

Pd-103 Plaque Brachytherapy for Treatment of Small Choroidal Melanoma

Low rate of metastasis in a series with more than 4 years' mean follow-up.

BY EKATERINA A. SEMENOVA, MD; AND PAUL T. FINGER, MD

Uveal melanomas of any size and location can metastasize.¹⁻⁵ However, the risk of metastasis for smaller melanomas is lower than for larger tumors.^{2,5} The Collaborative Ocular Melanoma Study found that increasing tumor size was related to increasing mortality risk.² Nonetheless, metastatic death from small choroidal melanomas has been reported in 12%, 29%, and in even higher percentages of patients with failure of local control.⁵ In a review of 7369 cases, the Ophthalmic Oncology Task Force of the American Joint Committee on Cancer (AJCC) also determined that melanoma size could be used to predict metastasis.⁵ Certainly, all can agree that any treatment that prevents metastasis, preserves eyes, and saves vision in patients with choroidal melanoma is highly desirable. However, all current treatments risk loss of vision.⁶

Earlier this year we reported results with the use of palladium-103 (Pd-103) brachytherapy for small choroidal melanoma in 72 patients.¹ More recently, we presented an update of those results.⁷ This paper recaps highlights of that presentation at the American Society of Retina Specialists meeting in Toronto, Canada.

STUDY POPULATION, DESIGN

A total of 91 patients with small choroidal melanoma were included in this retrospective case series. The maximum tumor apical height was 2.5 mm, maximum basal dimension was 10 mm, and all lesions fell within the T1 stage as defined by the *AJCC staging manual, 7th edition*.⁸

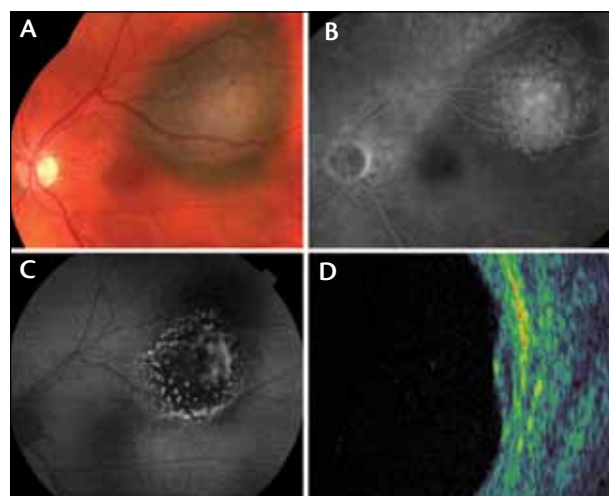


Figure 1. A small choroidal melanoma. Fundus photography reveals a small parafoveal melanoma with orange pigment lipofuscin (A). Fluorescein angiography shows mottled tumor hyperfluorescence (B). Fundus autofluorescence image shows hyperautofluorescence of the orange pigment lipofuscin and subretinal fluid (C). B-scan shows moderately reflective choroidal tumor (D).

In most cases, tumor location was equatorial (56%); 16% were subfoveal, 13% were in the anterior choroid, and 6% were juxtapapillary.

Diagnostic technologies used to identify and follow these tumors included color fundus photography, fun-

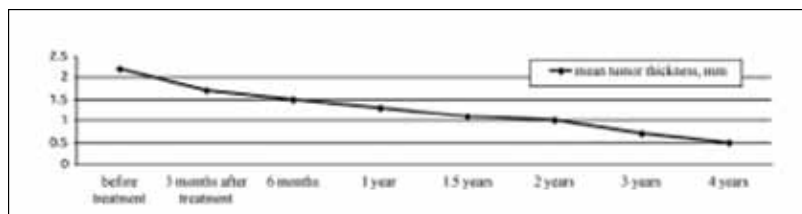


Figure 2. Mean tumor thickness regressed in 91 patients with small choroidal melanoma. Regression continues beyond 4 years.

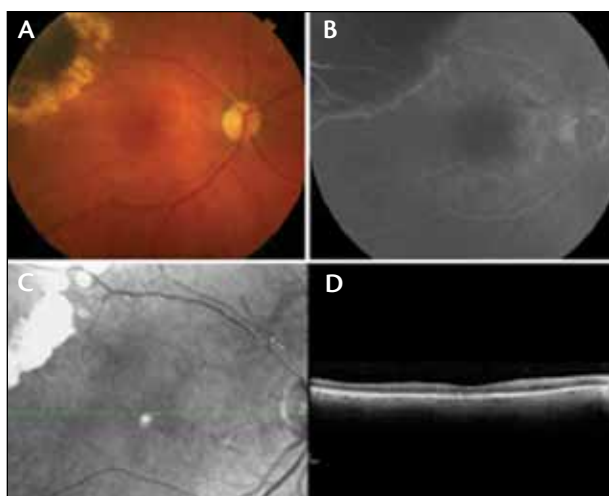


Figure 3. Case example of radiation retinopathy. Visual acuity 20/40. Fundus photography shows flat regressed choroidal melanoma, 9 years after Pd-103 plaque radiation therapy (A). Radiation maculopathy and radiation optic neuropathy are suppressed with monthly intravitreal anti-VEGF injections. Fluorescein angiography shows capillary dropout in the macula, retinal neovascularization, microaneurysms, and mild retinal edema (B). OCT shows flat fovea and slightly atrophic retina with no subretinal or intraretinal fluid (C,D).

dus autofluorescence imaging (FAF), optical coherence tomography (OCT), fluorescein angiography, and B-scan ultrasonography (Figure 1).

A metastatic survey was performed on all patients at initial staging using whole-body positron emission tomography/computed tomography (PET/CT) or contrast-enhanced chest and abdominal CT or MRI. Follow-up examinations included abdominal imaging studies with either CT or MRI, performed every 6 months for the first 3 years and then once yearly thereafter.

Plaques used for brachytherapy in this study included standard round plaques (n=75), notched plaques (n=13) before 2005, and more recently Finger's slotted plaques (n=3). The latter allow the optic nerve sheath to enter

the plaque so that it can be advanced more posteriorly. This posterior shift has been found to allow the plaque to surround the entire tumor, normalizing plaque radiation. It is key to remember that the Pd-103 seeds are the radioactive elements, not the plaque itself. Radioactive seeds within the plaque are located around the notch, providing complete irradiation of juxtapapillary tumor.

Radiation dose was calculated by medical physicists based on the recommendations of the American Association for Physicists in Medicine and the American Brachytherapy Society.⁹ Case selection conformed to the most recent consensus guidelines of the ABS Ophthalmic Oncology Task Force.¹⁰ The mean dose to the tumor apex was 82.3 Gy; the mean dose to the macula was 47.1 Gy, to the optic disc 39.0 Gy, and to the lens 5.6 Gy. The relatively high doses to the macula and optic nerve reflect the posterior positions of many of the tumors.

RESULTS

With a mean 54 months (range, 8–127) of observation, local tumor control was achieved in 90 of 91 patients (99%). Metastatic disease was seen in 1 patient (1%). Mean tumor thickness regressed over time (Figure 2). Regression also continued beyond the 4 years shown on the graph; the longest follow-up is currently more than 10 years.

No sight-limiting complications were seen in 44 patients (48.4%). Radiation maculopathy (RM) was noted in 47.3% of patients, in whom the mean radiation dose to the macula was 76.5 (range, 55.0–218.3) Gy. Radiation optic neuropathy (RON) was seen in 18 patients (19.8%), in whom the mean radiation dose to the optic disc was 86.9 (range, 54.2–219.0) Gy. There was comorbid RM and RON in some patients, so these percentages include some overlap (Figure 3).

The visual acuity results of these complications were analyzed based on the availability of anti-VEGF therapy at the time of initial brachytherapy treatment. In patients treated before 2004, 25 developed RM and/or RON, and none of these patients received anti-VEGF therapy. Among these patients, 11 maintained their initial visual acuity, and 14 lost a mean of 3 lines of visual acuity at a mean of 56 (range, 13–127) months. The mean last measured visual acuity in this group was 20/160 (range, 20/16–count fingers).

Of those treated after the introduction of anti-VEGF therapy, 21 patients developed RM and/or RON, and

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these patients received anti-VEGF therapy to suppress radiation-induced vasculopathy. In this group, visual acuity improved by a mean of 1 line in 7 patients, remained stable in 10 patients (mean 23 months follow-up on anti-VEGF therapy), and decreased by a mean of 2 lines in 4 patients (mean 35 months follow-up on anti-VEGF therapy). The mean last measured visual acuity in this treated group was 20/25 (range, 20/10–20/63).

It should be noted that the group receiving anti-VEGF therapy was treated more recently, so the follow-up periods are different between the 2 groups.

In the study population as a whole, 82 patients (90.1%) had a final visual acuity of 20/200 or better. Overall mean visual acuity prior to treatment was 20/40, and overall mean final visual acuity was 20/80. From baseline to final examination, in 19 patients (20.9%) visual acuity improved, in 40 (44%) it remained unchanged, and in 32 (38.5%) it declined.

Vision loss was related to RM or RON in most cases (n=28); other causes included preexisting foveal detachment (n=1), exudative macular degeneration (n=2), and secondary enucleation (n=1).

CONCLUSIONS

Treatment decisions for small choroidal melanomas are particularly difficult. Many of these melanomas are centrally located, where treatment carries the greatest risk for loss of visual acuity. This is why many eye cancer specialists suggest observation for growth before treating the tumor. On the other hand, patients must also be aware that waiting for a malignant tumor to grow carries a small and as yet unquantified risk of metastasis.

This study demonstrates the results of Pd-103 plaque radiation treatment of small (T1) choroidal melanomas. We achieved 99% local control and eye preservation at a mean 54 months of observation (range 8–127 months); 99% of the patients are free of metastasis. The low rate of metastasis is associated with our high rate of local control.

Anti-VEGF therapy was capable of suppressing RM and RON, resulting in preservation of vision. In the group treated with anti-VEGF therapy in this study, mean final visual acuity was 20/25.

Pd-103 plaque radiation of small choroidal melanoma offered excellent local control, a low rate of metastasis, and preservation of vision. ■

Ekaterina A. Semenova, MD, is a postdoctoral clinical research fellow at the New York Eye Cancer Center. She may be reached at esemenova@eyecancer.com.



Paul T. Finger, MD is the Director of The New York Eye Cancer Center and of Ocular Tumor Services at The New York Eye and Ear Infirmary, New York University School of Medicine, and affiliated hospitals. This research was supported by The Eye Cancer Foundation (<http://eyecancerfoundation.net>). Dr. Finger may be reached at +1 212 832 8170; or at pfinger@paultfingermd.com.



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