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Original Article

# Treatment of conjunctival palpebral lesions using ruthenium plaque brachytherapy "sandwich technique"



Shahar Frenkel,[1,2] Jacob Pe'er,[1,2] Yael Deckel,[1] Zvi Gur,[1] Shay Kehat Ofir,[1] Maya Eiger-Moscovich[1]

***Objective:*** Treatment of palpebral conjunctival lesions is problematic due to late diagnosis, difficult surgical approach, and the need to preserve eyelid integrity. We describe our treatment experience using plaque brachytherapy in the "sandwich technique."

***Design:*** A retrospective study.

***Participants:*** We reviewed the medical records of patients treated by plaque brachytherapy for conjunctival lesions at the Hadassah Medical Center between January 1, 2013, and January 1, 2024, and included in the analysis patients treated for palpebral conjunctival lesions.

***Methods:*** Ruthenium plaque was sutured to the palpebral conjunctiva. The matching nonradioactive "dummy" plaque was sutured to the external eyelid to flip the tarsal's curvature.

***Results:*** The study cohort included 5 patients, 2 men (40%) and 3 women (60%) at a median age of 68.11 years (range: 47-79.7 years). Three patients had conjunctival melanoma (60%), 1 had sebaceous carcinoma (20%), and 1 had extensive carcinoma in situ (20%). All lesions were in the left upper eyelid. Median follow-up was 37.6 months (range: 18.7-110.6 months). Four patients demonstrated a complete response (80%), while one had a partial response (20%). There was local recurrence in 1 patient (20%), and 1 patient had new foci elsewhere (20%). All patients had full local control after adding local treatments. One patient developed metastatic disease and died (20%). All patients had manageable madarosis and conjunctival scars.

***Conclusions:*** Treatment of palpebral conjunctival lesions using "sandwich" plaque brachytherapy is safe and effective. To the best of our knowledge, this treatment was never described before, and we believe it should be added to our armamentarium.

***Objectif:*** La prise en charge des tumeurs conjonctivales palpébrales est complexe : le diagnostic est tardif, et le traitement chirurgical, ardu, sans compter qu'il faut conserver l'intégrité de la paupière. Nous décrivons ici notre expérience sur l'utilisation d'une plaque de curiethérapie dans le contexte d'un traitement « en sandwich ».

***Nature:*** Étude rétrospective.

***Participants:*** Nous avons examiné les dossiers médicaux des patients dont les tumeurs conjonctivales ont été traitées par plaque de curiethérapie au Hadassah Medical Center entre le 1er janvier 2013 et le 1er janvier 2024. Notre analyse a inclus les patients qui ont été traités en raison de tumeurs conjonctivales palpébrales.

***Méthodes:*** Une plaque de ruthénium a été suturée à la conjonctive palpébrale. La plaque « placebo » appariée a été suturée à la paupière externe pour inverser la courbure tarsale.

***Résultats:*** La cohorte regroupait 5 patients, soit 2 hommes (40 %) et 3 femmes (60 %), dont l'âge médian était de 68,11 ans (fourchette : 47-79,7 ans). Les présentations se déclinaient comme suit : 3 cas de mélanome conjonctival (60 %), 1 cas de carcinome sébacé (20 %) et 1 cas de carcinome in situ extensif (20 %). Toutes les lésions touchaient la paupière supérieure gauche. Le suivi médian a été de 37,6 mois (fourchette : 18,7-110,6 mois). Par ailleurs, 4 patients ont bénéficié d'une réponse complète (80 %), tandis que le cinquième patient n'a eu qu'une réponse partielle (20 %). Une récurrence locale s'est produite chez 1 patient (20 %), et de nouveaux foyers sont apparus ailleurs chez 1 autre (20 %). Tous les patients ont obtenu une maîtrise locale complète après l'ajout de traitements locaux. Enfin, 1 patient est décédé après l'apparition de métastases (20 %). Tous les patients ont présenté une madarose traitable et des cicatrices conjonctivales.

***Conclusions:*** La prise en charge des tumeurs conjonctivales palpébrales par plaque de curiethérapie dans le contexte d'un traitement « en sandwich » est sûre et efficace. À notre avis, il s'agit de la première description de ce type de traitement, et nous estimons qu'il doit être ajouté à notre arsenal.

Conjunctival malignant neoplasms can be treated by different treatment modalities. The primary treatment modality is surgical excision, with added cryotherapy, chemotherapy drops (mitomycin C 0.02% for epithelial/0.03% for pigmentary lesions or 5-fluorouracil 1%), or immunotherapy (interferon $\alpha$-2), as needed. More extensive disease can be treated by localized treatments, including external beam radiotherapy (EBRT), proton beam radiation, or interventional radiotherapy, as high-dose interstitial brachytherapy.[1-3] In some patients, systemic treatments, such as chemotherapy and immunotherapy, are more appropriate, depending on malignancy type, size, and location. The treatment aim is to eradicate the tumor, while preserving visual function and aesthetic appearance and avoiding extensive disfigurement as orbital exenteration.[4]

Treatment of palpebral conjunctival lesions is specifically problematic. Since the diagnosis requires eversion of the eyelid, which is not done as part of a routine examination by

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most ophthalmologists, it is often diagnosed as an extensive disease. Treatment of the superior palpebral conjunctiva with topical adjuvant treatment with chemotherapy or immunotherapy may be less effective due to gravity. Also, the surgical approach may be difficult, and the need to preserve eyelid integrity limits treatment options.

At the Hadassah Medical Center, we treat relatively extensive palpebral conjunctival lesions, which cannot be removed surgically without extensive disfigurement, using a ruthenium-106 plaque brachytherapy in a procedure that we created called the "sandwich technique." In this treatment modality, we use both the radioactive ruthenium plaques (BEBIG Medical, Berlin, Germany), and their respective nonradioactive "dummy" counterparts, which are available at many ocular oncology centers. In this article, we describe this treatment method and our experience in using it for the treatment of palpebral conjunctival lesions.

## Methods

We retrospectively reviewed the medical records of all the patients treated by ruthenium-106 plaque brachytherapy for conjunctival and eyelid lesions at the Hadassah Medical Center Ocular Oncology Unit from January 1, 2013, to January 1, 2024. Inclusion criteria were conjunctival lesions located in the palpebral conjunctiva and treated by the "sandwich technique." Patients treated by ruthenium plaque brachytherapy for lesions located in the bulbar conjunctiva or eyelid skin were excluded from this analysis. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board.

In the "sandwich technique," a ruthenium plaque is sutured to the palpebral conjunctiva with its radioactive surface facing the conjunctiva, while the matching nonradioactive "dummy" plaque is sutured to the external eyelid to inverse the contour of the tarsus and approximate the palpebral conjunctival lesion to the irradiating surface of the plaque. An added benefit is that this technique blocks exposure of the surroundings to radiation. The plaques' ears are sutured to each other through the eyelid, enabling the plaque to remain in position (Figure 1).

Surveillance for local recurrence and metastatic spread to the regional lymph nodes or the orbit included 6 monthly visits in the Ocular Oncology Unit with anterior segment pictures of the entire ocular surface and palpebral surfaces upon eyelid eversion (Nikon D90 Digital SLR Camera), a full slit-lamp eye examination, assessment of eye movement, and palpation of the draining lymph nodes. Patients were routinely interviewed about any pain (which could indicate a perineural invasion). Additional imaging (i.e., a PET-CT) was not employed.

The medical records were reviewed by the investigators for patient demographics, clinical features, surgical treatment features, pathological diagnoses, radiation features, and clinical outcomes. Statistical analysis was performed using MedCalc (version 22.017, MedCalc software, Ostend, Belgium). Continuous variables were reported as median (range). Clinical data were evaluated for normality and analyzed using descriptive statistics. A $p$ value $<0.05$ was considered statistically significant.

## Results

There were 50 patients treated by 61 ruthenium-106 plaque brachytherapy procedures for conjunctival and eyelid lesions in the Hadassah Medical Center Ocular Oncology Unit during the study period. Five patients were treated for lesions in the palpebral conjunctiva and were included in our analysis. The study cohort included 2 men (40%) and 3 women (60%), diagnosed at a median age of 68.1 years (range: 47-79.7 years). All patients were Caucasians (100%), 3 were of Jewish faith (60%) and 2 were of Arab ancestry (40%).

All patients underwent surgical incisional or excisional biopsy, aimed to treat the lesion and provide a pathological diagnosis, and received adjuvant local treatment, as needed. In all patients, the tumor presented in the palpebral conjunctiva of the left upper eyelid (100%), and it was treated by plaque brachytherapy, using the "sandwich technique". The median follow-up was 37.6 months (range: 18.7-110.6 months) from the date first seen and 26.6 months (range: 8.8-98.3 months) from plaque brachytherapy.

Two patients presented to the oculoplastic service with raised eyelid lesions. Both patients underwent an incisional biopsy, one was diagnosed with sebaceous carcinoma and the other with extensive squamous carcinoma in situ (Figures 2, A and C). The patient diagnosed with sebaceous carcinoma had an excisional biopsy with negative margins. Upon

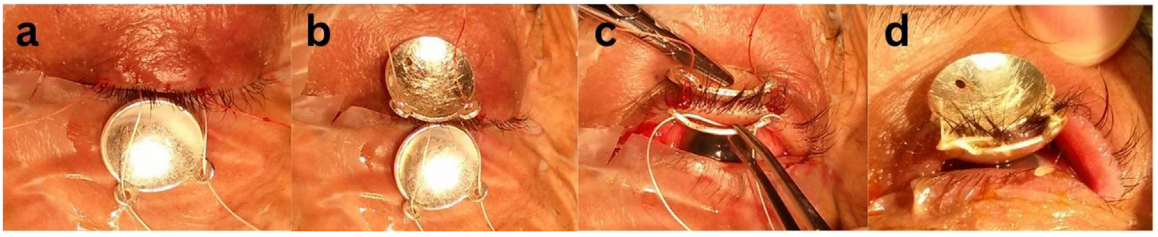


**Fig. 1—Surgical photos demonstrating the "sandwich technique." (A) A double-needle suture is placed through the ruthenium plaque ears and through the palpebral conjunctiva, out the eyelid skin, close to the eyelid margin. (B) The suture is placed through the ears of the matching non-radioactive "dummy" plaque. (C) The plaques are placed in appropriate position, with the radioactive surface facing the conjunctiva and covering the palpebral lesion. (D) The plaques ears are sutured to each other, enabling the plaque to remain in position.**

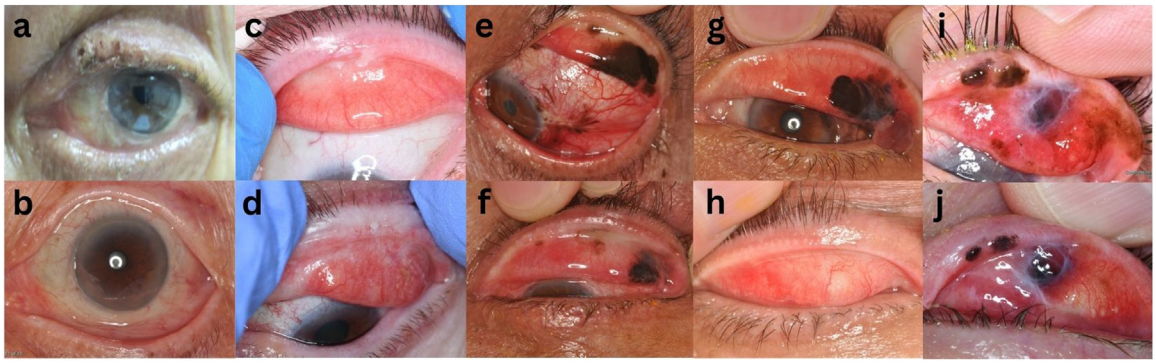


**Fig. 2—External photos of the study patients before and after treatment. (A and B) A 68- year-old male with an eyelid raised lesion diagnosed by incisional biopsy as sebaceous carcinoma, undergoing repeat surgery with clean margins. Upon recurrences (A) and 2 wedge biopsies with positive margins, he was treated by a plaque in the "sandwich technique" on 2 adjacent locations to cover the entire involved area with good local and systemic control (B). (C and D) A 73-year-old female with palpebral squamous carcinoma in situ treated by incisional biopsy and Imiquimod. Upon extensive recurrence (C), she was treated by a plaque in the "sandwich technique" with good local control. She later developed a recurrence treated by 0.02% mitomycin C drops with good local and systemic control (D). (E and F) A 59-year-old male with conjunctival melanoma, previously treated by bulbar plaque brachytherapy and 0.03% mitomycin C drops, with palpebral recurrence (E), treated by a plaque in the "sandwich technique" with good local control. Two new lesions that developed in another area of the palpebral conjunctiva, were treated by another sandwich plaque brachytherapy with good local control (F). He later developed systemic (including brain) metastatic disease, which led to his death. (G and H) A 79-year-old female with bulbar and palpebral conjunctival melanoma (G), previously treated by incisional biopsy to flatten the lesions toward plaque placement, was treated by a plaque in the "sandwich technique" and 0.03% mitomycin C drops with complete response and no local or systemic recurrence (H). (I and J) A 47-year-old female with conjunctival melanoma, previously treated by 0.03% mitomycin C drops, with a palpebral recurrence (I), treated by a plaque in the "sandwich technique" with partial response (J). She had no residual local or systemic disease after the addition of 0.03% mitomycin C drops and an excisional biopsy.**

recurrence in the left upper eyelid's palpebral conjunctiva, he underwent a wedge resection biopsy that was histopathologically found to have positive margins. Following a second recurrence after another wedge resection, it would have been very challenging to perform a third wedge resection, and he was referred to palpebral ruthenium plaque brachytherapy, using the "sandwich technique," on the palpebral conjunctiva. To cover the entire involved area, the plaque was placed on one part of the palpebral conjunctiva, and, at the completion of the irradiation, was immediately moved to cover the remaining untreated area. Radiation to lesions apex (1.5 mm deep) was 11,290-13,799 cGy with 13,365-16,335 cGy to the base. Following treatment, he had no residual disease and no recurrence or metastatic disease after 98.3 months of follow-up (Figure 2B). The patient diagnosed with squamous carcinoma in situ, was treated by Imiquimod with good local response. Upon recurrence, because of extensive disease without clear clinical margins, she was referred to palpebral ruthenium plaque brachytherapy, using the "sandwich technique." Radiation was 3,147 cGy to an apex 1.0 mm deep. She experienced a local recurrence 18 months later, diagnosed as squamous carcinoma in situ in an incisional biopsy. She was treated with 3 courses of 0.02% mitomycin C drops (qid, 2 weeks on—2 weeks off per course) with complete clinical response and no further recurrence or metastatic disease after 27.1 months follow-up (Figure 2D).

Three patients presented with bulbar pigmented lesions (Figure 2, E, G, I), which were resected and diagnosed as conjunctival melanoma. The residual bulbar lesions were treated by bulbar ruthenium plaque brachytherapy in one patient and 0.03% mitomycin C drops (qid, 2 weeks on-2 weeks off per course) in all 3 patients. At diagnosis of extensive left upper eyelid palpebral lesions, one patient had an incisional biopsy (for diagnosis and debulking of the tumor mass to allow for plaque placement), and all patients were treated by palpebral ruthenium plaque brachytherapy using the "sandwich technique." Radiation to lesions apex (1-2.5 mm deep) was 9,861-11,111 cGy with 10,055-21,355 cGy to the base. On follow-up, one patient had a good local response but developed new lesions in an adjacent untreated area of the palpebral conjunctiva, which were treated by another sandwich plaque brachytherapy with a good local response and no residual disease after 26.6 months of follow-up (Figure 2F). He unfortunately refused sentinel lymph node biopsy and later developed

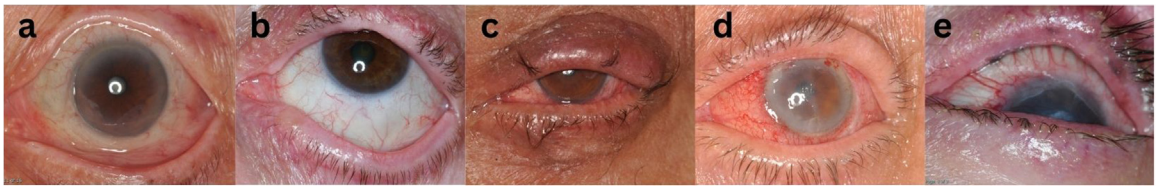


**Fig. 3—External photos of the study patients at the end of follow-up demonstrating side effects. All the patients had madarosis and conjunctival scars (A-E). Two patients experienced repeat corneal erosions (C and D), and 1 patient had limbal stem cell deficiency (E), which can be explained by the treatments they received for their bulbar disease.**

systemic metastatic disease, including brain metastases, which led to his death. The second patient had no residual disease and no recurrence through 17.4 months of follow-up (Figure 2H). She underwent a sentinel lymph node biopsy, which was negative. The third patient had only a partial response to brachytherapy, and to the addition of 0.03% mitomycin C drops (Figure 2J). She had a repeat excisional biopsy that revealed one focus of viable melanoma and two nonviable foci. After 8.8 months of follow-up, she had no recurrence or metastatic disease.

All patients suffered from madarosis and conjunctival scars in the treated area, which had minimal effect on their quality of life and eye function. Additional adverse effects, such as eyelid ptosis, restrictive strabismus, or diplopia were not observed in any of the patients. In the 3 patients who had conjunctival melanoma, it also involved the bulbar conjunctiva. One of whom was treated by bulbar plaque brachytherapy, and all 3 received 3 courses of 0.03% mitomycin drops. Two patients experienced repeat corneal erosions (one of whom for refusing to use artificial tears), and the third had limbal stem cell deficiency, which can be explained by the treatments they received for their bulbar disease (Figure 3). The repeat corneal erosions did influence their quality of life but were manageable.

## Discussion

In this study, we describe our experience with treating relatively extensive conjunctival malignancies using a ruthenium plaque brachytherapy in a procedure that we created called the "sandwich technique" as an alternative for extensive surgical procedures as orbital exenteration. In this procedure, we use the dummy plaque on the outer surface of the eyelid to alter the curvature of the tarsus and approximate the tarsal conjunctiva to the radioactive surface of the plaque facing it. This method eliminates the exposure of the ocular surface and the lens to the radiation, while minimizing the irradiation of people around the patient with the shield of the dummy plaque.

In some ocular oncology services, relatively extensive eyelid malignancies are treated by interventional radiotherapy. In some of those centers, they also treat relatively extensive conjunctival palpebral malignancies. Interventional radiotherapy can be delivered by different devices, depending on the size and location of the tumor. It includes either contact radiotherapy, using dedicated applicators and customized plaque,[5,6] or high-dose interstitial brachytherapy, using needles and catheters in high-risk areas.[4] Already in 1984, Daly et al. reported their experience with the use of iridium-192 wires for eyelid malignancies.[7] Most other centers that use high-dose interstitial brachytherapy also use iridium-192 wires,[8-15] but the use iodine-125 interstitial implant[16] have also been described. The use of interstitial wires necessitates appropriate equipment, a complicated planning procedure done by a dedicated radiation oncologist, not available in most hospitals,[4] and a delicate and intrusive surgical procedure, in which the wires are passed inside the eyelid through the tumor.[4]

In our study cohort, out of 5 patients treated by the "sandwich technique," 4 patients had a complete response (80%), while 1 patient had a partial response (20%). There was local recurrence in 1 patient (20%) and new disease foci in an adjacent untreated location on the palpebral conjunctiva in another patient (20%), possibly due to amelanotic PAM. All patients had a complete local response after the addition of plaque brachytherapy in 1 patient, 0.03% mitomycin C drops in 1 patient, and 0.03% mitomycin C drops plus an excisional biopsy in 1 patient. In studies describing high-dose interstitial wire brachytherapy for eyelid and palpebral conjunctival malignancies, local recurrence is reported in 3-29% of patients.[4,8,11-13,16] The local recurrence is lower when the treatments are for the frequently less aggressive eyelid carcinomas (3-17%),[8,11-13] comparing to the more aggressive conjunctival palpebral malignancies (25-29%),[4,8] similar and slightly higher than the local recurrence rate of the lesions treated in our study. One patient in our study (20%) developed metastatic disease and died after extended months of refusing sentinel lymph node biopsy. Metastatic disease is reported in 0-27% of patients treated by high-dose interstitial brachytherapy for a variety of malignant eyelid lesions.[8,12,15,16]

All the patients in our cohort experienced manageable madarosis and conjunctival scars. Two patients also experienced repeat corneal erosions (one of whom for refusing to use artificial tears), and 1 patient had limbal stem cell deficiency, which is mostly related to the treatment they received for their bulbar malignancy. In patients treated by high-dose interstitial iridium-192 wire brachytherapy, complications included eyelid erythema and edema, conjunctival chemosis, madarosis, eyelid skin depigmentation, ectropion, eyelid fibrosis, dry eye, epiphora, cataract, keratitis, and corneal ulcer with perforation,[8,13-16] frequently more severe complications than those described in our study cohort.

Our study has a number of limitations, including its retrospective nature and the small study group. Nevertheless, we were able to demonstrate this new surgical approach and to show its potential, as an alternative to disfiguring surgical procedures and complex interventional radiotherapy procedures.

In summary, the treatment of relatively extensive palpebral conjunctival lesions using the "sandwich" ruthenium-106 plaque brachytherapy is a relatively safe and effective treatment method. It can be widely used in ocular oncology services since it only necessitates a plaque in an appropriate size and its matching non-radioactive "dummy" plaque, sutured to the external eyelid to alter the curvature of the tarsus and prevent exposure of the surroundings to radiation. Those are available resources in many ocular oncology services that do not necessitate specialized equipment. To the best of our knowledge, this treatment method was never described before, and we believe it should be added as another tool in our armamentarium.

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## Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

From the [1]Division of Ophthalmology, Hadassah Medical Center, Jerusalem, Israel; [2]Faculty of Medicine, the Hebrew University of Jerusalem, Jerusalem, Israel.

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Correspondence to Shahar Frenkel, MD, Ocular Oncology Unit, Division of Ophthalmology, Hadassah Medical Center, P.O. Box 12,000, Jerusalem, Israel; shahar.frenkel@gmail.com.