

## Supplementary Online Content

Shields CL, Dalvin LA, Chang M, et al. Visual outcome at 4 years following plaque radiotherapy and prophylactic intravitreal bevacizumab (every 4 months for 2 years) for uveal melanoma: comparison with nonrandomized historical control individuals. *JAMA Ophthalmol*. Published online December 12, 2019. doi:10.1001/jamaophthalmol.2019.5132

**eTable 1.** Plaque Radiotherapy and Prophylactic Bevacizumab (Every 4 Months for 2 Years) for Uveal Melanoma in 1131 Eyes of 1131 Patients: Demographic Features

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Plaque radiotherapy and prophylactic bevacizumab (every 4 months for 2 years) for uveal melanoma in 1131 eyes of 1131 patients: Demographic features.**

<b>Demographic Features</b>	<b>Bevacizumab Group (n=1131) [n (%)]</b>	<b>Control Group (n=117) [n (%)]</b>	<b>p-values</b>
<b>Age (years)</b>			
Mean (median, range)	60 (61, 20-97)	59 (60, 19-87)	.55
<b>Race</b>			
Caucasian	1081 (96)	114 (97)	.74
African American	3 (<1)	0 (0)	
Hispanic	20 (2)	3 (3)	
Asian	1 (<1)	0 (0)	
Middle Eastern	3 (<1)	0 (0)	
Other/unknown	23 (2)	0 (0)	
<b>Sex</b>			
Male	557 (49)	59 (50)	.81
Female	574 (51)	58 (50)	
<b>Involved eye</b>			
Right	565 (50)	60 (51)	.79
Left	566 (50)	57 (49)	
<b>Medical History</b>			
Dysplastic nevus syndrome	4 (<1)	0 (0)	.13
Skin melanoma	36 (3)	3 (3)	.92
Diabetes	156 (14)	15 (13)	.77
Hypertension	478 (42)	48 (41)	.80
<b>Ocular history</b>			
Uveal melanoma (fellow eye)	1 (<1)	0 (0)	.16
Conjunctival melanoma	0 (0)	0 (0)	NA
Conjunctival primary acquired melanosis	2 (<1)	0 (0)	.45
Ocular melanocytosis	35 (3)	5 (4)	.50

**eTable 2. Plaque radiotherapy and prophylactic bevacizumab (every 4 months for 2 years) for uveal melanoma in 1131 patients: Plaque radiotherapy features.**

Plaque Radiotherapy Features	Bevacizumab Group (n=1131) [n (%)]	Control Group (n=117) [n (%)]	p-values
Total treatment duration (hours)			
Mean, (median, range)	101 (96, 21-173)	102 (97, 93-172)	.28
Plaque shape			
Round	849 (75)	91 (78)	<b>.04</b>
Notched	225 (20)	26 (22)	
Deep notched	57 (5)	0 (0)	
Distance from plaque (mm)			
Mean, (median, range)			
Tumor apex	6 (5, 3-14)	6 (5, 3-14)	.41
Tumor base	1 (1, 1-1)	1 (1, 1-1)	NA
Optic disc	12 (12, 5-23)	13 (13, 6-22)	.11
Foveola	11 (11, 1-23)	12 (11, 2-21)	.38
Lens	17 (17, 5-20)	16 (17, 9-20)	.26
Sclera	0 (0, 0-0)	0 (0, 0-0)	NA
Radiation Dose (Gy)			
Mean, (median, range)			
Tumor apex	70 (70, 35-83)	68 (70, 68-70)*	.09
Tumor base	184 (155, 46-605)	186 (149, 78-552)*	.93
Optic disc	38 (29, 4-217)	37 (31, 5-182)	.92
Foveola	57 (38, 4-508)	57 (40, 7-265)	.93
Lens	19 (11, 2-185)	22 (13, 3-103)	.14
Sclera	184 (155, 46-605)	212 (168, 89-631)	<b>.002</b>
Opposite retina	7 (5, 1-74)	7 (6, 2-21)	.43
Radiation Dose Rate (Gy/hour)			
Mean, (median, range)			
Tumor apex	72 (74, 38-99)	72 (74, 37-133)	.87
Tumor base	185 (164, 50-485)	189 (167, 62-434)	.55
Optic disc	38 (31, 4-230)	38 (31, 6-197)	.81
Foveola	58 (39, 2-374)	61 (40, 7-289)	.55
Lens	19 (12, 2-133)	22 (13, 1-103)	.06
Sclera	185 (164, 50-485)	209 (183, 96-434)	<b>.001</b>
Opposite retina	7 (5, 2-73)	7 (6, 2-17)	.08

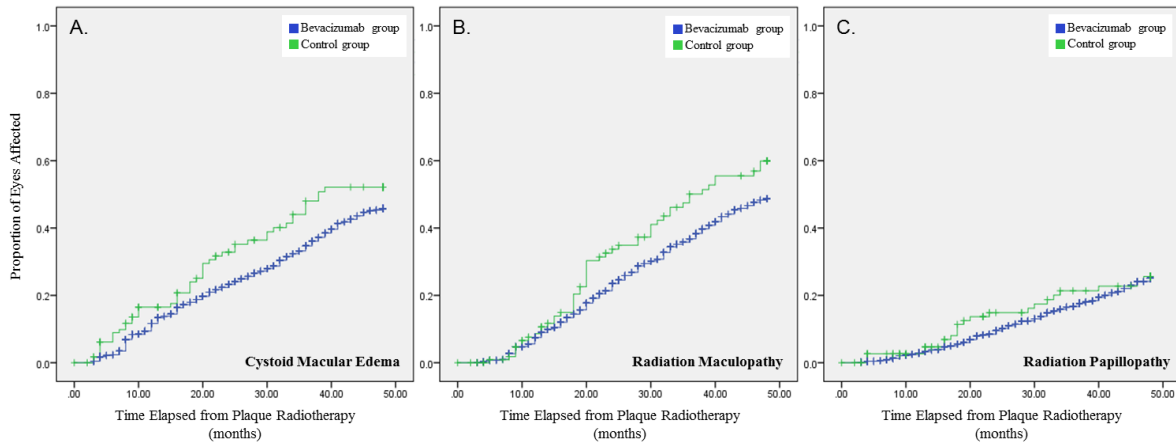
\*The definition of Gy changed in 2007, after which time our practice adjusted numerical radiation dosages to achieve equivalent radiation delivery to tumor apex and other structures. Patients in the control group were largely treated prior to this adjustment. When this is accounted for, mean radiation dose (median, range) to tumor apex and base in the control group is listed in the table. However, prior to this re-calculation the apex dose was recorded as 78 (80, 68-80), base dose as 212 (170, 89-631), apex dose rate as 80 (84, 43-152), and base dose rate as 207 (179, 71-434). Outcomes were adjusted in subsequent tables using multivariate analysis to account for the potential confounder of difference in radiation dosage. Bold type p values indicate significance.

**eFigure 1. Kaplan-Meier Analysis for Radiation Side Effects After Plaque Radiotherapy and Prophylactic Intravitreal Bevacizumab for Uveal Melanoma.**

(A) Comparison of patients treated with prophylactic intravitreal bevacizumab at 4-month intervals for a duration of two years versus controls managed with observation alone revealed the bevacizumab group was associated with reduced cumulative probability of OCT-evident CME at 4 months (2% vs. 6%, hazard ratio [HR]=3.49,  $p=0.002$ ), 24 months (28% vs. 37%, HR=1.52,  $p=0.02$ ) and 36 months (44% vs. 54%, HR=1.53,  $p=0.01$ ).

(B) The bevacizumab group was associated with reduced cumulative probability of clinically-evident radiation maculopathy at 24 months (27% vs. 36%, HR=1.5,  $p=0.03$ ), 36 months (44% vs. 55%, HR=1.48,  $p=0.01$ ) and 48 months (61% vs. 66%, HR=1.39,  $p=0.03$ ).

(C) The bevacizumab group was associated with reduced cumulative probability of radiation papillopathy at 4 months (0% vs. 3%, HR= 5.92,  $p=0.02$ ) and 18 months (6% vs. 12%, HR=2.02,  $p=0.04$ ).



Time interval	Bevacizumab Group (n=1131) n <sup>a</sup>	Control Group (n=117) n <sup>a</sup>
4 Months	33/1080	9/109
8 Months	61/978	7/94
12 Months	48/851	1/81
18 Months	42/674	11/72
24 Months	35/561	3/57
36 Months	45/369	6/42
48 Months	2/122	0/17

Time interval	Bevacizumab Group (n=1131) n <sup>a</sup>	Control Group (n=117) n <sup>a</sup>
4 Months	11/1090	1/111
8 Months	47/1012	7/103
12 Months	47/896	6/89
18 Months	67/721	16/76
24 Months	61/590	4/56
36 Months	44/374	6/40
48 Months	2/122	0/14

Time interval	Bevacizumab Group (n=1131) n <sup>a</sup>	Control Group (n=117) n <sup>a</sup>
4 Months	8/1083	3/111
8 Months	16/1005	0/100
12 Months	14/917	2/92
18 Months	29/776	6/79
24 Months	29/659	1/68
36 Months	18/436	1/58
48 Months	4/158	0/26

<sup>a</sup>Number of events/number at risk

**eFigure 2. Number of Patients with Available Follow-up Over the Course of Four Years After Plaque Radiotherapy and Prophylactic Intravitreal Bevacizumab for Uveal Melanoma.**

Comparison of patients treated with prophylactic intravitreal bevacizumab at 4-month intervals for a duration of two years versus controls managed with observation alone revealed 1131 versus 117 patients entering the study and 390 versus 66 patients with follow-up at four years.

