sized posterior uveal melanoma. *Br J Ophthalmol*. 2005;89(10):1306–1310. https://doi.org/10.1136/bjo.2005.068460.
12. Missotten L, Dirven W, Van der Schueren A, Leys A, De Meester G, Van Limbergen E. Results of treatment of choroidal malignant melanoma with high-dose-rate strontium-90 brachytherapy. A retrospective study of 46 patients treated between 1983 and 1995. *Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol*. 1998;236(3):164–173. https://doi.org/10.1007/s004170050059.
13. Cohen VML, Papastefanou VP, Liu S, Stoker I, Hungerford JL. The use of strontium-90 Beta radiotherapy as adjuvant treatment for conjunctival melanoma. *JAMA Oncol*. 2013;2013, 349162. https://doi.org/10.1155/2013/349162.
14. Cerezo L, Otero J, Aragón G, et al. Conjunctival intraepithelial and invasive squamous cell carcinomas treated with strontium-90. *Radiother Oncol J Eur Soc Ther Radiol Oncol*. 1990;17(3):191–197. https://doi.org/10.1016/0167-8140(90)90203-9.
15. Elkon D, Constable WC. The use of strontium-90 in the treatment of carcinoma in situ of the conjunctiva. *Am J Ophthalmol*. 1979;87(1):84–86. https://doi.org/10.1016/0002-9394(79)90196-x.
16. Lecuona K, Stannard C, Hart G, et al. The treatment of carcinoma in situ and squamous cell carcinoma of the conjunctiva with fractionated strontium-90 radiation in a population with a high prevalence of HIV. *Br J Ophthalmol*. 2015 Sep;99(9):1158–1161. https://doi.org/10.1136/bjophthalmol-2014-306327. Epub 2015 Mar 17. PMID: 25784215.
17. Viani GA, Stefano EJ, De Fendi LI, Fonseca EC. Long-term results and prognostic factors of fractionated strontium-90 eye applicator for pterygium. *Int J Radiat Oncol Biol Phys*. 2008;72(4):1174–1179. https://doi.org/10.1016/j.ijrobp.2008.02.075.
18. Yamada T, Mochizuki H, Ue T, Kiuchi Y, Takahashi Y, Oinaka M. Comparative study of different β-radiation doses for preventing pterygium recurrence. *Int J Radiat Oncol Biol Phys*. 2011;81(5):1394–1398. https://doi.org/10.1016/j.ijrobp.2010.07.1983.
19. Dhalla K, Cousens S, Bowman R, Wood M, Murdoch I. Is beta radiation better than 5 flurouracil as an adjunct for trabeculectomy surgery when combined with cataract surgery? A Randomised Controlled Trial. *PLoS One*. 2016;11(9), e0161674. https://doi.org/10.1371/journal.pone.0161674.
20. Kirwan JF, Rennie C, Evans JR. Beta radiation for glaucoma surgery. *Cochrane Database Syst Rev*. 2012;(6):CD003433. https://doi.org/10.1002/14651858.CD003433.pub3.
21. Miller MH, Rice NS. Trabeculectomy combined with beta irradiation for congenital glaucoma. *Br J Ophthalmol*. 1991;75(10):584–590. https://doi.org/10.1136/bjo.75.10.584.
22. Kirwan JF, Cousens S, Venter L, et al. Effect of beta radiation on success of glaucoma drainage surgery in South Africa: randomised controlled trial. *BMJ*. 2006;333(7575):942. https://doi.org/10.1136/bmj.38971.395301.7C.
23. de Fendi LI, Arruda GV, Costa VP, Paula JS. Meta-analysis of beta radiation augmentation for trabeculectomy - results in distinct ethnic groups. *Arq Bras Oftalmol*. 2011;74(4):300–305. https://doi.org/10.1590/s0004-27492011000400016.
24. Cook C, Perrott A, Mustak H, Courtright P, Wetter J, du Toit N. Randomised clinical trial of trabeculectomy with mitomycin-C versus trabeculectomy with beta radiation. *South African Ophthalmology Journal*. 2018-12-01;13(4):11–14. https://doi.org/10.10520/EJC-136ba7e6dd.
25. Tarr KH, Constable IJ. Late complications of pterygium treatment. *Br J Ophthalmol*. 1980 Jul;64(7):496–505. https://doi.org/10.1136/bjo.64.7.496. PMID: 6968590; PMCID: PMC1043747.
26. Murdoch I, Puertas R, Hamedani M, Khaw PT. Long-term safety and outcomes of β-radiation for trabeculectomy. *J Glaucoma*. 2023;32(3):171–177. https://doi.org/10.1097/IJG.0000000000002144. Epub 2022 Oct 31. PMID: 36375094.
27. Kearsley JH, Fitchew RS, Taylor RG. Adjunctive radiotherapy with strontium-90 in the treatment of conjunctival squamous cell carcinoma. *Int J Radiat Oncol Biol Phys*. 1988 Mar;14(3):435–443. https://doi.org/10.1016/0360-3016(88)90257-x. PMID: 3343150.
28. Arepalli S, Kaliki S, Shields CL, Emrich J, Komarnicky L, Shields JA. Plaque radiotherapy in the management of scleral-invasive conjunctival squamous cell carcinoma: an analysis of 15 eyes. *JAMA Ophthalmol*. 2014 Jun;132(6):691–696. https://doi.org/10.1001/jamaophthalmol.2014.86. PMID: 24557333.
29. Rao R, Honavar SG, Lahane S, Mulay K, Reddy VP. Histopathology-guided management of ocular surface squamous neoplasia with corneal stromal or scleral invasion using ruthenium-106 plaque brachytherapy. *Br J Ophthalmol*. 2023 May;107(5):621–626. https://doi.org/10.1136/bjophthalmol-2021-319201. Epub 2021 Nov 29. PMID: 34844918.
30. FDA. FDA Clearance Statement. https://www.accessdata.fda.gov/cdrh_docs/pdf19/K193602.pdf Accessed date June 26th, 2023.
31. Finger PT. High dose rate yttrium (90Y) episcleral plaque brachytherapy for Iris and iridociliary melanoma. *Ophthalmology Science*. 2024, 100513. https://doi.org/10.1016/j.xops.2024.100513. ISSN 2666-9145.
32. Finger PT, Tran HV, Turbin RE, et al. High frequency ultrasonographic evaluation of conjunctival intraepithelial neoplasia and squamous cell carcinoma. *Arch Ophthalmol*. 2003;121(2):168–172. https://doi.org/10.1001/archopht.121.2.168.
33. Finger PT, Reddy HS, Maheshwari A. Tarsoconjunctival flap for scleromalacia related to treatments for conjunctival melanoma. *Am J Ophthalmol Case Rep*. 2023 Jan 18;29, 101805. https://doi.org/10.1016/j.ajoc.2023.101805. PMID: 36714017; PMCID: Akova YA.
34. Koç F, Yalvaç I, Duman S. Scleromalacia following trabeculectomy with intraoperative mitomycin C. *Eur J Ophthalmol*. 1999 Jan-Mar;9(1):63–65. https://doi.org/10.1177/112067219900900110. PMID: 10230595.
35. Kwon HJ, Nam SM, Lee SY, Ahn JM, Seo KY. Conjunctival flap surgery for calcified scleromalacia after cosmetic conjunctivectomy. *Cornea*. 2013 Jun;32(6):821–825. https://doi.org/10.1097/ICO.0b013e318277ac92. PMID: 23263220.
36. Moshirfar M, McCaughey MV, Fenzl CR, Santiago-Caban L, Kramer GD, Mamalis N. Delayed manifestation of bilateral scleral thinning after I-BRITE (®) procedure and review of literature for cosmetic eye-whitening procedures. *Clin Ophthalmol*. 2015 Mar 4;9:445–451. https://doi.org/10.2147/OPTH.S78390. Erratum in: Clin Ophthalmol. 2016;10:187. PMID: 25784790; PMCID: PMC4356697.
37. Avila MP, Farah ME, Santos A, et al. Three-year safety and visual acuity results of epimacular 90 strontium/90 yttrium brachytherapy with bevacizumab for the treatment of subfoveal choroidal neovascularization secondary to age-related macular degeneration. *Retina*. 2012 Jan;32(1):10–18. https://doi.org/10.1097/IAE.0b013e31822528fc. PMID: 21817963.