A 12-Year Study of Slotted Palladium-103 Plaque Radiation Therapy for Choroidal Melanoma: Near, Touching, or Surrounding the Optic Nerve

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• **PURPOSE: To present our 12-year experience with low-energy-photon, slotted eye plaque radiation therapy.**

• **DESIGN: Retrospective interventional case series.**

• **METHODS: Setting: The New York Eye Cancer Center. Study Population: Fifty-two consecutive patients with uveal melanomas near, touching, or surrounding the optic disc. Intervention: Slotted eye plaque radiation therapy. Main Outcome Measures: Change in visual acuity, local tumor control, radiation side effects, eye salvage, and systemic metastases.**

• **RESULTS: Tumors were peripapillary within 1.5 mm of the optic disc (n = 8, 15%), juxtapapillary touching ≤180 degrees (n = 23, 44%), or circumpapillary >180 degrees and encircling the disc (n = 21, 41%). Mean follow-up was 47 months (median 34 months, range 6-146 months). Radiation induced a mean 41.2% reduction in tumor thickness. Life table analysis showed that 69% of patients retained their visual acuities ≥ 20/40 and had a vision loss–free survival 84 months after treatment. Also, 90% of patients retained their visual acuity between 20/50 and 20/200 and had a vision loss–free survival 36 months after treatment. Slotted plaque brachytherapy was associated with 4% secondary cataract, 11% neovascular glaucoma, and no dry eye or eyelash loss. Local tumor control (no recurrence) was achieved in 98.1% of patients. Life table analysis showed an overall enucleation-free survival of 93% and metastasis-free survival of 94%.**

• **CONCLUSIONS: Slotted plaque radiation therapy provided a normalized plaque-tumor position, such that the entire choroidal melanoma plus a 2- to 3-mm free margin of normal-appearing tissue was included in the targeted zone. At 12 years, slotted plaque radiation therapy resulted in high rates of local tumor control and vision and eye retention. (Am J Ophthalmol 2018;188: 60–69. © 2018 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).)**

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American Brachytherapy Society (ABS) consensus guidelines (2014) defined "normal" ocular plaque position as to cover the entire tumor plus a 2- to 3-mm margin of safety.[1] This is because the thin line between success and failure, particularly in treatment of juxtapapillary tumors, is dependent on the eye cancer specialist's definition of tumor size and extent in relation to episcleral plaque size and position.

That said, the optic nerve and its retrobulbar sheath present a unique obstacle to normal plaque placement.[2] Within the eye, the optic disc has a mean diameter (disc diameter, DD) of 1.8 mm. However, as the optic nerve exits the eye, it is enveloped by a 5- to 6-mm-wide optic nerve sheath (ONS).[3] A round episcleral plaque placed against the ONS edge will be at least 1.5 mm from the edge of the optic disc. Thus, all melanomas extending within 1.5 mm, touching, surrounding, or overlying the optic disc cannot be included beneath a round episcleral plaque during treatment. In addition, the "normal" 2- to 3-mm radiation safety margins are impossible.[1–4]

Notched plaques were a prior attempt to circumnavigate the optic nerve. The classic 4-mm plaque notch was likely designed to overcome the visible, intraocular 1.8-mm optic disc diameter. However, a 4-mm plaque notch could not overcome the 5- to 6-mm orbital optic nerve sheath diameter and thus cannot be seated in position to surround any tumor near, touching, or surrounding the optic disc (much less a posterior margin of safety). In fact, compared to round plaques, notched plaques increase the offset of the plaque from the optic nerve sheath. They actually increase the amount of tumor geographically missed.

Evidence of eye cancer specialists' difficulty in treating tumors near, touching, and surrounding the optic disc includes the widespread use of notched plaques, stereotactic radiotherapy, and transpupillary thermotherapy (TTT), in addition to plaque brachytherapy and proton beam irradiation.[5–8]

In 2005, the first 8-mm-wide and 8-mm-deep slot cut from the posterior aspect of an 18-mm Collaborative Ocular Melanoma Study (COMS)-type gold plaque shell was used and termed "*Finger's Slotted Eye Plaque*."[9] The slot was created to exceed the optic nerve sheath diameter (ONSD), to allow the ONS into the plaque and thus allow plaque extension beyond the ONS obstruction. We found that by altering the depth of the plaque

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slot, the distance the gold plaque extended beyond the optic nerve sheath could be modulated. Slot depth was calculated to allow for "ABS-normal" plaque positioning, which includes a 2- to 3-mm margin of safety beyond the tumor's posterior edge.[1]

A 5-year study, with detailed discussion about slot depth calculations, plaque construction, seed orientation, radiation dose calculation, and plaque insertion, was published in 2012.[10] In contrast, herein we describe our 12-year experience with Finger's Slotted Eye Plaque technique. We report its long-term effect on visual acuity, local tumor control, radiation side effects, rate of eye salvage, and metastases.

METHODS

THIS RETROSPECTIVE INTERVENTIONAL CASE SERIES involved 52 consecutive patients treated with slotted eye plaque radiation for uveal melanomas near, touching, or surrounding the optic disc. Selection criteria also included a minimum 6-month follow-up. All clinical data were collected and analyzed at The New York Eye Cancer Center. This study conformed to the Declaration of Helsinki and the United States of America Health Insurance Portability and Accountability Act (HIPAA) of 1996. It was approved by the internal review board and ethics committee of The New York Eye Cancer Center.

• **CASE SELECTION:** Patients were treated between 2005 and 2017. All patients included in the study had choroidal melanomas that extended within 1.5 mm of the edge of the optic disc. Informed consent involved a detailed discussion of the patient's potential for vision, life, and preservation of eye as compared to treatment alternatives. This included the risks and potential benefits of observation and the more commonly used definitive treatments like radiation (plaque or proton) and enucleation. Lastly, each patient was informed about the number of patients who had been treated with slotted radioactive plaque therapy at The New York Eye Cancer Center and their outcomes.

Patients were informed that slotted plaque therapy normalizes the target zone so as to be equivalent to treatment of more anteriorly located choroidal melanomas.[1,4,10] They were also informed that the optic nerve would be placed closer to or within the plaque, thus increasing their risk for radiation optic neuropathy (RON)-related vision loss.[11] They were also informed that RON is treatable (suppressed) with anti–vascular endothelial growth factor (anti-VEGF) therapy.[12] Patient characteristics included age, sex, eye, and medical history. Ophthalmic examinations included ETDRS visual acuity measurements, pupillary reaction, ocular motility, intraocular pressure, and anterior segment surveillance (primarily for cataract and iris neovascularization).

Tumor characteristics included tumor height, basal dimensions, and shape. Radiation parameters included plaque size, slot size, apical tumor dose, apical tumor dose rate, minimum tumor dose, hours of radiation exposure, and dose to critical ocular structures (lens, fovea, central optic disc, and sclera).

Ophthalmic testing included fundus photography, ultrasonography, and optical coherence tomography (OCT) every 3-4 months after brachytherapy. Fluorescein angiography was performed every 6 months to monitor tumor and optic disc vasculopathy as well as tumor regression. Tumor height was measured with ultrasound imaging and compared at each visit. Initial American Joint Committee on Cancer (AJCC) staging required whole-body positron emission tomography–computed tomography (PET-CT).[13] Posttreatment surveillance involved abdominal radiographic imaging every 6 months for the first 5 years and then every year thereafter.[14] Based on the American College of Radiology Appropriateness Criteria for hepatic metastasis, the order of sensitivity was contrast-enhanced magnetic resonance imaging, computed tomography, and, lastly, ultrasound imaging.[15]

For this study, local recurrence was defined as ≥0.5 mm of apical tumor growth (by ultrasonography) or ≥1.0 mm of vascularized marginal growth (by comparative fundus photography and fluorescein angiography).

• **TUMOR DEFINITIONS AND SLOT DIMENSIONS:** Choroidal melanomas were classified as peripapillary, juxtapapillary, and circumpapillary (Figure 1).

Peripapillary choroidal melanoma was defined as extending within 1.5 mm of the optic disc (Figure 1). If a choroidal tumor extends to exactly 1.5 mm of the disc, its posterior margin approximates the same position as the edge of the retrobulbar optic nerve sheath. Therefore, a round plaque placed against that optic nerve sheath would be perfectly aligned with the edge of the tumor. There would be no possible 2.5-mm posterior safety margin. To provide that normal margin, the plaque must overcome the optic nerve sheath obstruction by 2-3 mm. Therefore, we must cut an 8-mm-wide, 2- to 3-mm-deep slot to advance the ONS into the slot.

Juxtapapillary choroidal melanoma was defined as extending to, touching up to 180 degrees, but not starting to encircle the optic disc (Figure 1). The juxtapapillary choroidal melanoma extending to the disc has grown to a position 1.5 mm beyond the retrobulbar optic nerve sheath edge. Therefore, a round plaque placed against that optic nerve sheath edge would be at least 1.5 mm away from the posterior margin of the tumor (a marginal miss). In addition, there would be no 2.5-mm posterior margin of safety. In this case, to provide the normalized plaque position, the plaque must both overcome the optic nerve sheath width (5-6 mm) by cutting an 8-mm-wide slot, then deepen the slot considering the 1.5- to 2.5-mm tumor extension, plus the 2.5-mm safety margin, totaling a 4- to 5-mm-deep slot.