

The retinal breaks in our patients mostly were degenerative and rarely were flap or horse-shoe tears, because posterior vitreous detachment is unlikely to occur at such an early age at presentation.

The reported indications for surgical intervention in PDCL are the presence of RRD or phacolytic glaucoma and uveitis.^{1,4} Although most of the surgical patients in our study showed associated RRD, others underwent surgery for optical rehabilitation or to prevent or manage complications. The intervention type was decided by the age, lenticular changes, and presence of RRD. Most of the interventions were performed with a 25-gauge vitrectomy system. A 23-gauge system was used when lensectomy was planned before surgery with a vitrectomy cutter alone in relatively older patients (in the third decade of life or older). A 20-gauge phacolytic group because of the associated cataract changes. In patients with RRD, lensectomy was performed with the cutter itself. The visual outcome depended on the preoperative CDVA (visual potential) and associated complications. The visual outcome was limited mainly because of pre-existing amblyopia resulting from long-standing dislocation, coexistent glaucomatous neuropathy, and long-standing RRD.

To conclude, spontaneous PDCL can have multiple causes with additional ocular and systemic associations. Ophthalmologists should be able to identify the diagnostic clinical features, ocular associations and complications, and possible systemic associations in such patients.

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Abbreviations and Acronyms:

ACIOL = anterior chamber intraocular lens; AM = anterior megalophthalmos; CDVA = corrected distance visual acuity; EL = ectopia lentis; HMCF = hand movements close to face; IOP = intraocular pressure; MFS = Marfan syndrome; NSM = nonsyndromic myopia; PCIOL = posterior chamber intraocular lens; PDCL = posterior

dislocation of crystalline lens; PPV = pars plana vitrectomy; RRD = rhegmatogenous retinal detachment; SFIOL = scleral-fixated intraocular lens; SLT = selective laser trabeculoplasty.

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References

1. Nelson LB, Maumenee IH. Ectopia lentis. *Surv Ophthalmol.* 1982;27:143–160.
2. Cross HE. Differential diagnosis and treatment of dislocated lenses. *Birth Defects Orig Artic Ser.* 1976;12:335–346.
3. Nelson LB, Spaeth GL, Nowinski TS, et al. Aniridia. A review. *Surv Ophthalmol.* 1984;28:621–642.
4. Kumawat D, Alam T, Sahay P, Chawla R. Ocular abnormalities and complications in anterior megalophthalmos: a case series. *Eye (Lond).* 2019;33:826–832.
5. Loeys BL, Dietz HC, Braverman AC, et al. The revised Ghent nosology for the Marfan syndrome. *J Med Genet.* 2010;47:476–485.
6. Morris AAM, Kožich V, Santra S, et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. *J Inherit Metab Dis.* 2017;40:49–74.
7. Chen S-J, Lu P, Zhang W-F, Lu J-H. High myopia as a risk factor in primary open angle glaucoma. *Int J Ophthalmol.* 2012;5:750–753.



Anti-VEGF Therapy Immediately after Plaque Radiation Therapy Prevents or Delays Radiation Maculopathy



Radiation has become the treatment of choice for patients with intraocular melanoma.¹ However, radiotherapy causes site-specific collateral damage to surrounding structures, with radiation maculopathy (RM) causing irreversible vision loss.^{2,3} The risk of RM developing is related to total radiation dose, radiation dose rate, presence of synchronous systemic diseases, and use of radiation sensitizers.² Extraocular plaque location affects both the incidence and location of radiation complications.⁴ Specifically, radiation dose to the fovea has been used to predict RM and radiation-related vision loss.² Eyes at highest risk for RM include those with tumors in subfoveal or juxtafoveal locations as well as those where the radiation dose to the fovea is 50 Gy or more.^{2–4}

Early clinical signs of RM include cotton-wool spots, intra-retinal hemorrhages, and macular edema. Finger et al⁵ showed that treatment with anti-vascular endothelial growth factor (VEGF) at the onset of visually and clinically significant RM resulted in preservation of vision and less radiation-related retinal damage. We suspect that a dose-dependent, subclinical ischemic radiation vasculopathy begins at or immediately after the time of plaque placement, but only later becomes clinically apparent when it causes vision loss and progressive retinal ischemia. We evaluated whether early introduction of anti-VEGF therapy for eyes at

Table 1. Patient Demographics, Visual Acuity Characteristics, Radiation Maculopathy Features

Variables	Anti-Vascular Endothelial Growth Factor Group	Case-Matched Group	P Value*
Patient demographics			
Age (yrs)			
Median	60.5	69.5	
Mean (range)	60 (44–73)	69 (45–87)	0.055
Medical history (%) [†]			
Diabetes	7.1	0.0	0.500
Hypertension	28.6	14.3	0.242
AJCC uveal melanoma T-size category (%)			
T1	78.6	35.7	0.242
T2	21.4	64.3	0.242
Foveal dose (Gy)			
Mean (range)	108.0 (60.4–183.9)	108.4 (62.4–183.1)	0.971
Treatment interval (mos)			
Mean (range)	40 (26–60)	49 (24–98)	0.255
Time from plaque to anti-VEGF (days)			
Mean (range)	24 (7–113)	—	
Visual acuity characteristics			
Visual acuity at diagnosis			
Mean	20/25	20/40	
Proportion at 20/40 or better (%)	78.6	57.1	0.158
Visual acuity at final examination			
Mean	20/32	20/160	
20/40 or better (%)	85.7	28.6	0.003 [‡]
Equal to or better than VA at diagnosis (%)	64.3	28.6	0.054
Within 2 lines of VA at diagnosis (%)	35.7	0.0	0.020 [‡]
Loss of 3 or more lines of VA (%)	0.0	71.4	<0.001 [‡]
Radiation maculopathy			
Finger stage at final examination (%)			
0	50.0	14.3	0.045 [‡]
1	0.0	0.0	—
2	42.9	7.1	0.036 [‡]
3	7.1	64.3	0.002 [‡]
4	0.0	14.3	0.241

AJCC = American Joint Committee on Cancer; VA = visual acuity; VEGF = vascular endothelial growth factor; — = none.

*Fisher exact test.

[†]No patients had either diabetic or hypertensive retinopathy.

[‡] $P \leq 0.05$.

highest risk for radiation maculopathy can prevent or delay vision loss.

This retrospective, nonrandomized, interventional, comparative case-matched study was conducted at The New York Eye Cancer Center. This study adhered to the tenets of the Declaration of Helsinki and the Health Insurance Portability and Privacy Act of 1996. The ethics committee and institutional review board of The New York Eye Cancer Center approved this study. We retrospectively reviewed data for 14 consented patients from 2014 through 2017 diagnosed with choroidal melanoma, treated with palladium-103 (Pd^{103}) plaque radiotherapy, and subsequently treated every 4 to 6 weeks within 6 months of plaque placement with intravitreal injection of anti-VEGF bevacizumab before onset of RM. These patients were case matched—by radiation dose to fovea, proximity to fovea, and size of tumor—with 14 historical patients diagnosed with choroidal melanoma and treated with Pd^{103} plaque radiotherapy between 1999 and 2005, before the advent of anti-VEGF therapy.

Outcome measures include visual acuity (using Early Treatment Diabetic Retinopathy Study charts), clinical features of RM, macular anatomic measurements—specifically, central foveal

thickness on OCT using the Spectralis OCT2 Module (Heidelberg Engineering, Heidelberg, Germany)—and fluorescein angiography.

Descriptive statistics for the anti-VEGF treatment and case-matched groups are summarized for the following variables: demographics, tumor characteristics, and radiation dosage. The Fisher exact test was used to compare proportions between groups, and a *t*-test assuming unequal variances was used to compare means between groups.

Ophthalmic findings, radiation treatment parameters, visual acuity outcomes, and RM outcomes are outlined in Table 1. We studied those patients at highest risk of RM developing because of high foveal dose; mean foveal doses for the anti-VEGF and case-matched groups were similar, at 108.0 and 108.4 Gy, respectively.² According to the American Joint Committee on Cancer, 8th edition, staging system, tumor size ranged from T1 (anti-VEGF, $n = 11$; case matched, $n = 5$) to T2 (anti-VEGF, $n = 3$; case matched, $n = 9$).⁶ No significant difference was found in treatment interval, which was a mean of 40 months (range 26–60 months) for the anti-VEGF group and 49 months (range 24–98 months) for the case-matched group. Finally, although the anti-VEGF group showed a mean visual acuity at

diagnosis of 20/25 and the case-matched group started at 20/40, the difference between the two groups was not statistically significant.

In contrast, the visual acuities differed significantly at last follow-up. The anti-VEGF group showed an overall mean visual acuity of 20/32 at last follow-up, as compared with the case-matched group's mean visual acuity of 20/160. When compared with their visual acuities measured at the time of diagnosis, 9 patients (64.3%) in the anti-VEGF treated group showed improvement or no change in visual acuity, in contrast to only 4 patients (28.6%) in the case-matched group. At the last follow-up examination, 5 patients (35.7%) in the anti-VEGF group were within 2 lines of the pre-treatment visual acuity. In contrast, none of the patients in the case-matched group were within 2 lines of the pre-treatment visual acuity. No patient in the anti-VEGF group lost more than 3 lines of vision, compared with 10 patients (71.4%) in the case-matched group.

Improvements in visual acuity primarily were the result of resolution of the adjacent retinal detachment and intraretinal fluid associated with the subfoveal tumor. In this study, 5 of the anti-VEGF patients versus 2 case-matched eyes showed improvement in visual acuity. The mean visual acuity trend depicted in [Figure 1](#) (available at www.ophtalmologyretina.org) demonstrates relative stability over time for the anti-VEGF patients versus the case-matched patients. Initial visual acuities between the groups remained similar until 9 months after treatment. Then, the anti-VEGF group remained stable, whereas the case-matched group's vision declined.

Radiation retinopathy was graded using the Finger staging system for radiation retinopathy. At last follow-up, 7 anti-VEGF patients (50%) demonstrated RM, as compared with 12 patients (85.7%) in the case-matched group. Of the anti-VEGF patients, 6 showed a solitary cotton-wool spots, 1 with a single intraretinal cyst (evident on OCT) that subsequently resolved with continued anti-VEGF injections. The 7 patients who did not demonstrate RM had a mean of 33 months of follow-up.

OCT evaluations were available only for the anti-VEGF group because OCT imaging was not available when the case-matched patients were treated. During this study, central foveal thickness measurements decreased by a mean of 185 μm , which likely resulted from normalization of macular anatomic features in response to treatment, as shown in [Figure 2](#) (available at www.ophtalmologyretina.org).

This pilot study suggests that early administration of monthly intravitreal anti-VEGF medication (bevacizumab) was well tolerated and prevented or delayed vision-threatening RM in high-risk choroidal melanoma patients after plaque therapy. The limitations of this study include its retrospective design and small number of patients. This study supports the need for a prospective randomized clinical trial or retrospective multicenter registry and validates our hypothesis that intravitreal anti-VEGF injections can be used to prevent or delay RM-related vision loss.

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Abbreviations and Acronyms:

RM = radiation maculopathy; **VEGF** = anti-vascular endothelial growth factor.

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References

1. American Brachytherapy Society—Ophthalmic Oncology Task Force, ABS—OOTF Committee. The American Brachytherapy Society consensus guidelines for plaque brachytherapy of uveal melanoma and retinoblastoma. *Brachytherapy*. 2014;13:1–14.
2. Finger PT, Chin KJ, Yu G-P. Risk factors for radiation maculopathy after ophthalmic plaque radiation for choroidal melanoma. *Am J Ophthalmol*. 2010;149:608–615.
3. Finger PT. Radiation therapy for orbital tumors: concepts, current use, and ophthalmic radiation side effects. *Surv Ophthalmol*. 2009;54:545–568.
4. Finger PT. Tumour location affects the incidence of cataract and retinopathy after ophthalmic plaque radiation therapy. *Br J Ophthalmol*. 2000;84:1068–1070.
5. Finger PT, Chin KJ, Semenova EA. Intravitreal anti-VEGF therapy for macular radiation retinopathy: a 10-year study. *Eur J Ophthalmol*. 2016;26:60–66.

6. Kivelä T, Simpson ER, Grossniklaus HE, et al. Uveal melanoma. In: Amin MB, Edge S, Greene FM, et al., eds. *The AJCC Cancer Staging Manual*. 8th ed. New York: Springer; 2017: 805–817.



Neighborhood Deprivation and Adherence to Initial Diabetic Retinopathy Screening



Annual diabetic retinopathy screening is an essential and cost-effective strategy to prevent vision loss.¹ However, more than one third of patients with diabetes in the United States do not undergo annual dilated eye examinations.² Although individual-level socioeconomic factors such as insurance status and education level have been associated with adherence to diabetic retinopathy examinations, the impact of neighborhood-level deprivation has not been studied previously.² Therefore, we aimed to determine if a composite measure of neighborhood deprivation was associated with adherence to first-time ophthalmology referral for diabetic retinopathy evaluation.

This retrospective, single-institution analysis was conducted in compliance with the tenets of the Declaration of Helsinki and with approval from the institutional review board of Yale University. Informed consent was waived. The Yale-New Haven Health System electronic medical record system was queried for patients 18 years of age or older with diabetes who received a first-time referral for diabetic retinopathy evaluation in the primary care setting from 2013 through 2017.

This study used the Area Deprivation Index (ADI), a metric of neighborhood-level deprivation derived from 17 sociodemographic United States Census metrics.³ To obtain national-level ADI percentiles, patient addresses were geocoded to obtain 12-digit Federal Information Processing System codes, the geographical unit by which ADI values are assigned. The cohort was divided into quintiles based on ADI national percentiles. Quintile 1 comprised patients with national ADI percentiles ranging from 1% to 20% (least disadvantaged), quintile 2 comprised patients with national ADI percentiles ranging from 21% to 40%, and so on. The dependent variable of this study, adherence to referral for diabetic retinopathy evaluation, was determined by evidence of a dilated fundus examination received within 12 months of first-time referral or an indicator in a patient's chart that the examination was or was not conducted.

In preliminary data analysis, the 2 most disadvantaged quintiles (quintiles 4 and 5) demonstrated the lowest likelihood of adherence. Therefore, in secondary analysis, individuals residing in the 40% most disadvantaged neighborhoods, stratified by decile, were compared with the remaining cohort residing in the least disadvantaged 60% of neighborhoods to identify a potential ADI cutoff above which disadvantaged status was associated significantly with screening nonadherence. All statistical analyses were conducted in R software version 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria). A 2-sided *P* value of less than 0.05 was considered statistically significant.

Of 1397 patients included, 727 (52.0%) underwent a dilated eye examination as referred, 797 (57.1%) were women, 580 (41.5%) were black, and 642 (46.0%) were insured with Medicaid (Table S1, available at www.opthalmologyretina.org/). More disadvantaged

quintiles consisted of greater proportions of black and uninsured patients (Fig S1, available at www.opthalmologyretina.org/).

Table 1 shows primary unadjusted bivariate and multivariate analyses. Adjustment for individual factors with *P* values less than 0.2 on univariate analysis (age, insurance, and race) significantly attenuated the association between ADI and adherence when comparing the most disadvantaged and least disadvantaged quintile (odds ratio [OR], 1.39; 95% confidence interval [CI], 0.82–2.37; *P* = 0.216), although significance remained when comparing the most disadvantaged quintile with quintile 3 (OR, 1.80; 95% CI, 1.25–2.61; *P* = 0.0016) and quintile 2 (OR, 1.55; 95% CI, 1.05–2.31; *P* = 0.028).

In secondary analysis, when comparing the 4 most disadvantaged ADI deciles individually with the least disadvantaged 60% of neighborhoods, residence within each of the 3 most disadvantaged deciles was associated with an increased risk of nonadherence to diabetic retinopathy screening (Table S2, available at www.opthalmologyretina.org/). When these 3 deciles were combined into a single group, residence within the 30% most disadvantaged neighborhoods significantly increased risk of nonadherence compared with the remaining cohort (OR, 0.56; 95% CI, 0.42–0.72; *P* = 0.0033).

This study demonstrated that residence in more disadvantaged neighborhoods, as measured by ADI, is associated independently with nonadherence to first-time ophthalmology referrals for diabetic retinopathy screening after controlling for known individual-level predictors of adherence to annual dilated eye examinations. Furthermore, a threshold effect was observed whereby adverse effects of ADI on screening adherence arose as soon as a threshold level of neighborhood disadvantage was reached, which has been reported previously in the association between ADI and rehospitalization rates.⁴ Although research has shown the impact of neighborhood deprivation status on health outcomes,⁴ previous studies have not associated a United States population-derived metric with diabetic retinopathy screening adherence.

The association between ADI and diabetic eye screening adherence is likely multifactorial. First, more disadvantaged neighborhoods may lack proximity to ophthalmology clinics and may have limited means of transportation, as has been described previously in the context of mammography adherence.⁵ Second, perceived neighborhood quality in disadvantaged communities may be a barrier to diabetic eye screening adherence. Social disorganization and crime prevalence have been associated previously with cancer screening adherence.⁶ Third, more disadvantaged neighborhoods, which have demonstrated lower diabetes health literacy and prevalence of diabetes self-care practices,⁷ may lack normative values that reinforce diabetic screening behaviors.

The potential of ADI in clinical care is broad. Area Deprivation Index is publicly available and requires only an address as input. Integration of ADI within electronic medical systems could direct provision of additional discussion about screening importance or resources. For example, travel vouchers, assistance in arranging transportation, telephone prompts, or automated alerts in medical charts for screening reminders could be implemented in primary care settings for patients identified as being at high risk of nonadherence. In a population-based approach, ADI could be used to target communities below cutoff ADI percentiles with interventions such as education initiatives or mobile clinics.