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Annulus-shaped I-125 plaque brachytherapy for conjunctival melanoma

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ABSTRACT

Purpose: To report successful ring-shaped iodine-125 plaque brachytherapy for conjunctival melanoma.
Observations: Eye Physics (EP) plaque brachytherapy, designed with Plaque Simulator software, proved to be an effective treatment modality with some corneal irritation and no recurrence at 12-months post radiation.
Conclusion and importance: Management of conjunctival melanoma is complicated by the lack of gold standard adjuvant treatments. I-125 EP plaque brachytherapy represents a viable option for these malignancies. Specifically, ring-shaped plaque geometries allow for targeted radiotherapy.

1. Introduction

Conjunctival melanomas (CM) typically present with a brownish elevated mass on the bulbar conjunctiva.[1] CM is rare with an estimated incidence between 0.2 and 0.4 cases per million, though incidence may be increasing.[2] Older, Caucasian men are likely at higher risk for CM.[3,4] Series of CM demonstrate likely metastasis in 26% of patients and melanoma-related mortality of 13%[1] with concerning reports of distant metastasis without prior or concurrent lymph node disease.[5]

Conjunctival melanomas have been treated with a "no-touch" microsurgical excisional biopsy combined with cryotherapy and alcohol corneal epitheliectomy for corneal involvement.[1] Importantly, the rarity of CM and lack of consensus evidence for adjuvant treatment efficacy and side effect profile complicates management, and less aggressive treatment of CM may promote recurrence and poor outcomes.[6] In addition, multifocal disease has been associated with a fivefold increase in mortality.[7] These nuances warrant exploration of the specific method and construct for adjuvant radiotherapy.

Adjuvant treatment with radiotherapy for CM was described over one century ago, with common delivery methods of strontium applicator, ruthenium, iodine plaque, or external-beam.[8] Strontium-90 applicators allow local treatment and can minimize side effects,[8] though custom-made I-125 plaques are preferable for malignancies that penetrate the sclera.[9]

In addition to radiation source, there are significant geometric modeling differences for brachytherapy approaches in a curved line, ring, disk, sphere, dome, or annulus constructs.[10] Moreover, the arrangement of radionuclide seeds can create significant dose distribution heterogeneity for ocular melanoma plaques,[11] and, the specific carrier and insertion of radioactive seeds can create dosimetric uncertainty.[12] Unlike iris and ciliary body melanoma which may require plaque therapy on the overlying cornea,[13] plaque brachytherapy for CM can be targeted to avoid unnecessary complications from extraneous radiation. Therefore, intra-plaque ring radionuclide seed strength and arrangements should be carefully selected to avoid complications from uniformly-loaded I-125 plaques.[14]

Custom I-125 plaques in round, curvilinear, and donut shapes have been well described for nonresectable malignant iris tumors.[15,16] Moreover, annular modified Collaborative Ocular Melanoma Study (COMS) plaques are used at the Mayo Clinic, with 180, 270, and 360° plaque constructs with collimating lips to treat anterior tumors and prevent radiation injury to the cornea or non-involved portion of the globe.[17]

In terms of CM, iodine-125 plaque brachytherapy has been used in standard circular plaques centered on the tumor. Circular I-125 plaques (ROPES Ltd., Sydney, NSW, Australia) were effectively used as an adjuvant to tractional microdissection with minimal but important anterior segment side effects such as corneal ulceration, limbal stem cell failure, and reduced corneal vascularization.[18,19] Unshielded custom I-125 were fit to a silica mold to treat invasive conjunctival melanoma.[20] Although adjunctive brachytherapy with I-125 has been used widely for conjunctival melanoma,[21] the specific plaque construct details are not always well described in the literature. Therefore, the authors sought to describe a unique case of CM with multifocal lesions, on the bulbar and

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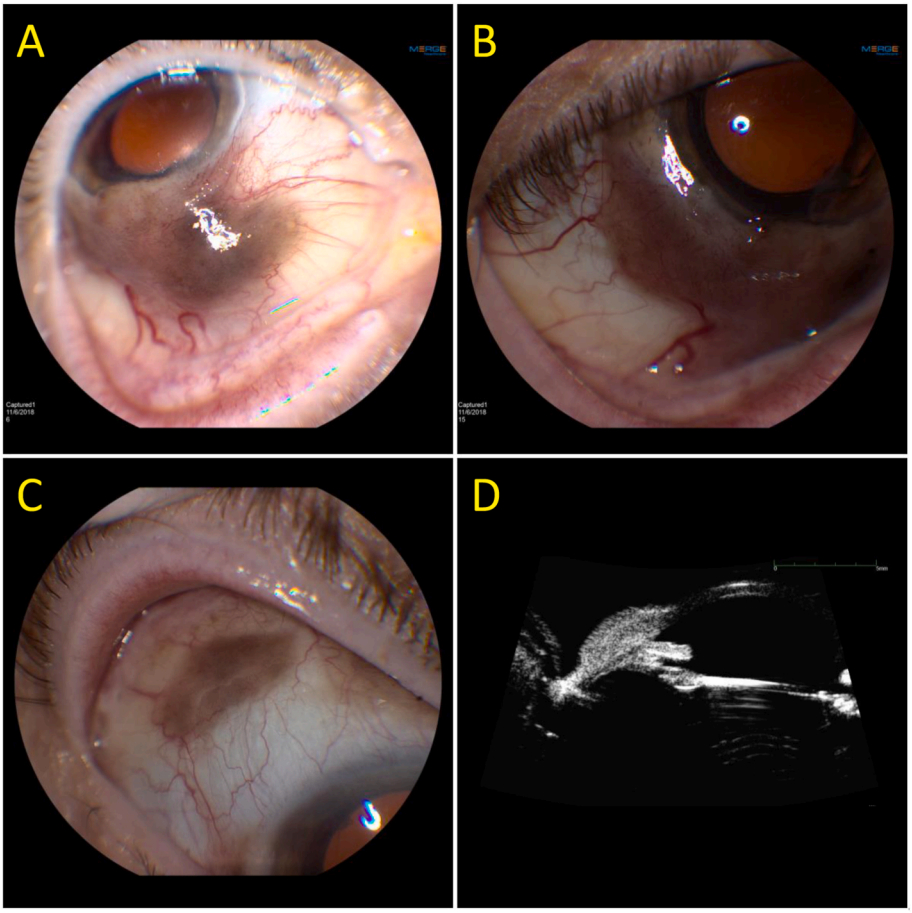

Fig. 1. Compilation of pre-operative clinical images A-B) Diffuse primary acquired melanosis from 4 o'clock to 11 o'clock with a 20 × 10 mm circumferential patch around the limbus. C) Large satellite conjunctival mass on superotemporal conjunctiva. D) Anterior B-Scan showing 2.1 mm echogenic mass with extension onto the cornea and sclera. Note the absence of extension into the globe.

deep forniceal conjunctiva, treated with novel annular I-125 plaque ring brachytherapy.

2. Case report

An 84-year-old, Caucasian female with history significant for diabetes, coronary artery disease, chronic kidney disease, and anemia, presented with a three-year history of a small discolored lesion on her right eye. Best-correct distance visual acuity was 20/40 -2. The anterior segment exam of the right eye showed a pigmented mass arising from multiple areas of primary acquired melanosis. The mass involved most of the bulbar conjunctiva and extended circumferentially around the

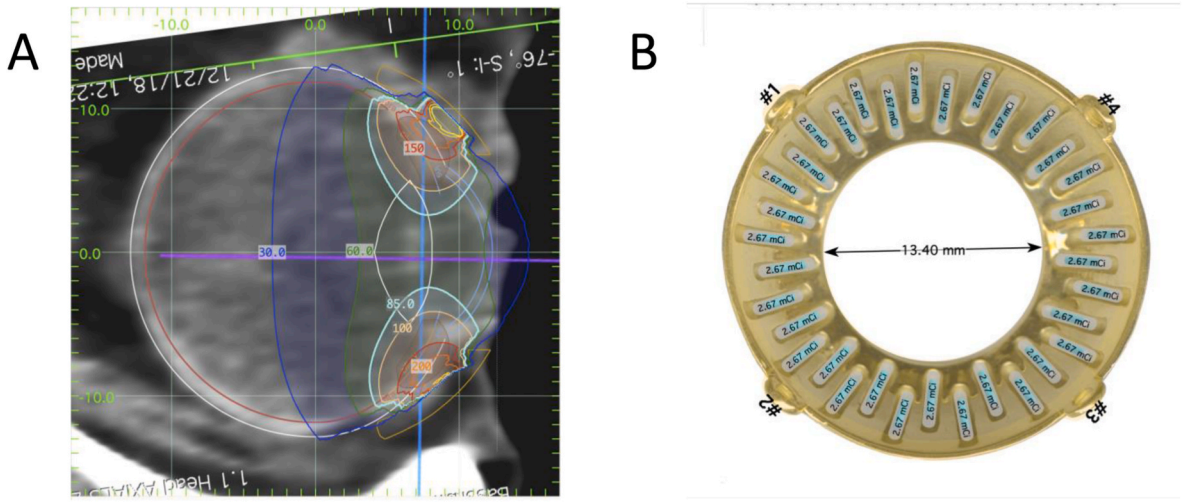

Fig. 2. Plaque Simulator Treatment Schematic A) Plaque simulator diagram showing anatomically correlated isodose curves B) Plaque ring model with 34 radially oriented, 2.67 mCi I-125 sources.

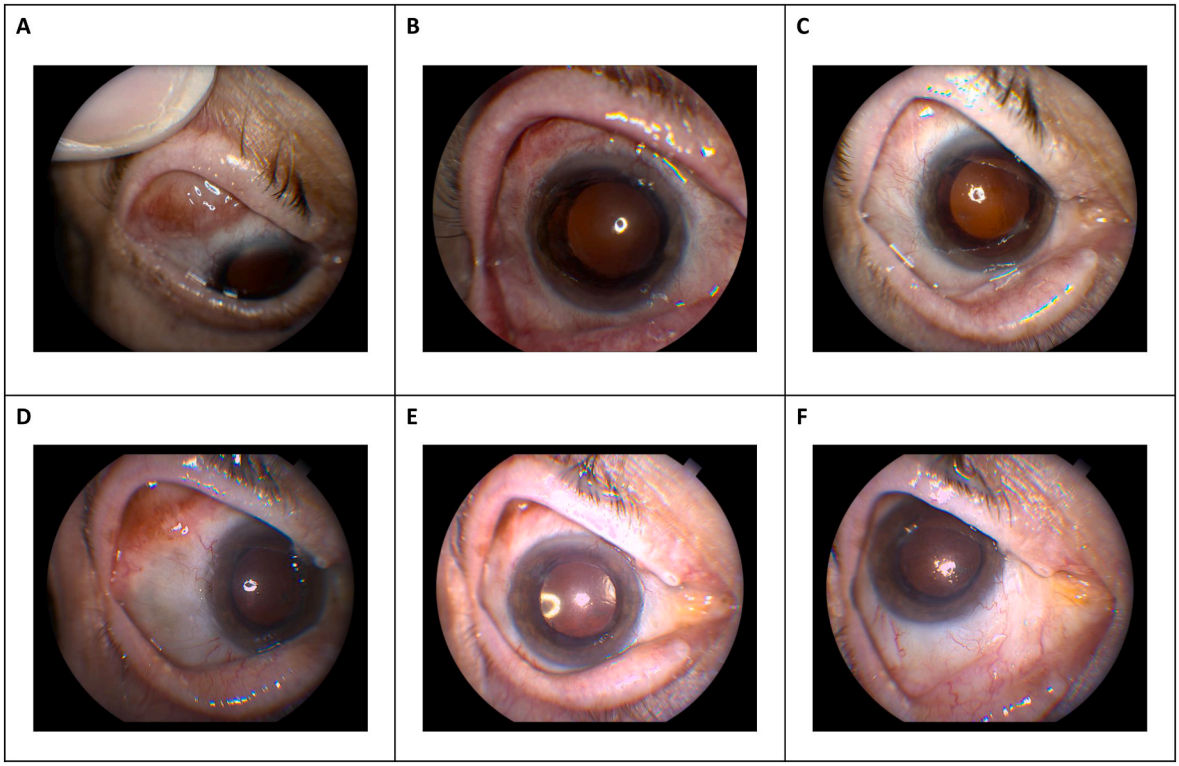

Fig. 3. Post operative anterior segment A-C) 6 months after plaque removal and D-F) 18 months after plaque removal.

limbus onto the cornea (Fig. 1A–C). An anterior B-Scan was performed showing a 2.1mm mass extending onto the cornea (Fig. 1D). CT of the orbits with contrast showed no intraorbital mass or pathologic enhancement.

Due to the size and extent of the lesion, operative resection of melanoma was performed by a partial lamellar scleroconjunctivectomy with supplemental double freeze-thaw cryotherapy and localized alcohol epitheliectomy, as previously described.[22] The corneal portion of the melanoma was removed with superficial keratectomy from 3 o'clock to 9 o'clock, and conjunctival portion was excised down to bare sclera. The tumor had invaded the episcleral and sclera, therefore complete resection was impossible. The episcleral underlying the excision was scraped with a 57 blade to remove as many melanoma cells as possible. Orbital biopsies were sent to evaluate for deep orbital spread of tumor, and the conjunctival edge was treated with cryotherapy. The conjunctiva was then reapproximated to the surgical limbus and closed with 7–0 Vicryl suture due to the large excision required. This constituted the conjunctivoplasty portion of the procedure. The biopsies were consistent with in-situ and invasive melanoma, with immunohistochemical stains positive for SOX10 and MelanA. To avoid exenteration the patient elected for I-125 plaque brachytherapy.

Three months after resection, I-125 plaque brachytherapy was used to treat the bulbar and deep forniceal conjunctival melanoma. A custom designed, annular Eye Physics plaque (EP donut) was designed using Plaque Simulator software with a diameter of 26.03 mm, with 34 I-125 sources, radially oriented, each with an average strength of 3.391U, designed to treat the entire conjunctival area over three days. The plaque had a scleral offset of 0.10 mm, with an apex of −2.50 mm, and radial and circumferential length of 6.03 mm by 8.69 mm, respectively. The prescription was 85.00 Gy, with an average dose rate of 118.1 cGy/hr to coordinates 5.35, −4.55, 0.00. The isodose curves provided diffuse, circumferential radiation with attenuation in the posterior segment (Fig. 2). Four conjunctival incisions were made deep in the fornix, and the underlying tenons was used to anchor the plaque posteriorly with interrupted suture. (An additional conjunctival biopsy was taken at the time of the plaque placement surgery.) The tarsal plate was sufficiently flexible to allow the plaque to cover the entire bulbar conjunctiva as well as the much of the deep forniceal conjunctiva. Though posterior pressure from the orbital tusse pushed the plaque anteriorly, a temporary tarsorrhaphy with multiple, interrupted sutures provided sufficient tension to secure plaque against the conjunctiva. (VIDEO 1) The plaque was removed three days later. Six months post-operative, the patient has had no recurrence of disease and has visual acuity 20/400 best corrected. One year post-operative, there was an area of skin pigmentation well managed with cryo therapy. She had subsequent cornea scarring and ocular discomfort, with best corrected visual acuity in the right eye of count fingers at one foot and count fingers at four feet, at nine months and eighteen months, respectively (see Fig. 3).

Supplementary video related to this article can be found at https://doi.org/10.1016/j.ajoc.2022.101512.

3. Discussion

While curved and annular I-125 plaques have been described for iris tumors,[15–17] these plaques are primarily modified Collaborative Ocular Melanoma Study (COMS) [23] plaque designs with concentrically oriented I-125 seeds. To the authors knowledge, an annular I-125 plaque brachytherapy with radially oriented I-125 seeds, designed with optimal thickness and geometry to treat the bulbar and deep forniceal conjunctiva, has not been previously reported for conjunctival tumors. Novel dome-shaped I-125 Eye Physics plaques were recently used for iris and ciliary body tumors, with unique radio seed orientation and geometric design with central holes to avoid the unnecessary contact and radiation to the cornea.[24] The novel annular Eye Physics plaque construct described here represents a further innovation on this design. Whereas the prior EP dome plaques created air gaps conducive to dosimetric error, the EP donut here can be sutured flush to the globe. In addition, these plaques utilize self-collimating seed slots allowing for a thinner design, which is ideal for conjunctival malignancy. Consequently, this plaque effectively managed diffuse, multifocal conjunctival

melanoma (CM), without unnecessary anterior sequela described with prior approaches.[18,19]

Importantly, the stage and level of invasion of CM must guide adjuvant plaque brachytherapy. The specific design employed here may not be well suited for later stage CM, and radiometric dosing may be further collimated for CM without involvement of the deep forniceal conjunctiva. Further design iterations should focus on reducing cornea scarring.

Adjunctive radiotherapy and chemotherapy are important therapeutics to prevent tumor recurrence in conjunctival melanoma.[25] Topical mitomycin C[26–28] as well as more recent small-molecule drugs and immunotherapy treatments have been explored for conjunctival melanoma.[29] Brachytherapy for CM is less well described in the literature[30] and specific applicators such as strontium-90 beta radiotherapy applicators are not regularly produced due to low demand.[31] While the rarity of CM has prevented robust clinical trials from determining a gold standard therapeutic regimen, adjunctive radiotherapy remains an important approach to sterilize the orbit and avoid exenteration.

4. Conclusions

This case describes successful use of annular EP plaques with Plaque Simulator software used to treat conjunctival melanoma (CM). Given the rarity of CM and concomitant lack of robust clinical studies, this case demonstrates a viable adjuvant brachytherapy approach.

Patient consent

The patient consented to publication of the case orally. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The following authors have no financial disclosures: STB, AB, DAR.

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