Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma
Treatment Complications and Visual Outcomes in 650 Consecutive Cases

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The choice of treatment for choroidal melanoma near the optic disc (juxtapapillary melanoma) is often influenced by the expected outcomes and complications of available methods. Such treatment modalities include plaque radiotherapy,1-3 proton beam radiotherapy,4,5 stereotactic radiosurgery,6-8 transpupillary thermotherapy (TTT),9 or enucleation.10 In a previous report, equivalent survival of patients with juxtapapillary melanoma treated by enucleation vs plaque radiotherapy has been documented.11 Detailed information on the radiotherapy risks to these eyes has received little attention in the literature. Known complications of plaque radiotherapy with or without TTT include retinopathy, maculopathy, papillopathy, cataract, glaucoma, retinal vascular occlusion, and secondary enucleation.12-16 In some centers, plaque radiotherapy is commonly followed with adjunctive TTT to consolidate regressed melanoma or to reduce intraocular exudative response.9,16 In this report, we analyze treatment-related complications and visual acuity outcomes in the same cohort as our previous report on tumor control.17

Methods

Our methods of clinical examination, diagnosis, and treatment have been described elsewhere.18 After Wills Eye Hospital Institutional Review Board approval, the electronic database of patients treated at the Ocular Oncology Service was searched for juxtapapillary choroidal melanoma with a posterior margin within 1 mm of the optic disc and treated with plaque radiotherapy. We retrospectively collected data on pa...
tient age, sex, medical history (hypertension, diabetes mellitus, hypercholesterolemia, dysplastic nevus syndrome, and skin melanoma), family history (choroidal or skin melano- 
ma), ocular symptoms, examination findings (visual acuity, anterior segment details, and intraocular pressure), and tumor 
findings (quadrant of tumor epicenter, number of clock 
hours encompassing the optic nerve, distance in millimeters 
to the optic disc, percentage of overhang of the optic disc by 
the tumor, distance in millimeters to the foveola, largest basal 
diameter in millimeters, shape, growth pattern, color, extra-
ocular extension, retinal invasion, subretinal fluid, orange pig-
ment, optic disc swelling, and retinal vascular congestion). 
Plaque radiation details included radioactive isotope (iodine 
125, ruthenium 106, cobalt 60, or iridium 192), shape (round, 
notched, or postage stamp), distribution (full or posterior), time 
of radiation exposure (hours), total radiation dose and dose 
rates to the tumor apex, tumor base, optic disc, foveola, and 
len. Adjunctive treatment details included the number of TTT 
sessions and treatment to the foveolar area. Early cases that 
had argon or krypton laser photocoagulation as adjunctive 
therapy and argon laser photocoagulation or TTT as a pri-
mary treatment were excluded from outcomes analysis. Fol-
low-up data included radiation-related nonproliferative and 
proliferative retinopathy, maculopathy, papillopathy, cata-
ract, neovascular glaucoma, scleral necrosis, and central or 
branch arterial and venous occlusion. Nonproliferative reti-
opathy was defined as the presence of retinal microangiopa-
thy in the absence of retinal, optic disc, or iris neovasculariza-
tion and in the absence of known retinal vascular occlusion. 
Secondary enucleation rates were also ascertained.

The cumulative probability of each complication was es-
timated at different follow-up points using Kaplan-Meier analy-
sis. A series of univariate analyses using the Cox propor-
tional hazards model were performed to identify factors predictive 
of complications based on clinical features at presentation and 
treatment parameters. Subsequent multivariate analyses using 
the Cox proportional hazards model were performed using the 
forward stepwise method for factors identified to be signifi-
cant at \( P \leq .05 \) in the univariate analyses. Hazard ratios (HRs) 
with 95% CIs were calculated for each risk factor. Compari-
sions between groups receiving TTT and not receiving TTT were 
performed using an independent sample \( t \) test (continuous vari-
ables), Wilcoxon rank sum test (nonparametric numerical vari-
ables), and \( \chi^2 \) test (categorical variables).

**Results**

From October 1, 1974, through November 30, 2005, a total of 650 
eyes with juxtapapillary choroidal melanoma received plaque 
radiotherapy. There were 549 eyes with a minimum follow-up 
of 3 months treated with primary plaque radiotherapy and in-
cluded in the analysis. The median follow-up was 40 months 
(range, 3-284 months). Demographic and tumor features at pre-
sentation and plaque radiotherapy parameters have been re-
ported for this group in our previous report.17

Complication rates were assessed by Kaplan-Meier analy-
sis (Table 1). By 5 years, 66% of eyes developed nonprolifica-
tive radiation retinopathy, and 24% developed proliferative ra-
diation retinopathy. Radiation maculopathy occurred in 56% 
of eyes and radiation papillopathy in 61% of eyes by 5 years. 
Neovascular glaucoma developed in 15% of eyes by 5 years. 
Secondary enucleation became necessary in 16% of eyes by 5 
years. There were no cases of scleral necrosis.

Although this was not a case-control study, outcomes of 
eyes receiving plaque radiotherapy plus TTT (n = 307) were 
compared with those treated with plaque radiotherapy alone 
(n = 242). Maculopathy and papillopathy developed in a higher 
proportion in the TTT vs no TTT group (65% vs 46% at 5 years; 
\( P < .001 \), log-rank test; and 66% vs 53% at 5 years, respec-
tively; \( P = .002 \)) and neovascular glaucoma in a lower propor-
tion (9% vs 19% at 5 years; \( P = .004 \)). Secondary enucleation 
rates were lower in the TTT group at 5 years after treatment 
(10% vs 21%; \( P = .01 \), log-rank test). The remaining complica-
tion outcomes revealed no difference with respect to TTT.

At a median follow-up of 40 months, secondary enucle-
lation was required in 69 eyes (13%), giving a globe retention 
rate of 87%. In the TTT group, 21 eyes (7%) were enucleated 
at a median follow-up of 33 months. Reasons for enucleation 
in this group were tumor recurrence in 10 eyes (48%), neovas-

![Table 1. Outcomes for Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma in 549 Consecutive Patients*](https://example.com/table1)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>At 1 y</th>
<th>At 2 y</th>
<th>At 5 y</th>
<th>At 10 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinopathy, non-proliferative</td>
<td>67/417(13)</td>
<td>185/240(40)</td>
<td>267/61(66)</td>
<td>278/6(75)</td>
</tr>
<tr>
<td>Retinopathy, proliferative</td>
<td>16/454(3)</td>
<td>42/344(9)</td>
<td>86/145(24)</td>
<td>97/35(32)</td>
</tr>
<tr>
<td>Maculopathy</td>
<td>58/425(11)</td>
<td>156/260(34)</td>
<td>222/90(56)</td>
<td>235/23(65)</td>
</tr>
<tr>
<td>Papillopathy</td>
<td>49/430(9)</td>
<td>147/259(32)</td>
<td>233/68(61)</td>
<td>252/13(77)</td>
</tr>
<tr>
<td>Cataract</td>
<td>75/359(16)</td>
<td>133/248(31)</td>
<td>235/64(66)</td>
<td>253/10(80)</td>
</tr>
<tr>
<td>Neovascular glaucoma</td>
<td>11/460(2)</td>
<td>23/360(5)</td>
<td>50/155(15)</td>
<td>58/39(22)</td>
</tr>
<tr>
<td>Vitreous hemorrhage</td>
<td>36/437(7)</td>
<td>86/312(19)</td>
<td>134/122(35)</td>
<td>143/31(42)</td>
</tr>
<tr>
<td>Enucleation</td>
<td>13/460(3)</td>
<td>27/362(6)</td>
<td>54/153(16)</td>
<td>64/35(26)</td>
</tr>
<tr>
<td>Visual acuity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final visual acuity ≤20/200(^a)</td>
<td>30/404(7)</td>
<td>75/320(18)</td>
<td>201/138(54)</td>
<td>289/30(87)</td>
</tr>
<tr>
<td>Visual loss, &gt;5 Snellen lines(^b)</td>
<td>15/404(3)</td>
<td>48/320(12)</td>
<td>148/138(45)</td>
<td>217/30(78)</td>
</tr>
</tbody>
</table>

\(^a\) Of the 650 patients with juxtapapillary choroidal melanoma, 549 were treated with primary plaque radiotherapy and had adequate follow-up for this analysis. 
\(^b\) Excludes previous pseudophakia and nonradiation cataract cases. 

Enucleations excluded.

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*Choroidal Melanoma Plaque Radiotherapy*
Comparison of eyes receiving TTT with those that did not revealed that the proportion with visual acuity of 20/200 or less was greater in the TTT group (61% vs 46% at 5 years; 5% < .001, log-rank test), and the proportion of eyes losing more than 5 Snellen visual acuity lines was also greater in the TTT group (52% vs 37% at 5 years; 5% < .001, log-rank test).

Factors predictive of complications and visual acuity outcomes were examined using the Cox proportional hazards model (Tables 2, 3, 4 and 5). The predictive factors that carried the highest HRs were hypertension for nonproliferative radiation retinopathy (HR, 1.37; 95% CI, 1.05-1.80), mean tumor thickness for proliferative radiation retinopathy (HR, 1.19; 95% CI, 1.11-1.28), and vision at presentation of 20/60 or better vs worse than 20/60 for radiation maculopathy (HR, 1.57; 95% CI, 1.09-2.25). Mean plaque size was the parameter with the highest HR (HR, 1.08; 95% CI, 1.02-1.14) for radiation papillopathy. Mean tumor thickness was the factor with the highest predictive value for radiation neovascular glaucoma (HR, 1.41; 95% CI, 1.19-1.66).

Factors predictive of retinal vein and artery occlusion are listed in eTable 1 and eTable 2 in the Supplement. A greater number of TTT sessions was a predictive factor for minor branch vein, major branch vein, and combined vein occlusion types and for minor branch artery and major branch artery occlusion. However, the number of TTT sessions was not predictive of central retinal vein occlusion. Instead, the strongest factor was optic disc swelling on presentation. Clinical factors and treatment parameters predictive of enucleation by multivariable analysis included tumor recurrence (HR, 40.98; 95% CI, 11.63-144.40), presence of radiation neovascular glaucoma (HR, 30.83; 95% CI, 8.96-106.10), and absence of nonproliferative radiation retinopathy (HR, 8.13; 95% CI, 3.56-18.58).

Factors predictive of final visual acuity of 20/200 or less included the presence of radiation papillopathy (HR, 1.45; 95% CI, 1.07-1.95) and radiation cataract (HR, 1.66; 95% CI, 1.23-2.25). Factors predictive of loss of more than 5 Snellen visual acuity lines included initial visual acuity of 20/60 or better (HR, 5.08; 95% CI, 2.78-9.27) and radiation cataract (HR, 1.72; 95% CI, 1.22-2.42). The use of TTT laser was not significant for visual loss in the multivariable analysis.

### Table 2. Factors at Initial Presentation and Treatment Predictive of Complications for Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma in 549 Consecutive Patientsa

<table>
<thead>
<tr>
<th>Complication</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonproliferative radiation retinopathy (n = 278)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (yes v no)b</td>
<td>1.37 (1.05-1.80)</td>
<td>.02</td>
</tr>
<tr>
<td>Radiation rate at disc</td>
<td>1.03 (1.00-1.05)</td>
<td>.03</td>
</tr>
<tr>
<td>Proliferative radiation retinopathy (n = 96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor thickness</td>
<td>1.19 (1.11-1.28)</td>
<td>.01</td>
</tr>
<tr>
<td>Radiation dose at base</td>
<td>1.00 (1.00-1.01)</td>
<td>.01</td>
</tr>
<tr>
<td>Radiation maculopathy (n = 311)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual acuity (≥20/60 vs &lt;20/60)</td>
<td>1.57 (1.09-2.25)</td>
<td>.02</td>
</tr>
<tr>
<td>Plaque size</td>
<td>1.07 (1.01-1.14)</td>
<td>.03</td>
</tr>
<tr>
<td>Radiation dose at apex</td>
<td>0.98 (0.96-0.99)</td>
<td>.002</td>
</tr>
<tr>
<td>Radiation papillopathy (n = 253)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque size</td>
<td>1.08 (1.02-1.14)</td>
<td>.01</td>
</tr>
<tr>
<td>Duration of radiotherapy</td>
<td>0.93 (0.88-0.98)</td>
<td>.005</td>
</tr>
<tr>
<td>Radiation cataract (n = 258)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.02 (1.01-1.03)</td>
<td>.001</td>
</tr>
<tr>
<td>Diabetes mellitus (yes v no)b</td>
<td>1.52 (1.02-2.27)</td>
<td>.04</td>
</tr>
<tr>
<td>Tumor thickness</td>
<td>1.17* (1.09-1.25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Plaque size</td>
<td>1.10 (1.02-1.19)</td>
<td>.01</td>
</tr>
<tr>
<td>Radiation neovascular glaucoma (n = 59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor thickness</td>
<td>1.41b (1.19-1.66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation dose at base</td>
<td>1.00 (1.00-1.01)</td>
<td>.04</td>
</tr>
<tr>
<td>Vitreous hemorrhage (n = 146)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extraocular extension (&gt;3 mm vs none)</td>
<td>27.12 (3.36-2.20)</td>
<td>.002</td>
</tr>
<tr>
<td>Radiation dose at base</td>
<td>1.00 (1.00-1.01)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation dose at lens</td>
<td>1.01 (1.00-1.02)</td>
<td>.02</td>
</tr>
</tbody>
</table>

* Of the 650 patients with juxtapapillary choroidal melanoma, 549 were treated with primary plaque radiotherapy and had adequate follow-up for this analysis.

b Reference variable.

### Table 3. Clinical Factors Predictive of Enucleation for Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma in 549 Consecutive Patientsa

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enucleation (n = 69)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior distribution (no v yes)b</td>
<td>3.90 (1.58-9.65)</td>
<td>.003</td>
</tr>
<tr>
<td>Radiation rate at base</td>
<td>1.07 (1.02-1.12)</td>
<td>.001</td>
</tr>
<tr>
<td>Tumor recurrence (yes v no)b</td>
<td>40.98 (11.63-144.40)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation retinopathy, nonproliferative (absent v present)b</td>
<td>8.13 (3.56-18.58)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation neovascular glaucoma (present v absent)</td>
<td>30.83 (8.96-106.10)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Of the 650 patients with juxtapapillary choroidal melanoma, 549 were treated with primary plaque radiotherapy and had adequate follow-up for this analysis.

b Reference variable.

Per 1 Gy/hour increase.
Table 4. Clinical Factors Initially Predictive of Poor Final Visual Acuity (Visual Acuity Loss >5 Snellen Lines) for Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma in 549 Consecutive Patients^a,b

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final visual acuity of ≥20/200 (n = 313)</td>
<td>1.16 (1.08-1.25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Plaque size</td>
<td>1.16 (1.08-1.25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation dose at apex</td>
<td>0.97 (0.95-0.98)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation rate at foveola</td>
<td>1.02 (1.01-1.04)</td>
<td>.002</td>
</tr>
<tr>
<td>Final tumor thickness</td>
<td>1.21 (1.10-1.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiation papillopathy (no v yes)</td>
<td>1.45 (1.07-1.95)</td>
<td>.02</td>
</tr>
<tr>
<td>Radiation cataract (no v yes)</td>
<td>1.66 (1.23-2.25)</td>
<td>.001</td>
</tr>
</tbody>
</table>

^a Of the 650 patients with juxtapapillary choroidal melanoma, 549 were treated with primary plaque radiotherapy and had adequate follow-up for this analysis.

^b Excludes enucleations.

^c Per 1-mm/y increase.

^d Per 100-cGy increase.

^e Per 10-cGy/h increase.

^f Reference variable.

Table 5. Clinical Factors Initially Predictive of Poor Final Visual Acuity (Visual Acuity Loss >5 Snellen Lines) for Plaque Radiotherapy for Juxtapapillary Choroidal Melanoma in 549 Consecutive Patients^a,b

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity loss &gt;5 lines (n = 238)</td>
<td>1.39 (1.01-1.92)</td>
<td>.04</td>
</tr>
<tr>
<td>Hypertension (yes v no)</td>
<td>1.39 (1.01-1.92)</td>
<td>.04</td>
</tr>
<tr>
<td>Visual acuity of ≥20/60 vs &lt;20/60^c</td>
<td>5.08 (2.78-9.27)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Plaque size</td>
<td>1.12^d (1.04-1.22)</td>
<td>.004</td>
</tr>
<tr>
<td>Radiation dose at apex</td>
<td>0.97^e (0.95-0.99)</td>
<td>.001</td>
</tr>
<tr>
<td>Radiation cataract (no v yes)</td>
<td>1.72 (1.22-2.42)</td>
<td>.002</td>
</tr>
<tr>
<td>Final tumor thickness</td>
<td>1.38^f (1.22-1.56)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

^a Of the 650 patients with juxtapapillary choroidal melanoma, 549 were treated with primary plaque radiotherapy and had adequate follow-up for this analysis.

^b Excludes enucleations.

^c Reference variable.

^d Per 1-mm increase.

^e Per 10-cGy/h increase.

Discussion

The treatment of juxtapapillary choroidal melanoma (tumor within 1 mm of the optic disc) is challenging because of the proximity of the tumor to visually important structures. A variety of treatment techniques have been developed, including plaque radiotherapy,^1,3 proton beam^4,5 or charged particle irradiation,^19 stereotactic radiosurgery,^6,7 TTT,^9,14 and enucleation.10 Optimal treatment choice is dictated by success rate and measured by tumor control and complication rates. In the current study, we report complication rates from plaque radiotherapy in a large series of eyes with juxtapapillary melanoma. Earlier reports^14 found equivalent survival rates for these patients when treated with plaque radiotherapy or primary enucleation. A detailed analysis of treatment complications after plaque radiotherapy in such a large cohort of this type of choroidal melanoma has been lacking in the literature. Analyses of treatment outcomes in special situations, where juxtapapillary melanoma circumscribes^20 or overhangs^21 the optic disc, have been previously reported.

Kaplan-Meier estimates at 5 years revealed nonproliferative retinopathy in 66% and proliferative retinopathy in 24% of eyes, with no significant difference between the TTT and no TTT groups. In a series of eyes with melanoma at any quadrant treated with combined plaque radiotherapy and TTT, the 5-year estimate for retinopathy has been reported at 39%.^16 The median proximity to the optic disc was 2 mm in that series and 0 mm in the current series. Other parameters, such as presence of diabetes (12% in the current study), tumor proximity to the fovea, tumor thickness, and radiation doses, were similar. Radiation retinopathy in 573 eyes with choroidal melanoma within 1.5 mm of the optic disc treated with proton beam irradiation was estimated at 60%.^5 For eyes with a melanoma within 2 mm of the optic disc treated with stereotactic radiosurgery, the 5-year rate of radiation retinopathy was 88%.^7

The 5-year probability by Kaplan-Meier analysis was 56% for maculopathy and 61% for papillopathy. Both of these outcomes were higher in the TTT group, reaching statistical significance (maculopathy P < .001; papillopathy P = .002, log-rank test). Maculopathy in the TTT group is the clinical end point of two possible processes: from radiation damage to the parafoveal capillaries and from retinal vein occlusions that occurred more frequently in TTT-treated eyes. However, the no TTT group is a historically earlier group, when optical coherence tomography was not available to detect subclinical macular edema. The higher probability of papillopathy could be related to the additional thermal damage that occurs with TTT. In an earlier report, the 5-year estimates for maculopathy and papillopathy were 18% and 38%, respectively, for melanomas at all choroidal locations treated with combination plaque radiotherapy and TTT.16 The Collaborative Ocular Melanoma Study (COMS) reported a 5-year prevalence of optic neuropathy of 27% and fluorescein angiographic evidence of maculopathy of 75%.23 In the current study, these estimates are higher because of the proximity of treatment delivery to visually important structures. In eyes with juxtapapillary melanoma undergoing ruthenium 106 plaque radiotherapy, the 5-year risk of at least some degree of optic neuropathy was 66%,^23 similar to our results. In eyes with tumors that touched the optic disc treated with proton beam irradiation, optic neuropathy was found in 81% at 5 years, and in 93 eyes with tumors within 1 disc diameter of the optic disc, papillopathy occurred in 68% at a median of 1.5 years.24,25 In a report on the outcomes of proton beam radiotherapy, the cumulative rates of maculopathy or papillopathy in 573 eyes with melanoma within 1.5 mm of the optic disc were 49% at 5 years and greater than 60% at 10 years.^5

For neovascular glaucoma, the 5-year risk was 15%, with a significantly lower proportion in the TTT group by 5 years (9% vs 19% for the TTT group vs no TTT group) and beyond. In a series of 270 eyes with choroidal melanoma at all locations treated with combined plaque radiotherapy and TTT, the 5-year risk of neovascular glaucoma was 7%,^16 similar to the 9% found in the TTT group in our current series. For proton beam irradiated eyes, although not specifically for juxtapap-
illary melanomas, neovascular glaucoma was reported in 15% by 3 years.24 Other studies reported higher rates of neovascular glaucoma for proton beam or charged particle irradiation compared with eyes undergoing iodine 125 plaque brachytherapy19,26 and a 42% occurrence in stereotactic radiosurgery-treated eyes.27,28

Branch retinal artery occlusion and branch retinal vein occlusion were related to the use of TTT. This is a result of the thermal collateral damage that occurs to normal tissues when TTT is applied for tumor treatment. A similar effect on branch vascular occlusion has been reported in eyes with small choroidal melanoma treated with TTT alone.14

Our secondary enucleation rate at 5 years was 16%, with a significantly lower proportion in the TTT group compared with the no TTT group. Reasons for enucleation included tumor recurrence and neovascular glaucoma. Our results indicate that the effect of TTT on neovascular glaucoma and enucleation is protective, possibly because of reduction of intraocular edema after radiation to the tumor, and we recommend the use of adjuvant TTT for this reason.

In the COMS trial, one of the exclusion criteria for plaque radiotherapy was juxtapapillary melanoma contiguous with the optic disc.29 Such cases were advised to receive primary enucleation, but noncontiguous tumors that were within 2 mm of the optic disc and spanned less than 90° were enrolled in the radiotherapy arm, highlighting the difficulty of treating this subtype of melanoma. The 5-year estimate for secondary enucleation after plaque radiotherapy in the COMS trial was 13%.30 In the current series of eyes with juxtapapillary melanoma within 1 mm of the optic disc, our 5-year estimate for secondary enucleation was 16% overall, with a lower enucleation rate in the adjunctive TTT group at 5 years. In another study16 on combined treatment with plaque radiotherapy and TTT for all choroidal melanomas, enucleation for radiation complications was necessary in 3% at a median of 29 months of follow-up. In a series of juxtapapillary melanomas treated with ruthenium 106 plaque radiotherapy, secondary enucleation rates varied from 8% to 15% because of inadequate tumor regression.3,23 It is known that iodine 125 plaques emitting X-ray and γ radiation have deeper penetration than the β-rays of ruthenium 106, and in a comparative series between these isotopes used to treat choroidal melanoma in all locations, tumor control was lower in the ruthenium 106 group.26 The secondary enucleation rate in a series of eyes with melanomas within 3 mm of the optic disc or fovea, treated with proton beam irradiation with at least a 2-year follow-up, was 8%.30 A more recent analysis3 of proton beam treatment of 573 melanomas within 1.5 mm of the optic disc found a 5-year enucleation rate of 13%. For stereotactic radiosurgery, the 5-year enucleation rate was 16%.7 Our results in eyes with tumors closer to the optic disc reveal that a similar eye retention rate can be achieved with plaque radiotherapy.

A randomized clinical trial of plaque radiotherapy vs proton beam or heavy charged particle irradiation for juxtapapillary melanoma does not exist. Case-controlled studies for all choroidal melanomas report lower enucleation rates in plaque radiotherapy–treated eyes compared with eyes irradiated with either protons26 or heavy charged particles.19 In these and other reports,2,12,27 tumor recurrence and radiation complications are usually the reasons for requiring enucleation, which concurs with our findings.

Visual acuity in retained eyes was 20/200 or less in 54% at 5 years, and the number of eyes losing more than 5 Snellen visual acuity lines was 45% at 5 years, updating the results of our previous smaller study.7 A higher proportion lost vision in the TTT group by Kaplan-Meier analysis, but the use of TTT was not significant for visual loss in the multivariable analysis. Significant risk factors by multivariable analysis included radiation papillopathy, cataract, radiation rate to fovea, and final tumor thickness. Use of a wide-notched plaque reports visual loss to a median of 20/40 at 23 months, with use in some eyes of intravitreal antiangiogenic endothelial growth factor injections to suppress radiation maculopathy or optic neuropathy.31 With proton beam–treated patients, the 2-year risk of visual loss to 20/200 or less was 47% if tumors were near the optic disc or fovea30 and appears not to be radiation dose dependent at 5 years.32 In an additional report of tumors within 1 disc diameter of the optic disc, two-thirds of eyes had visual acuity of 20/200 or less.5 Visual field defects with enlargement of absolute scotoma occurred in more than 67% of eyes receiving proton beam radiation, related to retinal radiation field rather than development of radiation optic neuropathy.33 With stereotactic radiosurgery, visual loss can be anticipated in 90% at 5 years,7 although this appears to be radiation dose dependent.8 In the COMS trial, 43% of the iodine 125–treated eyes had visual acuity of 20/200 or worse at 3 years, and 49% lost 6 Snellen visual acuity lines, related to size and posterior location of the tumor.34 Our results are compatible with those of this series, although the inclusion criteria for the COMS trial were different than the criteria used for our study.

During the past 15 years, TTT has been used for choroidal melanoma management either in isolation in selected cases14 or more commonly as an adjunctive treatment in association with plaque radiotherapy.9,16 Our no TTT group represents a historically earlier group of eyes that received plaque radiotherapy using iodine 125, ruthenium 106, cobalt 60, or iridium 192, whereas those in the TTT group were treated with our current preferred radioisotope, iodine 125. Similarly, in the no TTT group, there was a lower proportion of eyes treated with notched plaque, but our current preferred plaque shape is a notched plaque, which is supplemented by TTT to cover the entire tumor margin in eyes with pigmented tumors and in situations where doubt might exist on the effectiveness of irradiation at the posterior margin on follow-up.

Conclusions

Our outcomes from this large series support the use of plaque radiotherapy for juxtapapillary melanoma because this treatment modality is associated with a high rate of globe retention. Not surprisingly, radiation-related papillopathy and maculopathy are common events, occurring in more than half of the cases by 5 years. The planned use of TTT appears to protect against neovascular glaucoma and secondary enucleation in the first 5 years after treatment.
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