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Efficacy and Toxicity of Intravitreous Chemotherapy for Retinoblastoma: Four-Year Experience

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Purpose: To investigate the efficacy and toxicity of intravitreous melphalan for treatment of retinoblastoma, as a single agent or with concomitant topotecan.

Participants: A total of 130 eyes of 120 patients with retinoblastoma receiving 630 intravitreous (melphalan, topotecan) or topotecan periocular injections. A total of 83 (64%) of these eyes were treated with concomitant ophthalmic artery chemosurgery (OAC).

Design: Retrospective cohort study.

Methods: Indirect ophthalmoscopy and clinical imaging were used to evaluate clinical response. Ocular survival and disease-free survival were estimated using Kaplan–Meier methods in 130 eyes. Ocular toxicity was evaluated by clinical findings and electroretinography (ERG) on 244 evaluable injections in 63 patients using 30-Hz flicker responses. Analysis was performed using linear mixed effects models with a random intercept and slope for each patient and a fixed effect for number of injections, in addition to any other fixed effect of interest.

Main Outcome Measures: Ocular survival, disease-free survival, ERG: peak-to-peak ERG amplitudes in response to 30-Hz photopic flicker stimulation.

Results: There were no disease- or treatment-related deaths, and no patient developed externalization of tumor or metastatic disease. Two-year Kaplan–Meier estimates of ocular survival and disease-free survival were 94.2% (95% confidence interval, 89.2–99.4) and 86.2% (95% confidence interval, 78.7–94.5), respectively. There was a significant association between the number of injections and diminished ERG responses, such that on average each intravitreous melphalan injection was associated with a 5.3-μV decrease in ERG amplitude ($P < 0.001$). Concomitant intra-arterial chemotherapy ($P = 0.01$) and greater inherent ocular pigment also were significantly associated with a reduction in ERG ($P = 0.045$). Patient age and weight, new injection site location, addition of topotecan, concomitant focal treatment, and time interval between injections were not significantly associated with toxicity.

Conclusions: Intravitreous melphalan is an effective treatment for vitreous seeding in retinoblastoma, resulting in high rates of ocular survival and disease-free survival. However, in this study, each injection of melphalan was associated, on average, with a decrement in ERG response. The findings suggest increased toxicity (1) when OAC is given within 1 week of the intravitreous injection and (2) in more deeply pigmented eyes. *Ophthalmology 2017;124:488-495 © 2017 by the American Academy of Ophthalmology*

Intravitreous chemotherapy effectively treats retinoblastoma vitreous seeds and saves eyes that once would have been enucleated.[1] However, as we have previously described, this comes at the expense of ocular toxicity.[2] The posterior segment is involved, and retinal damage occurs such that for every injection, we have reported a 5.8-μV decrease in the electroretinography (ERG) recording.[2] Furthermore, toxic effects also may occur in the anterior segment of the eye, including iris recession, cataracts, iris depigmentation, and iris thinning along with scleromalacia.[3]

The alternative management for vitreous seeds (or recalcitrant subretinal and retinal tumor) includes ophthalmic artery chemotherapy or enucleation. Intra-arterial chemotherapy can be effective for vitreous disease and causes minimal retinal toxicity.[4,5] However, ophthalmic artery chemotherapy requires a team of specialists and resources that are not available to all retinoblastoma centers. For many centers that rely on intravitreous chemotherapy or centers that are deciding between intravitreous and intra-arterial chemotherapy, the question becomes, how can we maintain the efficacy of intravitreous chemotherapy while limiting its toxicity? We have done more than 600 intravitreous injections for retinoblastoma since 2012 and have an extensive database of electroretinogram recordings, so we undertook a retrospective analysis of 630 chemotherapy injections in an attempt to help answer this question. In addition to evaluating the efficacy of the injections, we investigated a number of patient and treatment characteristics to determine whether these influenced retinal toxicity.

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Methods

This institutional review board–approved study included all eyes that received injections of melphalan or topotecan for the management of intraocular retinoblastoma at Memorial Sloan Kettering Cancer Center between September 2012 and September 2016. Informed consent was obtained for each patient from their guardian, caregiver, or parent. The study was Health Insurance Portability and Accountability Act compliant. Research adhered to the tenets of the Declaration of Helsinki.

The intravitreous injections were performed as follows: After induction of anesthesia, the intraocular pressure was lowered by digital massage to a target pressure of less than 10 mmHg. Intravitreous melphalan (25–30 μg in 0.05–0.072 mL) was injected through the conjunctiva, sclera, and pars plana with a 33-gauge needle, usually 3 mm from the limbus. A total of 32 injections of 25-μg melphalan were given in 8 eyes, and in 7 of these eyes, melphalan was administered with concomitant intravitreous topotecan; the remaining injections were 30-μg melphalan. Before needle withdrawal, the injection site was sealed and sterilized with cryotherapy.[1] The ocular surface was submerged in irrigating sterile water for 3 minutes.[6] Periocular injections of 1-mg topotecan were performed in a manner previously described.[7] Periocular or intravitreal topotecan was used to supplement intravitreal melphalan in patients in whom intravitreal melphalan was not resulting in the desired response and it was believed that additional treatment was warranted. Ophthalmic artery chemosurgery (OAC) was given as concomitant treatment in 84 eyes in a manner previously described.[8] In brief, melphalan (2.5–8 mg), topotecan (0.3–2 mg), and carboplatin (20–70 mg) were used. The number of drugs and doses were determined by a number of factors, including laterality of disease, age of the patient, prior response to treatment, and so forth.

The clinical status was evaluated under anesthesia with indirect ophthalmoscopy, RetCam fundus photography (Clarity, Pleasanton, CA), B-scan ultrasonography (Ellex, Adelaide, Australia), and ultrasonic biomicroscopy (Ellex). At each subsequent examination, the burden of residual disease was reevaluated and additional injections were given on a weekly or monthly schedule. Additional injections were given if the seeds were not in a state of regression by clinical examination. Seeds that enlarged in size without dismantling and dispersing into smaller pieces were deemed active.

Patient data included sex, laterality, age and weight at the start of the injection course, degree of ocular pigmentation (blue = blue iris with blonde fundus, light brown = brown iris with moderate fundus pigment, dark brown = brown iris with deep fundus pigment), eye status (salvaged or enucleated), indication for chemotherapy injection (vitreous seeds, subretinal seeds, or retinal tumor), and follow-up time from the beginning of the injection course. Treatment data included the number of injections, the number of clock hours when injections were administered, the time interval between injections, clock hours of salt-and-pepper retinopathy, concomitant OAC or focal treatment (laser or cryotherapy) defined as occurring within 1 week of the injection but exclusive of the injection site cryotherapy, and concomitant periocular/intravitreous topotecan injection at the time of melphalan injection. For ocular survival, an adverse event was defined as enucleation (no eyes received external beam radiation as salvage treatment). For disease-free survival, an event was defined as recurrence of seeds requiring enucleation or a subsequent course of injections. Tumor data included Reese-Ellsworth classification, Children's Oncology Group version of the International Classification, and seed classification at presentation (class 1 = dust, class 2 = spheres ± dust, or class 3 = clouds ± spheres or dust).

Ocular Toxicity

The ERG recordings were obtained during regularly scheduled examinations under anesthesia, according to an International Society for Clinical Electrophysiology of Vision standard protocol that had been modified to limit anesthesia time, as previously described.[2,9] We report the amplitudes of responses to 30-Hz photopic flicker stimulation, which are representative of the full protocol.[10] Electroretinogram responses were measured at baseline, immediately before each injection, and at each follow-up visit. The ERG studies were deemed inevaluable if the baseline recording amplitudes were not sufficient enough to allow demonstration of ERG change over the injection course (e.g., each injection has the potential to decrease the ERG by ~5 μV^2; therefore, an eye with an 8-μV amplitude at baseline would not have sufficient baseline ERG signal strength to demonstrate change over 6 injections) or if there was no ERG testing performed (because of the absence of an electrophysiologist).

Statistical Analysis

Ocular survival and disease-free survival were estimated using Kaplan–Meier methods in 130 eyes of 120 patients. Ocular toxicity was evaluated by clinical findings and ERG for 244 evaluable injections in 63 patients. We explored trends in the data through a line plot of each individual patient's trajectory of ERG over injections, with a locally weighted scatterplot smoothing line showing the overall trend in the data. Then, linear mixed effects models with a random intercept and slope for each patient and a fixed effect for the number of injections, in addition to any other fixed effect of interest, were fit to the ERG data. All statistical analyses were conducted using R software version 3.2.5 (R Core Development Team, Vienna, Austria), and a P value < 0.05 was considered statistically significant.

Results

A total of 56 patients had unilateral disease, and 64 patients had bilateral disease (10 patients had injections in both eyes). There were no disease- or treatment-related deaths, and no patient developed externalization of tumor or metastatic disease. One patient died of trauma. The median follow-up among those eyes that were not enucleated was 14.3 months (range, 0.3–47.4 months), and the median age at initial treatment was 25.8 months (range, 5.2–216.3 months). A total of 630 injections in 130 eyes (Reese-Ellsworth Classification IA = 2 eyes, IB = 2 eyes, IIA = 3 eyes, IIB = 1 eye, IIIA = 4 eyes, IIIB = 4 eyes, IVA = 1 eye, VA = 16 eyes, VB = 97 eyes; International Classification A = 2 eyes, B = 8 eyes, C = 4 eyes, D = 83 eyes, and E = 33 eyes) were included in this study. The median interval between injections was 12 days (range, 6–44 days). Classifications of vitreous seeds, delivery, and drugs used in the injection and indication for the injection are shown in Table 1. Treatment and disease characteristics are demonstrated in Table 2 and show that the majority of eyes received prior treatment (OAC, external beam radiation, or intravenous chemotherapy before intravitreal injections), and the majority of eyes received concomitant OAC. All eyes received intravitreous chemotherapy after prior treatment or with concomitant OAC (Table 3).

As shown in Figure 1, the overall 2-year Kaplan–Meier estimate for ocular survival was 94.2% (95% confidence interval,

Table 1. Number, Delivery, and Indication for 630 Chemotherapy Injections

Indication for Injections	No. Eyes	No. Intravitreal Melphalan Injections	No. Concomitant Intravitreal Topotecan Injections
Vitreous disease	94	374 (4.0)	26 (0.3)
1	27	63 (2.3)	0 (0)
2	46	207 (4.5)	16 (0.3)
3	21	104 (5.0)	10 (0.5)
Nonvitreous disease	36	118 (3.3)	28 (0.8)
Anterior chamber	1	3 (3.0)	0 (0)
Subretinal seeds	17	52 (3.1)	10 (0.6)
Retinal tumor	18	63 (3.5)	18 (1.0)
Total	130	492 (3.8)	52 (0.4)

Mean numbers of injections per eye are shown in parentheses.

89.2–99.4). The 2-year Kaplan–Meier estimate for disease-free survival was 86.2% (95% confidence interval, 78.7–94.5).

The 63 patients evaluable for ERG each received between 2 and 9 injections for a total of 295 observed injections. The change in ERG for each injection of melphalan ranged from an increase of 43.4 μV to a decrease of 68.5 μV, as shown in Figure 2. Individual patient trajectories of ERG over time, as measured by the number of injections, are plotted in Figure 3. The locally weighted scatterplot smoothing line shows that there is an overall downward trend in ERG over time. In a linear mixed model with a random effect for patient and both a random and fixed effect for injection number, there was a significant association between the number of injections and ERG decrement, such that on average each intravitreous melphalan injection was associated with a 5.3-μV degradation in ERG response ($P < 0.001$). When additional fixed effects variables were added to the model one at a time, we found that concomitant intra-arterial chemotherapy was associated with an 8.0-μV decrease in ERG. Light brown or dark brown versus blue ocular pigment also was significantly associated with a reduction in ERG ($P = 0.045$) (Fig 4). Both concomitant OAC and ocular pigment were confirmed to be statistically significant on multivariate analysis. Age, weight, new injection site clock hour, addition of topotecan, concomitant focal treatment, and time interval between injection were not significantly associated with toxicity.

Discussion

Initial concerns regarding the use of intravitreous chemotherapy for retinoblastoma centered on questions of its safety and the risk of externalization of tumor. Because of a resurgence of interest stimulated by Munier et al[11] and a coordinated effort to adopt enhanced safety techniques, intravitreous chemotherapy injections have proven relatively safe in practice.[12] As the technique has been more widely implemented, it has proven to be very effective for treating vitreous seeds.[1,13,14] However, although intravitreous chemotherapy can save eyes, it is also toxic to the eye and the retina.[2] In further refining the intravitreous chemotherapy technique, the question now arises as to how can we make these injections less toxic and more amenable not only to saving the eye but also to potentially saving vision.

Patient characteristics potentially related to the size of the eye (age and weight) were not associated with increased toxicity. This may come as a surprise, because it might be that younger, smaller patients have an increased concentration of drug (because of a smaller volume of vitreous due to less axial elongation at a younger age[15]) or more viscous vitreous, resulting in less drug diffusion and "pockets" of higher drug concentration in proximity to the retina, both of which might increase toxicity.

In a porcine model, it has been shown that a higher concentration of melphalan accumulated in the retinal pigment epithelium choroid than in the retina after intra-arterial chemotherapy, suggesting melphalan may be preferentially taken up by pigmented tissues.[16] We previously speculated that more deeply pigmented eyes may absorb increased levels of melphalan, resulting in more retinal pigment epithelium toxicity and, by extension, retinal and choroidal toxicity.[2] Our current findings align with this theory: Using iris and fundus pigment as a proxy for inherent ocular pigmentation demonstrated a statistical impact on retinal toxicity such that eyes with brown irides had more retinal toxicity compared with eyes with blue irides. This raises the question as to whether more deeply pigmented eyes may benefit from melphalan dose

Table 2. Treatment and Disease Characteristics for 130 Eyes

Treatment and Disease Details	All (n = 130)	Vitreous (n = 94)	Nonvitreous (n = 36)
Disease status			
Primary	60 (45%)	42 (45%)	18 (50%)
Recurrent	70 (55%)	52 (55%)	18 (50%)
Treatment status			
Naïve	22 (17%)	19 (20%)	3 (8%)
Prior treatment	108 (83%)	75 (80%)	33 (92%)
OAC	38	25	13
IVC	34	24	10
OAC + IVC	32	22	10
EBR + IVC	1	1	
EBR + OAC	1	1	
EBR + IVC + OAC	2	2	
Concomitant OAC			
Yes	83 (64%)	66 (70%)	17 (47%)
No	47 (36%)	28 (30%)	19 (53%)

EBR = external beam radiation; IVC = intravenous chemotherapy; OAC = ophthalmic artery chemosurgery.
Percentage shown in parentheses.

Table 3. Details of 69 Eyes of 63 Patients Who Had Evaluable Electroretinogram Responses

Gender	Laterality	RE	ICRB	Prior Treatment	Disease Status	Indication for Injection*	Concomitant OAC	No. of OAC Drugs	No. of OAC Cycles	No. of M Injections	No. of Intravitreal T Injections	No. of Periocular T Injections
M	B	5B	E	OAC, Sc	Recurrent	3	Yes	M, T, C	3	8		
F	B	5B	E	OAC, EBR	Recurrent	2	Yes	M, T, C	2	6		
F	B	5B	D	OAC	Recurrent	1	No			5		
F	B	1B	B	None	Primary	R	No			2		
F	B	1A	B	OAC, Sc	Primary	R	No			3		
F	B	5B	D	OAC, Sc, EBR	Recurrent	2	Yes	M, T, C	2	3		
M	B	5B	C	OAC, Sc	Recurrent	2	No			5		4
F	U	5B	D	OAC, Sc	Recurrent	2	Yes	M, T, C	2	6		
F	B	5B	C	Sc	Recurrent	2	Yes	M, T	3	3		
M	B	5B	D	OAC	Recurrent	R	No			2		
M	B	5B	D	Sc, EBR	Recurrent	2	Yes	M, T, C	3	8		
M	B	5B	E	OAC, Sc	Recurrent	2	Yes	M, T, C	3	4	4	3
F	U	5D	E	None	Primary	3	Yes	M, T, C	3	7		
M	B	5B	D	Sc	Recurrent	2	Yes	M, T, C	2	2		
M	U	5B	D	OAC	Recurrent	1	Yes	M, T, C	5	2		
F	U	5B	D	OAC	Primary	3	Yes	M, T, C	3	3		
M	B	5B	D	OAC	Primary	2	Yes	M, T, C	2	2		4
M	B	5B	E	OAC	Recurrent	2	No			8		
M	U	5B	D	OAC	Primary	1	Yes	M, T, C	3	2		
F	B	5B	D	Sc	Primary	2	Yes	M, T, C	7	3		
M	U	5B	D	None	Primary	3	Yes	M, T	2	7	2	
F	U	5B	D	Sc	Primary	3	Yes	M, T, C	2	5		
M	B	2A	B	OAC	Recurrent	R	Yes	M, C	2	7		
F	B	5B	E	OAC	Primary	1	No	M, T, C	3	3		
F	B	5B	D	Sc	Recurrent	2	No			7		7
F	B	5B	D	OAC	Recurrent	R	Yes	M, T, C	7	2	2	
F	U	5B	D	None	Primary	3	Yes	M, T, C	2	4		
M	U	5B	E	Sc	Primary	2	Yes	M, T, C	3	6		8
F	U	5B	D	OAC	Recurrent	2	Yes	M, T, C	2	7		
M	B	5B	D	Sc	Primary	2	Yes			8		
F	U	5B	D	None	Primary	1	Yes			1		
M	B	5B	E	None	Primary	1	Yes			4		
F	B	5A	E	OAC, Sc	Recurrent	2	No	M, T, C	3	8		
M	U	5B	D	OAC	Primary	1	No			1		
F	U	5B	D	Sc	Primary	3	Yes	M, T, C	2	8		
M	B	5B	D	OAC, Sc	Recurrent	2	No			3		
M	B	5B	D	OAC, Sc	Recurrent	2	No			1		1
F	U	5B	C	None	Primary	1	Yes	M	3	5		2
M	U	5B	D	Sc	Recurrent	2	Yes	M, T, C	1	8		
M	B	5B	D	OAC, Sc	Recurrent	2	No			6		
F	B	5B	E	Sc	Primary	1	Yes	M, C	1	3		
M	U	5B	D	None	Primary	3	Yes	M, T, C	3	4		
F	B	1B	B	OAC, Sc	Recurrent	R	Yes	M, T, C	3	5	5	
F	B	2A	D	OAC	Recurrent	R	No			4	2	
M	B	5B	D	OAC	Recurrent	2	No			5		

(*Continued*)

Table 3. (Continued.)

Gender	Laterality	RE	ICRB	Prior Treatment	Disease Status	Indication for Injection*	Concomitant OAC	No. of OAC Drugs	No. of OAC Cycles	No. of M Injections	No. of Intravitreal T Injections	No. of Periocular T Injections
M	B	5B	D	OAC, Sc	Recurrent	R	Yes	M, T, C	4	8	2	5
F	B	5B	E	OAC	Recurrent	2	Yes	M, T, C	3	3		
M	U	5B	E	OAC	Primary	1	No			3		
M	U	5B	E	Sc	Primary	3	Yes	M, T, C	3	3		
M	U	5B	D	None	Primary	3	Yes	M, T, C	3	2		
M	U	4A	D	OAC, Sc	Recurrent	2	No			4		
M	U	5B	D	Sc	Primary	2	Yes	M, C	2	2		2
F	B	3B	D	OAC, Sc	Recurrent	SRS	No			3		
F	B	3B	D	OAC, Sc	Recurrent	SRS	No			3		
M	U	3A	D	Sc	Primary	SRS	Yes	M, T, C	4	3		
M	U	3B	C	OAC	Primary	R	No			2		
M	U	5B	E	None	Primary	1	Yes	M, T, C	2	1		
F	U	5B	E	Sc	Primary	3	Yes	M, T, C	3	6		
M	U	5B	D	None	Primary	2	Yes	M, T, C	3	1		
M	B	5B	D	Sc	Primary	1	Yes	C, T	2	1		
M	B	5A	D	OAC	Recurrent	SRS	No			3		
M	B	5B	D	Sc	Recurrent	2	Yes	M, T, C	3	6		
M	U	5B	D	OAC, Sc	Primary	2	No			2		
M	B	3A	B	None	Primary	R	Yes	M, T, C	1	3		
F	B	5B	E	None	Primary	3	Yes	M, T, C	4	3		
M	U	5B	D	OAC	Recurrent	R	No			2		
M	B	5B	D	Sc	Primary	R	Yes	M, T, C	2	2		
F	U	5B	E	OAC, Sc	Primary	SRS	No			2		
M	B	2B	B	OAC	Primary	R	No			3		

B = bilateral; C = carboplatin; EBR = external beam radiation; F = female; ICRB = International Classification of Retinoblastoma; M = melphalan; OAC = ophthalmic artery chemosurgery; R = retinal tumor; RE = Reese-Ellsworth; Sc = systemic chemotherapy; SRS = subretinal seed; T = topotecan; U = unilateral.
*Class of vitreous seed.

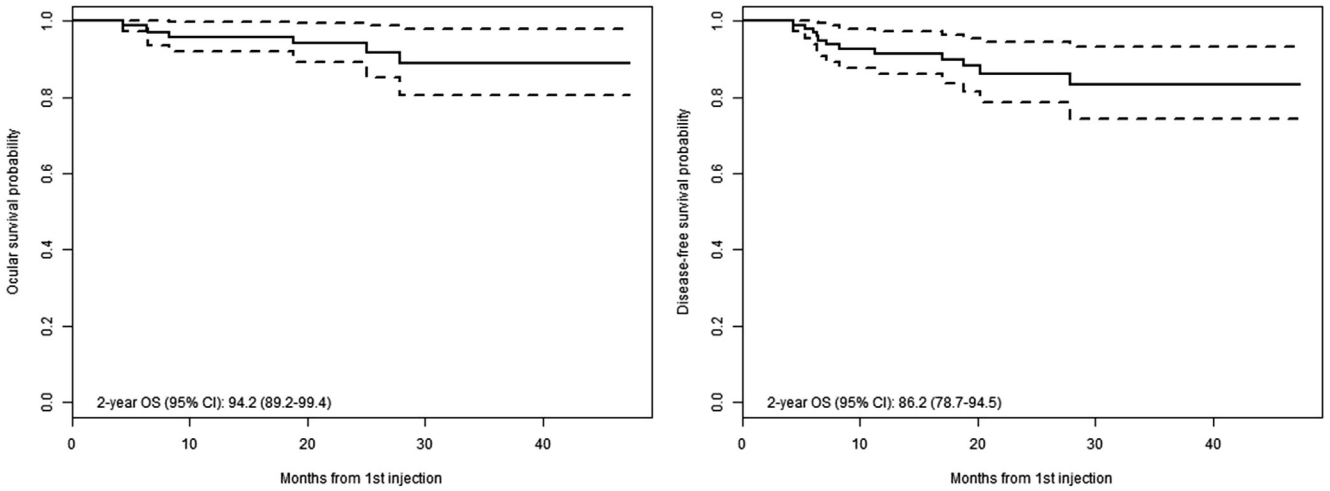

Figure 1. Kaplan–Meier survival curves for (*left*) ocular survival (OS) of all eyes and (*right*) event-free survival of all eyes. CI = confidence interval.

reduction. However, it is to be determined whether a lower dose of melphalan in more pigmented eyes would result in lower toxicity while, more important, still being efficacious.

It is commonly found that concomitant treatments are additive in their efficacy but also in their toxicity, and that toxicity may be worse with a shorter interval between modalities. Our results demonstrate no statistically significant impact on retinal toxicity when melphalan injections are given within 1 week of concomitant focal treatment or topotecan injections. However, although OAC alone has only a minimal impact on electroretinogram recordings,[5] it seems that concomitant administration within 1 week of intravitreous melphalan heightens the retinal toxicity of intravitreous melphalan to a statistically significant extent. Presumably, the melphalan delivered via OAC is additive with the drug administered intravitreally, and although this may result in more toxicity, it may have enhanced efficacy. The question of the ideal interval between these 2 drug delivery modalities, such that efficacy is optimized and toxicity minimized, would benefit from further investigation.

In addition to concomitant therapies, other treatment factors were evaluated for their influence on toxicity. Our current results confirmed our previous findings that more numerous intravitreous injections result in a statistically significant increase in toxicity. More specifically, for every melphalan injection, the electroretinogram recordings decrease by 5.3 μV (which is close to our previous finding of a 5.8-μV decrement for each injection in a smaller cohort[2]). We previously demonstrated that retinal toxicity was observed promptly (detectable 1 week after the injection) and was stable without further decline after that initial 1-week interval. This may explain our present finding that the interval between injections does not significantly influence toxicity. One could deduce that the toxicity is recordable and stable by at least 1 week after the injection, and

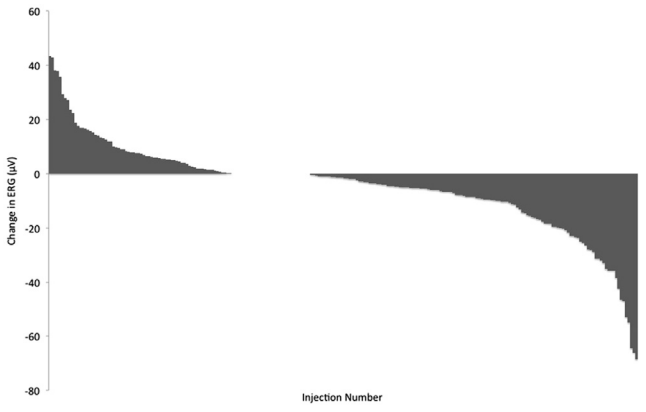

Figure 2. Waterfall plot demonstrating change in electroretinogram (ERG) response recorded after each intravitreal injection of melphalan.

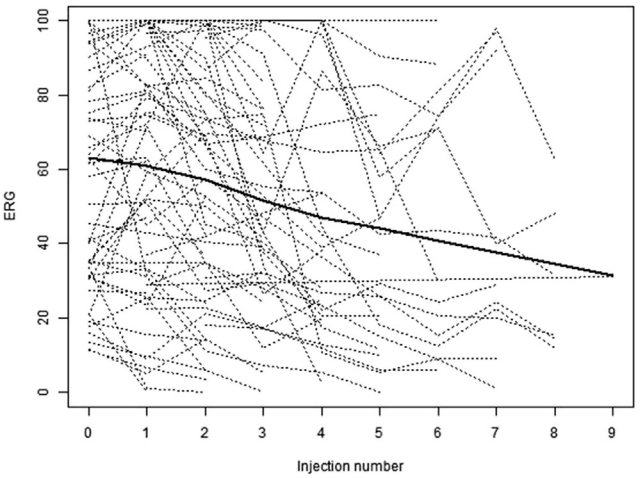

Figure 3. Individual patient trajectories of electroretinograms (ERGs) over time, as measured by the number of injections (*dotted lines*), with a locally weighted scatterplot smoothing line depicting the overall trend (*solid line*).

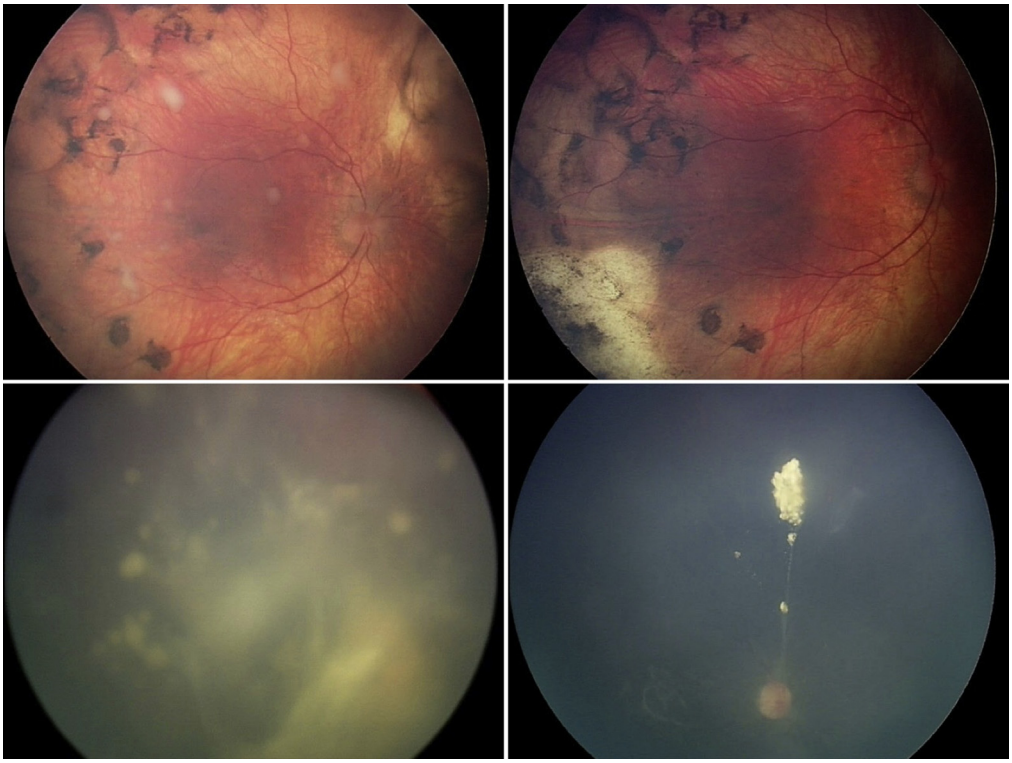

Figure 4. Representative cases of each seed classification (classes 1, 2, and 3) and response to intravitreous melphalan. Representative eye with a blue iris and class 2 (spheres) vitreous seeds (*upper left*) had a degradation of 3.6 μV after 3 melphalan injections (*upper right*). Representative eye with a dark brown iris and class 3 (cloud predominant) vitreous seeds (*lower left*) had comparatively more degradation (26.4 μV) after 3 melphalan injections (*lower right*).

adding additional injections at 1 week, 2 weeks, or 1 month would have little influence on the toxicity of that prior injection. It is still to be determined whether monthly injections afford more time for tumoricidal seed response, thereby resulting in fewer injections and less toxicity.

Studies have suggested that there is an increased concentration of the drug at the site of the injection as clinically demonstrated by salt-and-pepper retinopathy (sometimes referred to as "melphalan pigment epitheliopathy").[2] There is a belief that repeated injections in the same clock hour may limit exposure of the drug to a single portion of the retina and thereby reduce toxicity. However, our results do not support this and in fact show no statistically significant relationship between the number of clock hour injection sites and retinal toxicity. Perhaps each melphalan injection creates an area of vitreous liquefaction in which the drug concentrates and remains in proximity to the retina, and each subsequent injection into this same location expands this area of vitreous liquefaction while also expanding drug exposure and impact on the retina.

Our current study validates our prior, smaller case series that showed that each intravitreous melphalan (30 μg) injection results in approximately 5-μV degradation in retinal response. This larger cohort demonstrates a patient characteristic (ocular pigment) and a treatment factor (concomitant OAC within 1 week) that influence toxicity and thereby provides a potential avenue for future modifications to limit toxicity.

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Abbreviations and Acronyms:
ERG = electroretinography; **OAC** = ophthalmic artery chemosurgery.

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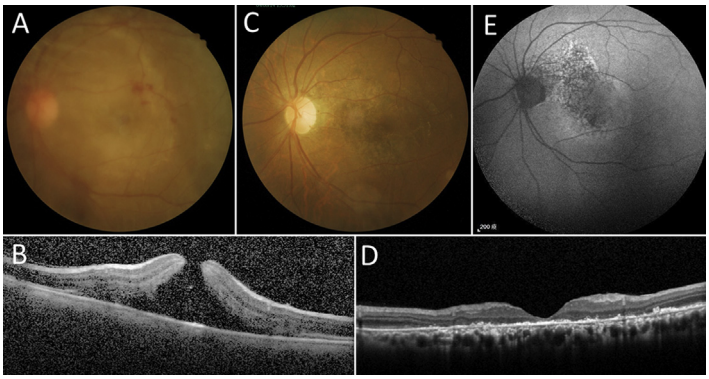
Pictures & Perspectives



Traumatic Maculopathy with Macular Hole

A 61-year-old man sustained blunt injury to his left eye, decreasing visual acuity to count fingers. Examination revealed mild vitreous hemorrhage, Berlin's edema with retinal hemorrhage, and a macular hole (Fig 1**A**). Spectral-domain optical coherence tomography (SD OCT) demonstrated a full- thickness macular hole with increased parafoveal thickness (Fig 1**B**). Two months later, his vision was 2/200, and examination showed resolution of macular edema with spontaneous closure of traumatic macular hole (Fig 1**C**). Spectral-domain OCT demonstrated loss of the ellipsoidal zone and external limiting membrane (Fig 1**D**). Fundus autofluorescence revealed interposed, reduced, and increased macular and peripapillary autofluorescence (Fig 1**E**).

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