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# Regression Patterns of Iris Melanoma after Palladium-103 ($^{103}$Pd) Plaque Brachytherapy

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***Purpose:*** To evaluate the patterns of regression of iris melanoma after treatment with palladium-103 ($^{103}$Pd) plaque brachytherapy.

***Design:*** Retrospective, nonrandomized, interventional case series.

***Participants:*** Fifty patients with primary malignant melanoma of the iris.

***Methods:*** Palladium-103 plaque brachytherapy.

***Main Outcome Measures:*** Changes in tumor size, pigmentation, and vascularity; incidence of iris neovascularization; and radiation-related complications.

***Results:*** The mean age in the case series was 61.2±14.9 years. The mean tumor thickness was 1.4±0.6 mm. According to the American Joint Committee on Cancer, eighth edition, staging criteria for iris melanoma, 21 tumors (42%) were T1a, 5 tumors (10%) were T1b, and 24 tumors (48%) were T2a. The tumor was melanotic in 37 cases (74%) and amelanotic in 13 cases (26%); of these, 13 tumors (26%) showed variable pigmentation. After brachytherapy, mean tumor thickness decreased to 0.9±0.2 mm. Pigmentation increased in 32 tumors (64%), decreased in 11 tumors (22%), and was unchanged in 6 tumors (12%). For intrinsic vascularity (n = 19), 12 tumors (63%) showed decrease and 7 tumors (37%) showed complete resolution. Appearance of ectropion uveae showed diminution in 15 tumors (43%); newly present corectopia was observed in 6 patients (12%). On high-frequency ultrasound imaging, of the 42 tumors (84%) with low to moderate internal reflectivity, 30 tumors (60%) showed an increase in internal reflectivity on regression. Iris stromal atrophy was noted in 26 patients (52%), progression or new-onset cataract was noted in 22 patients (44%), neovascular glaucoma was noted in 1 patient (2%), and there were no cases of corneal opacity. There was no clinical evidence (0%) of radiation-induced retinopathy, maculopathy, or optic neuropathy. Mean follow-up in this series was 5.2 years (range, 0.5–17 years).

***Conclusions:*** The most common findings related to iris melanoma regression after $^{103}$Pd plaque brachytherapy included decreased intrinsic tumor vascularity, increased tumor pigmentation, and decreased tumor thickness with synchronous increase in internal ultrasonographic reflectivity. No irreversible sight-limiting complications were noted. *Ophthalmology 2017;■:1–8 © 2017 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Iris melanoma is the least common type of uveal melanoma, constituting only 2% to 3% of cases.[1,2] Early studies suggested that because of their anatomic location and tendency for slow growth, they were presumed to have low metastatic potential of 3.5% to 5%.[1–3] Thus, smaller iris and iridociliary melanomas have been observed for documentation of growth before intervention. However, a relatively recent single-center and multicenter international studies have found that biopsy-proven iris melanomas are more dangerous, with metastatic rates of 10.7% to 11%.[2,4] These findings support the treatment of iris melanomas.

Clinical signs suggesting that a pigmented iris tumor is a melanoma include intrinsic tumor vascularity, stromal involvement of more than 3 clock hours (or measuring >5 mm), thickness larger than 1 mm, sentinel vessels (iris and episcleral), sector cataract, pigment dispersion, secondary glaucoma, and extrascleral extension.[4] Although a clinical diagnosis can be acceptable, both aspiration cutter-assisted or needle biopsy have been performed safely in cases with high suspicion of malignancy or with atypical clinical features, as well as for obtaining a specimen for histopathologic and genetic studies.[5–7]

The management of iris melanoma has depended on several clinical features: tumor size, location, or extent; tumor seeding; as well as the presence of tumor-related glaucoma.[4,8] Treatment options include iridectomy, iridocyclectomy, plaque brachytherapy, proton beam radiotherapy, and enucleation.[9–19] Smaller tumors have been managed with local resection (iridectomy, iridocyclectomy) to achieve tumor-free margins, whereas larger tumors, multifocal tumors, or those tumors causing uncontrollable glaucoma were managed with plaque radiotherapy or enucleation.[13,17–19] Of these, local resection invariably causes a dysmorphic, dystonic pupil or large optical opening with associated anisocoria, accommodative symptoms, and photophobia. Local control after local resection of iris melanomas has been reported to be 90% to 94%.[18,19]

In 1991, we treated the first iris melanoma with epicorneal palladium-103 ($^{103}$Pd) ophthalmic plaque radiation therapy in an effort to preserve normal iris tissue and



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function.[16] More recent literature reveals a trend towards conservative treatment with radiation therapy.[10–17] In consideration of this trend, it is important to examine and document the patterns of change after plaque radiation therapy for iris melanoma.

In a search and review of National Library of Medicine and PubMed findings using the terms *iris*, *plaque*, *radiation*, and *regression*, we could find no studies describing the clinical patterns of regression of iris melanoma after plaque brachytherapy. Therefore, we describe the clinical features of regressing iris melanomas after $^{103}$Pd plaque brachytherapy.

## Methods

This study adhered to the tenets of the Declaration of Helsinki and the Health Insurance Portability and Accountability Act of 1996. We obtained approval from The New York Eye Cancer Center Internal Review Board to perform a retrospective chart review of ophthalmic plaque brachytherapy for iris melanomas between 1998 and 2015. This included 50 patients with iris melanoma who underwent $^{103}$Pd plaque brachytherapy with at least 6 months of follow-up. Patients diagnosed with ciliary body melanoma extending to the iris were excluded from the study.

### History and Ophthalmic Examination

All patients were referred to The New York Eye Cancer Center with a history of iris lesion with (1) evidence of documented growth or (2) suspicion of malignant melanoma. The demographic data involving age at presentation, gender, race, and associated ocular and systemic diseases (hypertension, diabetes mellitus, cardiac illness, and malignancies involving other systems) were recorded.

Ophthalmologic examinations were inclusive of, but not limited to, visual acuity with the Early Treatment Diabetic Retinopathy Study charts and rooms, slit-lamp biomicroscopy with photography, tonometry, gonioscopy, scleral transillumination, high-frequency ultrasonography (20–50 MHz), and indirect ophthalmoscopy. Of these, visual acuity, slit-lamp photography, gonioscopic photography, high-frequency ultrasound imaging, and ophthalmoscopy testing were performed at each visit.

### Informed Consent, Biopsy, and Systemic Evaluations

All patients were counselled about the most common methods of management (observation for growth, confirmation of histopathologic diagnosis with biopsy, radiation therapy, iridectomy or iridocyclectomy, and enucleation). Biopsy was performed in 37 eyes (74%) having either atypical morphologic features or after patient request for a histopathologic diagnosis using the Finger Iridectomy Technique (FIT).[5] A histopathologic diagnosis of malignant melanoma was established in all 37 eyes. All 50 patients subsequently underwent treatment with $^{103}$Pd plaque brachytherapy.

Pretreatment radiographic metastatic surveys (initial whole-body 18-fluorodeoxyglucose positron emission tomography/computed tomography [PET/CT]) imaging or contrast-enhanced chest and abdominal radiographic imaging (computed tomography or magnetic resonance imaging) were performed. Follow-up systemic examinations were repeated every 6 months for the first 5 years and every year thereafter and typically were limited to radiographic abdominal imaging.[7]

### Primary Data Parameters

Ocular data at presentation included initial best-corrected visual acuity, anterior segment findings, iris color, intraocular pressure, tumor pigmentation (melanotic, amelanotic [e.g., tapioca colored]), nature of pigmentation (uniform, variable), tumor epicenter quadrant (superior, temporal, inferior, nasal, or diffuse), anterior and posterior tumor margins (pupil, midzone, iris root, angle), tumor configuration (nodular, dome, diffuse), tumor base measurements (in millimeters), tumor thickness (in millimeters), intrinsic vascularity, pigment dispersion, corectopia, ectropion uveae, tumor seeds in the anterior chamber angle, ciliary body invasion, and extraocular extension. Ultrasound characteristics included tumor thickness (in millimeters), defined as the highest tumor height as measured by high-frequency ultrasound. We also determined and recorded internal tumor reflectivity (low, moderate, high), iris pigment epithelium (IPE) anterior displacement or posterior bowing, iris pigment epithelium erosion, and invasion of supraciliary space. The radiation prescription point was defined by ultrasonography as the effective tumor height in millimeters or the distance from the corneal epithelium to deepest intraocular tumor extension as measured by high-frequency ultrasonography after mydriasis.

### Palladium-103 Plaque Radiation Therapy

After careful analysis of the comparative intraocular radiation distribution to critical structures (iodine 125 [$^{125}$I] vs. $^{103}$Pd]), the latter was the radionuclide selected for every case.[20] The radiation parameters included plaque shape (round, custom-designed shape), plaque diameter, number of seeds used, duration of treatment (hours), prescribed radiation dose (Gray), and radiation rate (Gray per hour) to tumor apex, lens, optic disc, and foveola.

Plaque surgery was comprised of tumor localization and plaque insertion. Scleral transillumination and preoperative high-frequency ultrasound measurements were used to define tumor margins. Each plaque was placed as to cover the entire tumor plus a 2- to 3-mm tumor-free margin. Epicorneal plaque touch was buffered with a 0.1-mm thick amniotic membrane held in position by the plaque. The anterior aspect of the plaque was covered by conjunctiva to form a Gunderson flap. This buffering technique was used for all cases (74%) after its discovery in 2008.[21] All patients received continuous radiation starting at insertion and ending when the prescription dose was delivered to the point of deepest intraocular tumor extension (as measured by high-frequency ultrasonography after mydriasis) over 5 to 7 days. Periocular steroid injection, topical Atropisol 1% (Iolab, USA), and epibulbar antibiotic–steroid ointment were placed at the end of surgery. Topical Cyclogyl 1% (Alcon Laboratories, Inc, Fort Worth, TX) and antibiotic–steroid drops were instilled 4 times daily during the treatment interval.

### Follow-up

Follow-up examinations were performed at 4 to 6-month intervals during the first 5 years and then at 6 to 12-month intervals thereafter. A detailed clinical evaluation and photographic documentation were performed at each visit. The outcome measures were changes in tumor size, pigmentation, vascularity, intraocular pressure, incidence of iris neovascularization, and radiation-related complications.

## Results

Analysis of the 50 cases of iris melanoma revealed that their median follow-up was 48 months (mean, 63 months; range, 6–204 months). Demographic characteristics are described in Table 1.

Table 1. Patient Demographic Data

| Features | Data |
|---|---|
| Age (yrs) | |
| Median | 65 |
| Mean | 61.2 |
| Range | 10–85 |
| Race, no. (%) | |
| White | 47 (94) |
| Hispanic | 2 (4) |
| Asian | 1 (2) |
| Gender, no. (%) | |
| Male | 21 (42) |
| Female | 29 (58) |
| Associated comorbidities, no. (%) | |
| Hypertension | 10 (20) |
| Diabetes mellitus | 8 (16) |
| Cardiac illness | 10 (20) |
| Dysplastic nevus syndrome | 2 (4) |
| Skin melanoma | 5 (10) |
| Breast carcinoma | 4 (8) |
| Colon carcinoma | 2 (4) |

Table 2. Pretreatment Tumor Characteristics

| Features | No. | % |
|---|---|---|
| Morphologic features | | |
| Tumor epicenter quadrant location | | |
| Superior | 6 | 12 |
| Nasal | 15 | 30 |
| Inferior | 15 | 30 |
| Temporal | 12 | 24 |
| Diffuse | 2 | 4 |
| No. of quadrants involved | | |
| 1 | 46 | 84 |
| 2 | 2 | 4 |
| 3 | 0 | 0 |
| 4 | 2 | 4 |
| Anterior tumor margin | | |
| Pupil | 26 | 52 |
| Midzone | 22 | 44 |
| Root | 0 | 0 |
| Angle | 2 | 4 |
| Posterior tumor margin | | |
| Pupil | 0 | 0 |
| Midzone | 15 | 30 |
| Root | 5 | 10 |
| Angle | 25 | 50 |
| Ciliary body | 5 | 10 |
| Tumor configuration | | |
| Nodular | 34 | 68 |
| Dome | 10 | 20 |
| Diffuse | 6 | 12 |
| AJCC staging at presentation* | | |
| T1a | 21 | 42 |
| T1b | 5 | 10 |
| T2a | 24 | 48 |
| High-frequency ultrasonography | | |
| Internal reflectivity | | |
| Low | 23 | 46 |
| Moderate | 19 | 38 |
| High | 8 | 16 |
| Iris pigment epithelium | | |
| Bowing | 22 | 44 |
| Erosion | 25 | 50 |
| Iris root | | |
| Displacement | 6 | 12 |
| Disinsertion | 4 | 8 |
| Invasion of supraciliary space | 24 | 48 |

*According to American Joint Committee on Cancer (AJCC) cancer staging manual, eighth edition.[23]

## Pretreatment Characteristics

Iris melanoma affected the right eye in 19 patients (38%) and the left eye in 31 patients (62%). Iris color was blue in 20 eyes (40%), green or hazel in 22 eyes (44%), and brown in 8 eyes (16%). Multiple ipsilateral iris nevi were noted in 20 affected eyes (40%), whereas choroidal nevus was noted in 17 affected eyes (34%). Pre-existing cataract was noted in 21 eyes (42%), whereas 4 eyes (8%) were pseudophakic. Pretreatment visual acuities were 20/16 to 20/40 in 45 eyes (90%), 20/50 to 20/200 in 3 eyes (6%), and worse than 20/200 in 2 eyes (4%). Mean pretreatment intraocular pressure was 15.4 mmHg (range, 11–20 mmHg).[22]

Tumors were predominantly melanocytic in 37 eyes (74%) and amelanotic in 13 eyes (26%). Variable pigmentation was noted in 13 tumors (26%); pigmentation was uniform in the remaining 37 tumors (74%). Corectopia and ectropion uveae were noted in 29 eyes (58%) and 35 eyes (70%), respectively. Pigment dispersion was noted on the iris stroma in 27 eyes (54%) and in the angle in 12 eyes (24%). Intrinsic vascularity was present in 19 tumors (38%); sentinel blood vessels were noted in 3 eyes (6%) (Table 2).

## Pretreatment Ultrasound Imaging

Melanomas in this series had mean ultrasonographic transverse width of 5.3 mm (range, 1.7–9.6 mm) and a longitudinal length of 5.4 mm (range, 2–12 mm). Mean tumor thickness was 1.4 mm (range, 0.7–2.8 mm). High-frequency ultrasonography imaging revealed 23 tumors (56%) that exhibited low internal reflectivity, 19 tumors (38%) that exhibited moderate internal reflectivity, and 8 tumors (16%) that exhibited high reflectivity. Ciliary body involvement with the invasion of supraciliary space was found in 24 eyes (48%) (Table 2). According to the American Joint Committee on Cancer, Eighth Edition, staging criteria for iris melanoma, 21 tumors (42%) were stage T1a, 5 (10%) were stage T1b, and 24 (48%) were stage T2a.[23]

## Pretreatment Tumor Biopsy

Tumor biopsy using the aspiration-cutter FIT was performed in 37 eyes (74%), and histopathologic examination confirmed the diagnosis of malignant melanoma in all cases.[5] No vision loss, secondary glaucoma, or long-term complications could be attributed to this method of tumor biopsy. No extraocular extension of tumor (n = 0) or distant metastasis (n = 0) was present before or during this study.

## Radiation Treatment

Palladium-103 plaque brachytherapy was performed with a mean prescription dose of 84.5 Gy (range, 74.6–100 Gy) for a mean duration of 163.3 hours (range, 111.5–170 hours). The mean duration of follow-up after $^{103}$Pd plaque brachytherapy was 63 months (i.e., 5.2 years); the median was 48 months and the range was 6 to 204 months. The dosimetry and treatment parameters are described in Table 3.

Table 3. Dosimetry and Plaque Treatment Parameters

| Variable | Value |
|---|---|
| Radiation dose to tumor apex (Gy) | |
| Median | 85 |
| Mean | 84.5 |
| Range | 74.6–100 |
| Plaque size (mm), no. (%) | |
| Round | |
| 10 | 17 (34) |
| 12 | 7 (14) |
| 14 | 1 (2) |
| 16 | 1 (2) |
| 18 | 1 (2) |
| Custom designed | 23 (56) |
| Effective tumor height (mm) | |
| Median | 2.5 |
| Mean | 2.4 |
| Range | 2–3.6 |
| $^{103}$Pd Seeds, No. | |
| Median | 5 |
| Mean | 6.8 |
| Range | 5–21 |
| Radiation rate at the tumor apex (Gy/hr) | |
| Median | 58.2 |
| Mean | 59 |
| Range | 54.5–81 |
| Dose to lens (Gy) | |
| Median | 43.4 |
| Mean | 44.7 |
| Range | 18.2–59 |
| Dose to fovea (Gy) | |
| Median | 1.7 |
| Mean | 1.8 |
| Range | 0.2–5.2 |
| Dose to optic nerve (Gy) | |
| Median | 1.6 |
| Mean | 1.8 |
| Range | 0.3–4.7 |
| Duration of treatment (hrs) | |
| Median | 166.5 |
| Mean | 163.6 |
| Range | 111.5–170 |

1Gy = 100 cGy.

## Follow-up after Irradiation

Data were available from this cohort of 50 patients for 45 patients at 1 year, 33 patients at 3 years, 20 patients at 5 years, and 8 patients at 10 years of follow-up. The data were analyzed for regression pattern with respect to changes in tumor thickness, pigmentation, intrinsic vascularity, corectopia, ectropion uveae, and iris neovascularization for 1-, 3-, 5-, and 10-year follow-up (Table 4).

## Posttreatment Findings

**Color.** At the last follow-up, tumor pigmentation was found to be increased in 32 eyes (64%) (Fig 1A-D). The sites of previous tumor biopsy showed presence of fibrous scarring in 26 eyes (n = 37 [70%]), whereas 11 eyes (n = 37 [30%]) showed a small, persistent biopsy-related iridotomy. Iris stromal atrophy was documented in 26 eyes (52%). Pigment dispersion on iris stroma was found to increase in 20 eyes (n = 27 [74%]) (Fig 2A-B).

**Tumor Vascularity.** All 19 melanomas that revealed intrinsic vascularity (on slit-lamp and gonioscopic evaluation documented by photography) before radiation demonstrated decreased vascularity over time (Fig 3A-B). Of these, 7 tumors (37%) showed complete resolution and 12 tumors (63%) showed diminished vascularity (Fig 3A-B).

**Corectopia and Ectropion Uveae.** At the last follow-up after a mean of 5.2 years, 6 eyes (12%) showed newly developed corectopia. Of the 29 irises with corectopia before treatment, 6 (20%) showed an increase, whereas 22 (76%) showed persistent corectopia. Of the 35 irises with ectropion before radiation, 15 (43%) showed a decrease, whereas 2 (6%) showed an increase (Fig 2C-D).

**Intraocular Pressure.** The mean intraocular pressure at 3 months (n = 50) was 14.7 mmHg, at 1 year (n = 45) was 16.0 mmHg, at 3 years (n = 33) was 15.5 mmHg, at 5 years (n = 20) was 15 mmHg, and at 10 years (n = 8) was 14.8 mmHg. At the mean follow-up of 5.2 years, intraocular pressure was 14.7 mmHg, with a mean reduction of 4.5%. Neovascular glaucoma was diagnosed at the 1-year follow-up visit in 1 eye (2%) and was managed with topical antiglaucoma medications for 9 years.

**Ultrasonographic Findings.** The mean tumor thickness was 0.9 mm at regression (Fig 3C-D). Therefore, radiation induced a mean 36% reduction in thickness in this series. Note that the decrease in tumor thickness stabilized (within 0.1 mm) after 3 years (Fig 4). Of the 42 tumors (84%) with low to moderate internal reflectivity, 30 (60%) showed increase in internal reflectivity at last follow-up.

**Visual Acuity.** The final visual acuity was 20/16 to 20/40 in 42 eyes (84%), 20/50 to 20/200 in 4 eyes (8%), and worse than 20/200 in 4 eyes (8%). Forty eyes (80%) were within 2 lines or equal to the pretreatment visual acuity, whereas 4 eyes (8%) showed improvement of more than 2 lines. Overall, 88% were found to have stable to improved visual acuity at a mean 63 months of follow-up. Three or more lines of vision were lost in 4 patients, attributable to development of glaucomatous optic atrophy secondary to neovascular glaucoma (n = 1) and the development of choroidal neovascularization related to age-related macular degeneration (n = 3). Progressive or newly documented cataract (after plaque brachytherapy) was seen in 22 eyes (44%).[24] Each was treated with cataract surgery. No radiation-associated difficulty was reported by the cataract surgeons.

**Radiation Complications.** Focal superficial corneal epitheliopathy was found in 3 eyes (6%) at the 3- to 6-month follow-up. No eyes showed corneal, scleral, or corneoscleral necrosis (n = 50 [0%]), nor any corneal opacity at the last follow-up. The aforementioned cataracts were considered an acceptable and safely treatable consequence to iris brachytherapy. There was no clinical evidence of radiation-induced retinopathy, maculopathy, or optic neuropathy (n = 50 [100%]). The complications and visual, ocular, and systemic outcomes are listed in Table 5.

**Local and Systemic Outcomes.** In this series of 50 tumors, there was no evidence of local tumor recurrence (n = 0 [0%]) or distant metastasis (n = 0 [0%]) at a mean follow-up of 63 months. As classified by the eighth edition of the American Joint Committee on Cancer staging system, there was no difference in local or systemic outcome in comparison between T1- and T2-stage iris melanomas.

## Discussion

Slit-lamp biomicroscopy-assisted photography and gonioscopy were indispensable tools for documenting the presence and progress of clinical signs of tumor regression.

Table 4. Regression Pattern Analysis at 1, 3, 5 and 10 Years

| Feature | Before Surgery (n = 50) | 1 Year (n = 45) | 3 Years (n = 33) | 5 Years (n = 20) | 10 Years (n = 8) | Last Follow-up (Mean, 5.2 Years; n = 50) |
|---|---|---|---|---|---|---|
| Mean tumor thickness (mm) | 1.4 | 1.0 | 0.9 | 0.9 | 0.8 | 0.9 |
| Pigmentation, no. (%) | 50 (100) | n = 45 | n = 33 | n = 20 | n = 8 | n = 50 |
| Decrease | | 10 (22) | 10 (30) | 8 (40) | 4 (50) | 11 (22) |
| Increase | | 24 (53) | 19 (58) | 11 (56) | 4 (50) | 32 (64) |
| Persistent | | 11 (24) | 3 (10) | 1 (5) | 0 (0) | 6 (12) |
| Intrinsic vascularity, no. (%) | 19 (38) | n = 19 | n = 13 | n = 9 | n = 4 | n = 19 |
| Decrease | | 17 (90) | 8 (62) | 4 (45) | 0 (0) | 12 (63) |
| Resolved | | 2 (10) | 5 (38) | 5 (55) | 4 (100) | 7 (37) |
| Persistent | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Correctopia, no. (%) | 29 (58) | n = 29 | n = 21 | n = 7 | n = 7 | n = 29 |
| Persistent | | 25 (86) | 17 (80) | 4 (57) | 4 (57) | 22 (76) |
| Increase | | 3 (10) | 3 (14) | 2 (29) | 2 (29) | 6 (20) |
| Newly present | | 1 (3) | 1 (4) | 1 (14) | 1 (14) | 6 (12) |
| Ectropion uveae, no. (%) | 35 (70) | n = 35 | n = 27 | n = 15 | n = 6 | n = 35 |
| Persistent | | 20 (57) | 13 (48) | 10 (67) | 5 (83) | 18 (51) |
| Decrease | | 13 (37) | 12 (44) | 5 (33) | 1 (17) | 15 (43) |
| Increase | | 2 (6) | 2 (8) | 0 (0) | 0 (0) | 2 (6) |
| Iris neovascularization, no. (%) | 0 (0) | n = 45 | n = 33 | n = 20 | n = 8 | n = 50 |
| | | 2 (4) | 1 (3) | 1 (15) | 1 (13) | 1 (2) |

Side-by-side comparison of documented slit-lamp and gonioscopy photographs from each follow-up visit was a sensitive method for detecting changes in pigmentation, pigment dispersion, vascularity, corectopia, and ectropion uveae. Both clinical and ultrasonographic signs of tumor regression were documented after $^{103}$Pd plaque irradiation of iris melanoma. Most tumors (64%) showed an increase in visible pigmentation, as opposed to decreased (22%) and persistent (12%) pigmentation. The sites of previous tumor biopsy showed presence of fibrous scarring (70%) that did not affect the patency of the 30% with small iridotomies after biopsy. Corectopia was a common presenting feature in iris melanomas that remained persistent during follow-up in most patients (76%). Six patients (12%) showed new-onset corectopia. Pre-existing ectropion uveae were documented to be persistent in 51% of patients and decreased in

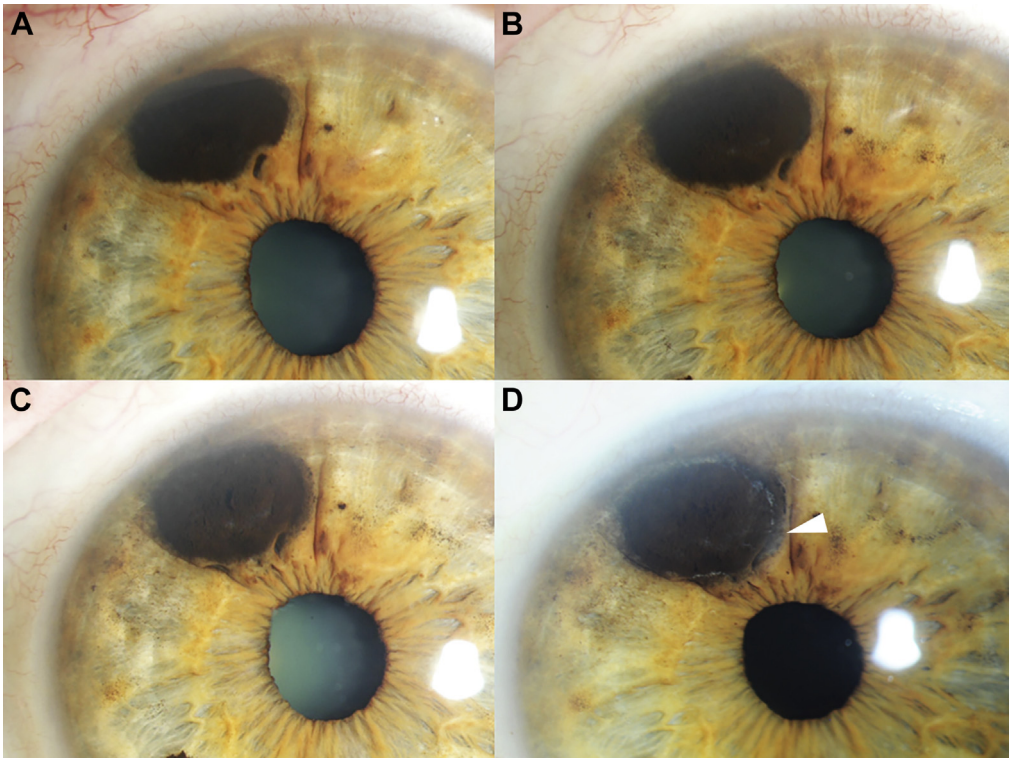


**Figure 1.** Slit-lamp photographs of a pigmented iris melanoma (**A**) before surgery, (**B**) 3 years after brachytherapy, (**C**) 5 years after brachytherapy, and (**D**) 10 years after brachytherapy. Note the progressively darkened pigmentation, surrounding atrophy (*arrowhead*), and result of the uneventful cataract repair.

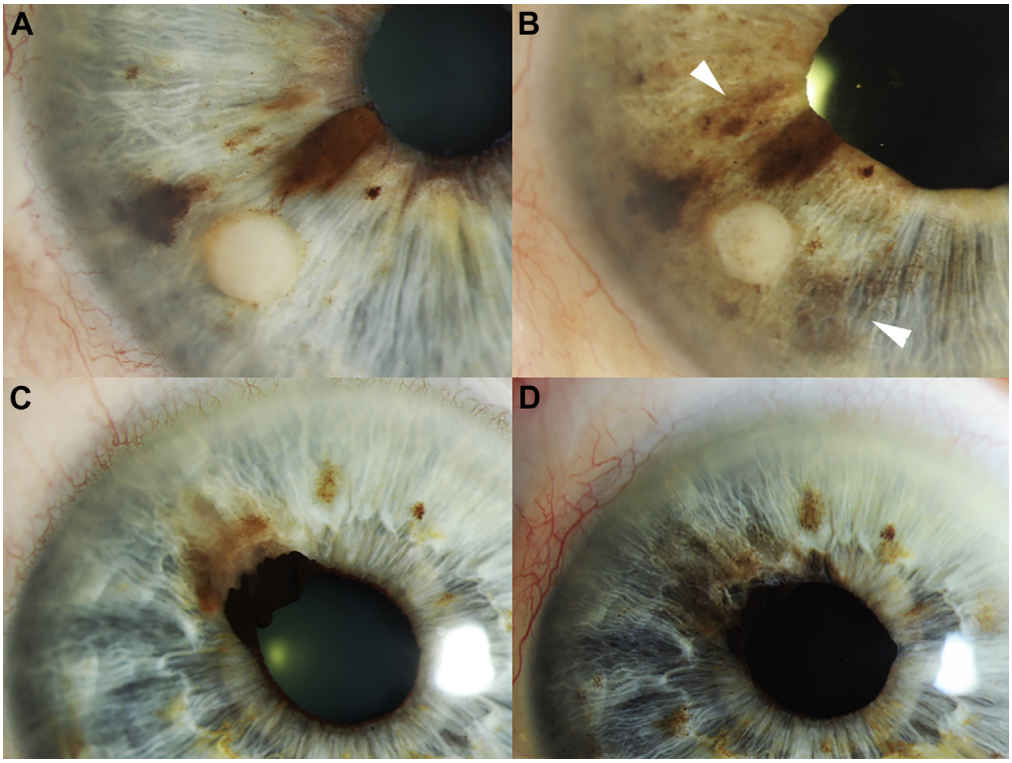


**Figure 2.** Slit-lamp photographs of an amelanotic iris melanoma (**A**) before surgery and (**B**) at 8 years after brachytherapy. Note pigment liberation onto the iris stroma (*arrowheads*) and reduced tumor size. Slit-lamp images of variably pigmented biopsy-proven iris melanoma (**C**) before palladium-103 plaque radiation and (**D**) at 10 years of follow-up. Note increased tumor pigmentation, partial resolution of ectropion uveae, and iris stromal atrophy.

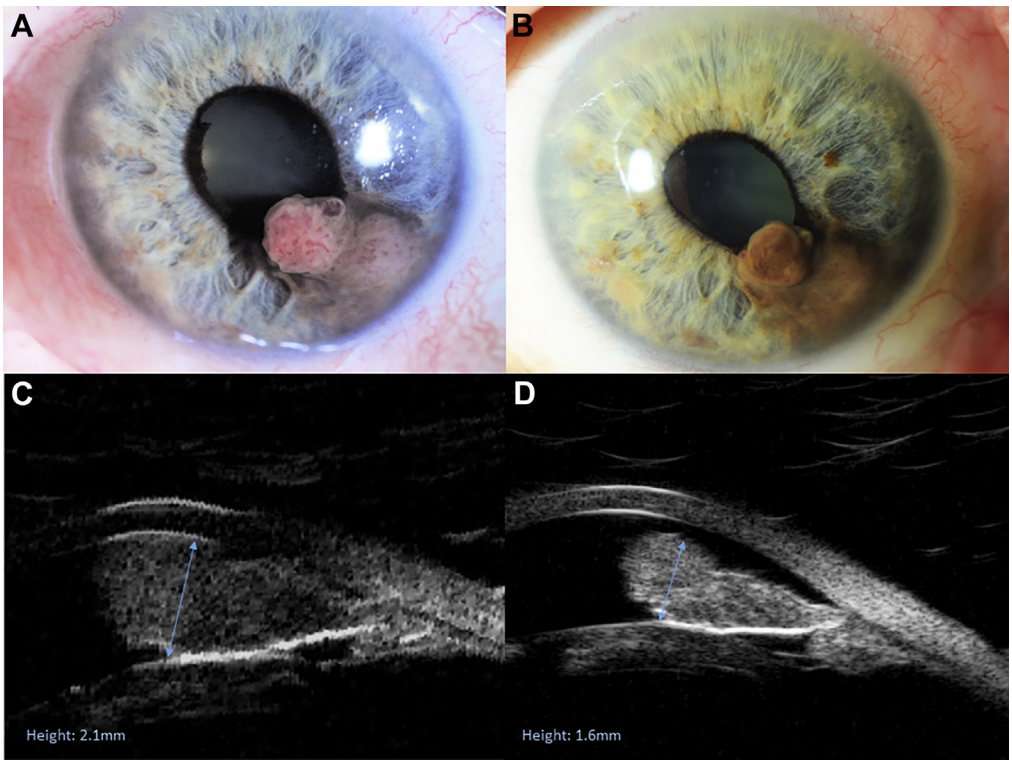


**Figure 3.** Slit-lamp photographs of an iris melanoma (**A**) before surgery and (**B**) at 1 year after brachytherapy. Note the progressively diminished intrinsic vascularity, increased tumor pigmentation, and persistent corectopia. Longitudinal sections of high-frequency ultrasound imaging (**C**) before surgery and (**D**) at 1 year of follow-up showing decreased tumor thickness (blue arrow measures tumor height in mm) and opening of the iridocorneal angle.

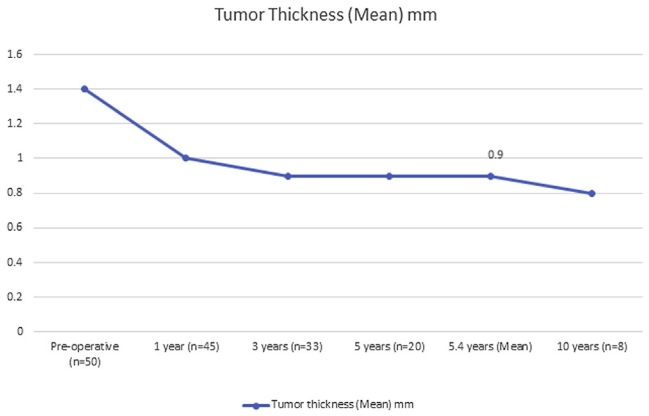


**Figure 4.** Graph showing tumor thickness uniformly declining until year 3, then tending to remain stable (within 0.1 mm).

43% of patients. Iris neovascularization developed in 2 patients (4%) within 1 year of radiation. It gradually resolved in 1 patient, whereas it progressed to cause neovascular glaucoma in the other patient at 3 years of follow-up.

It is important to note that partial reduction or complete elimination of intrinsic tumor vascularity was found to be the most consistent finding related to tumor regression. All eyes with visible pretreatment intratumoral vascularity (n = 19 [100%]) demonstrated a gradual decrease; of those, 37% (n = 7) showed complete resolution.

Table 5. Side Effects, Complications, and Vision, Ocular, and Systemic Outcomes*

| Variable | No. (n = 50) | % |
|---|---|---|
| Complication | | |
| Cornea | | |
| Focal corneal epitheliopathy | 3 | 6 |
| Corneal stromal edema | 0 | 0 |
| Persistent corneal opacity | 0 | 0 |
| Corneal necrosis | 0 | 0 |
| Scleromalacia | 0 | 0 |
| Iris stromal atrophy | 26 | 52 |
| Cataract† | 22 | 44 |
| Glaucoma, including neovascular glaucoma† | 1 | 2 |
| Nonproliferative retinopathy | 0 | 0 |
| Proliferative retinopathy | 0 | 0 |
| Maculopathy | 0 | 0 |
| Optic neuropathy | 0 | 0 |
| Vitreous hemorrhage | 0 | 0 |
| Outcomes | | |
| Visual outcome‡ | | |
| Good (20/16–20/40) | 42 | 84 |
| Intermediate (20/50–20/200) | 4 | 8 |
| Poor (<20/200) | 4 | 8 |
| Ocular outcome | | |
| Tumor recurrence | 0 | 0 |
| Enucleation | 0 | 0 |
| Eye salvage | 50 | 100 |
| Systemic outcome | | |
| Distant metastasis | 0 | 0 |
| No distant metastasis | 50 | 100 |

*At last follow-up.
†New-onset or worsening of pre-existing disease.
‡Final best-corrected visual acuity.

In the literature review, descriptions of regression of iris and iridociliary melanoma after brachytherapy have been limited mostly to ultrasonographically measured change in thickness.[25–27] For example, our present series showed gradual reduction in tumor thickness from a mean of 1.4 mm to 0.9 mm (−36%) over a median follow-up of 48 months. In addition, of the 42 tumors (84%) with low to moderate ultrasonographic internal reflectivity, 30 tumors (60%) showed an increase in internal reflectivity on regression. Similarly, Torres et al[27] found a 1.1-mm reduction in 4 ciliary body tumors in 23 months, and Shields et al[13] found that nonresectable iris and iridociliary melanomas decreased in ultrasonographically measured thickness after $^{125}$I plaque brachytherapy. Also, we previously reported a mean reduction of 1.4 mm in 24 cases of iris and iridociliary melanoma with a median follow-up of 30 months.[25] Commonly reported, increased ultrasonographic intratumoral reflectivity has been reported in prior studies as an indication of tumor regression.[25–27] Weisbrod et al[26] theorized that high reflectivity was histopathologically correlated with poorly cohesive cells with resultant large intercellular spaces. Therefore, the finding of increased internal reflectivity after plaque brachytherapy may represent a decrease in the density or discohesion of the uveal melanoma cells within treated tumors, a finding supported by our observations of postirradiation pigment dispersion. But as pointed out in 2007, these changes in internal reflectivity do not always correlate with reduction in tumor thickness, and reflectivity changes should be monitored along with change in tumor dimensions.[25] Moreover, iris and iridociliary melanomas have been reported to appear in various shapes: nodular, dome, flat, and diffuse. Their surface configuration can be smooth or irregular. Their color can be melanotic or amelanotic or can demonstrate variable pigmentation. They can be unifocal or multifocal as well as have satellite lesions.[4,7,8] Thus, a single measure of change in measured thickness does not comprehensively describe findings associated with regression of iris melanomas.

In this study, $^{103}$Pd plaque brachytherapy of iris melanomas has demonstrated diminution of intrinsic tumor vascularity, darkening of tumor surface, and decreased tumor thickness. Although the finding of ectropion uvea showed diminution (43%), there was new-onset corectopia (12%). Iris stromal atrophy and cataract formation were the most common radiation-related complications. However, the atrophy was not severe enough to affect vision and the cataracts were repaired without complication. Neovascular glaucoma occurred in 1 patient (2%). There was no evidence of radiation-related corneal opacity, scleromalacia, retinopathy, maculopathy, or optic neuropathy.[28] With 100% local and systemic control at a mean duration of 63 months after $^{103}$Pd plaque brachytherapy, we found this to be a safe and effective pupil-sparing treatment for iris melanomas. Both clinical and ultrasonographic findings can be used to monitor regression of iris melanomas after radiation therapy.

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Abbreviations and Acronyms:
**FIT** = finger iridectomy technique; **Gy** = gray; **IPE** = iris pigment epithelium; **$^{125}$I** = iodine 125; **$^{103}$Pd** = palladium 103.

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