Review

Surgical Approach in Intraocular Tumors

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Abstract

Surgery in intraocular tumors is done for excision/biopsy and the management of complications secondary to the treatment of these tumors. Excision/biopsy of intraocular tumors can be done via fine-needle aspiration biopsy (FNAB), transretinal biopsy (TRB), partial lamellar sclerouvectomy (PLSU), and endoresection. FNAB, TRB, and PLSU can be used in tumors that cannot be diagnosed by clinical examination and other ancillary testing methods. PLSU is employed in tumors involving the iridociliary region and choroid anterior to the equator. Excisional PLSU is performed for iridociliary and ciliary body tumors with less than 3 clock hours of iris and ciliary body involvement and choroidal tumors with a base diameter less than 15 mm. However, for biopsy, PLSU can be employed with any size tumor. Endoresection is a procedure whereby the intraocular tumor is excised using vitrectomy techniques. The rationale for performing endoresection is based on the fact that irradiated uveal melanomas may cause complications such as exudation, neovascular glaucoma, and intraocular pigment and tumor dissemination (toxic tumor syndrome), and removing the dead tumor tissue may contribute to better visual outcome. Endoresection is recommended 1-2 weeks after external radiotherapy. Pars plana vitrectomy is also used in the management of complications including vitreous hemorrhage, retinal detachment, and epiretinal membrane that can occur after treatment of posterior segment tumors using radiotherapy and transpupillary thermotherapy. It is important to make sure the intraocular tumor has been eradicated before embarking on such treatment.

Keywords: Intraocular tumors, ciliary body tumor, choroidal tumor, fine needle aspiration biopsy, partial lamellar sclerouvectomy, endoresection, pars plana vitrectomy, radiotherapy

Introduction

Surgical approaches related to intraocular tumors can be summarized under two main headings: procedures performed for tumor excision/biopsy and procedures to manage complications secondary to treatment of the tumor.

The first intraocular biopsy was performed by Hirschberg in 1868.[1] Intraocular biopsy techniques have evolved over the years and are used in the diagnosis of malignant tumors before treatment. The intraocular biopsy technique used may vary depending on tumor location, size, and tumor-associated findings.[2] Intraocular tumor biopsy is performed by fine-needle aspiration biopsy (FNAB), pars plana vitrectomy (PPV) with transretinal biopsy (TRB), and partial lamellar sclerouvectomy (PLSU).

The first experiences with intraocular tumor excision date back approximately 100 years. The first excision of malignant tumors in the iris and ciliary body region was performed by Zirm in 1911.[3] In 1961, Stallard[4] introduced a new approach to intraocular tumor surgery. After forming a scleral flap, he excised the choroidal tumor by performing diathermy to the underlying sclera, choroid, and retina.[4] Foulds[5] also described a similar surgical technique. In the opposing school, Meyer-schwickerath[6] and Peyman et al.[7] excised tumors by performing a full-thickness eye wall (including sclera) excision including the tumor tissue. Of these two techniques, the method based on excising the underlying tumor after forming a scleral flap (i.e., the technique pioneered by Stallard and Foulds) was more widely adopted.[3] This surgical technique has been given various names, such as iridocyclectomy, PLSU, transscleral local resection, and exoresection. Regarding PLSU surgery, reports with large case numbers from Shields and Shields,[8] Shields et al.,[9] Damato,[10] made especially enlightening contributions to the ocular oncology literature.

Today, PLSU surgery is mainly performed for uveal melanomas. It can also be utilized for various tumors that are confused for melanoma or are known to be benign but still require excision, such as melanocytoma, medulloepithelioma, pigmented ciliary body adenoma, non-pigmented ciliary body adenoma (Fuchs' adenoma), schwannoma, and leiomyoma. External resection is widely used for iris and ciliary body tumors. This type of surgical resection can also be performed with peripheral choroidal and ciliochoroidal tumors. However, most surgeons avoid external tumor resection for choroidal tumors close to the optic disc and fovea.

Endoresection surgery refers to intraocular tumor excision using vitreoretinal surgery methods. This procedure was first described in 1988 by Peyman and Charles,[12] who used the term "internal eyewall resection" for this surgery. Damato et al.[13,14] further developed this surgical technique in the following years and named it endoresection.

Surgical procedures related to tumor excision/biopsy are grouped under the headings of FNAB, TRB, PLSU, and endoresection. In our review, these procedures will be discussed in turn. Surgical procedures for treatment complications will also be reviewed.

Fine-needle Aspiration Biopsy

FNAB, which is the most commonly used biopsy method for the diagnosis of intraocular tumors, can be performed via a transvitreal or transscleral approach. Transvitreal FNAB is performed for tumors posterior of the equator and transscleral FNAB is performed for tumors anterior of the equator. For tumors posterior to the equator, FNAB is performed by inserting a 22-27 gauge (G) needle into the eye at a distance of 3.5-4.0 mm from the limbus and advancing it into the tumor under indirect ophthalmoscopy.[15] Biopsy material is aspirated by pulling back the injector connected to the needle with a tubing line. At the end of the procedure, balanced salt solution is drawn into the syringe to collect fragments remaining in the needle and connector tubing.

The main limitations of the FNAB technique are the difficulty of navigating the needle into the tumor under indirect ophthalmoscopy and the possibility of obtaining insufficient material for pathological examination. Rates of obtaining adequate cytological material from FNAB have been reported as between 64.7% and 88.1%.[16,17,18] Complications such as vitreous hemorrhage, subretinal hemorrhage, and extraocular spread of tumor cells may occur after FNAB.[19,20,21] Considering these complications, it is essential that the material obtained by FNAB is evaluated by an experienced cytologist.

Transretinal Biopsy with Pars Plana Vitrectomy

In ciliary body and choroidal tumors, biopsy can be performed via the scleral route (i.e., using the PLSU approach described previously) or via PPV (Figure 1a-f and Figure 2a, b). TRB via PPV was originally performed with 20G vitrectomy, whereas 23G, 25G, and 27G vitrectomy systems are used today. A 3-port vitrectomy is performed. The vitrector is advanced into the tumor via the transretinal route and tumor tissue is aspirated using an injector connected to the vitrector to obtain material for cyto/histopathology. During this surgery, some clinicians perform additional procedures such as posterior hyaloid removal, total vitrectomy endolaser application to the biopsy area, laser photocoagulation endocerclage, fluid-air exchange, and gas-air exchange. Iatrogenic retinal tears can be treated effectively with this approach. However, performing minimal surgery is the more common approach in TRB. In minimal surgery, TRB is also performed via a three-port vitrectomy approach.[22] However, only ocutome-assisted retinal/choroidal tumor biopsy is performed, while other surgical procedures such as vitrectomy and intraocular gas injection are not employed. Performing all vitreoretinal surgical procedures is more appropriate in patients with significant exudative retinal detachment overlying and surrounding the tumor. In contrast, TRB alone can be performed if there is no or minimal fluid over the tumor. Applying endolaser around the biopsy entry site during TRB is also useful to create chorioretinal adhesions.

In cases of suspected primary vitreoretinal lymphoma in which vitreous aspiration does not provide sufficient yield, a retinal and choroidal biopsy should be performed because lymphoma infiltration is present under the retinal pigment epithelium. In
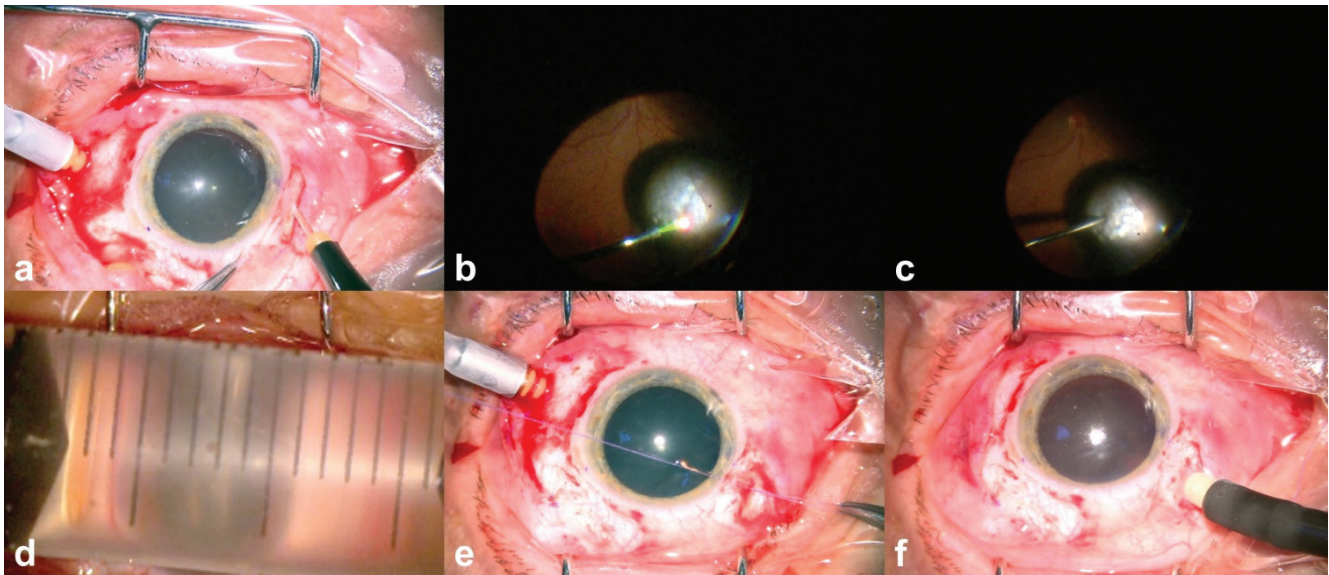
Figure 1. Intraoperative images from transretinal biopsy surgery. a) The trocar is advanced into the eye. b) Endolaser photocoagulation spots are seen on the tumor surface. c) The vitrector is inserted into the tumor during biopsy. d) After transretinal biopsy, the injector is checked for sufficient biopsy material. e) The sclerotomy is sutured. f) At the end of the procedure, triple freeze-thaw cryotherapy is performed after suturing
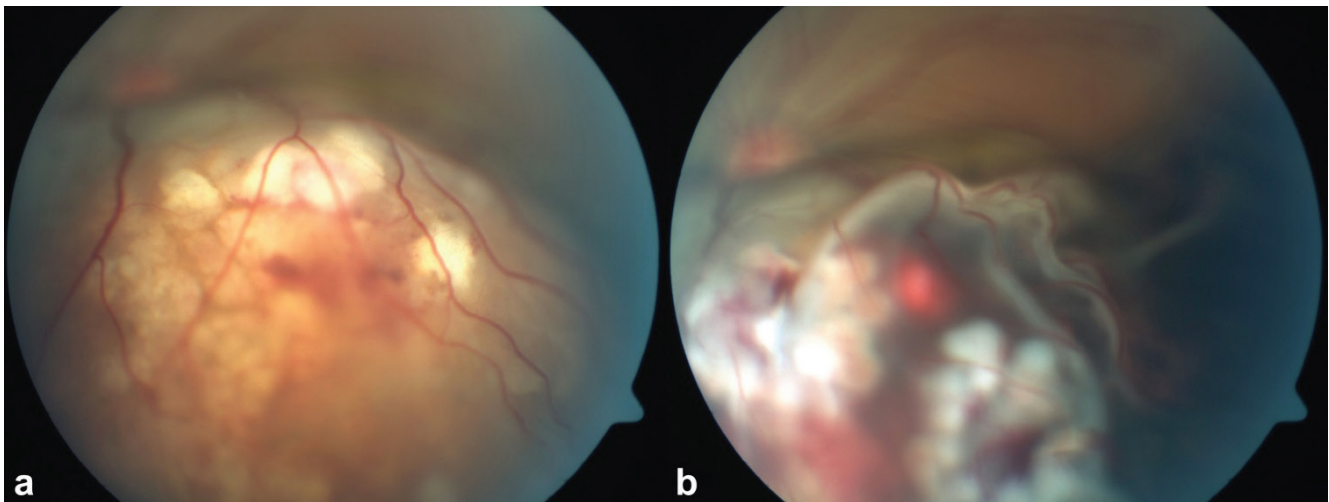

Figure 2. Preoperative and postoperative fundus photographs of a 56-year-old woman with metastatic choroidal tumor who underwent transretinal biopsy. a) An amelanotic tumor that could represent choroidal metastasis is observed on the inferotemporal aspect of the optic disc. However, since the possibility of melanoma could not be completely ruled out, it was decided to perform a transretinal biopsy of the tumor. b) At 1 week after pars plana vitrectomy and transretinal biopsy, endolaser spots and subretinal hemorrhage are observed around the tumor entry site

these cases, the minimal surgery approach discussed above may be insufficient, and all necessary vitreoretinal surgical procedures need to be performed.

In the series reported in the literature, TRB provided sufficient material for pathological examination in 88.9% to 100% of cases.[22,23,24,25,26,27,28,29] Choroidal melanoma was detected in 50-100% of cases in cyto/histopathological examination of TRB material.[22,23,24,25,26,27,28,30,31,32] Therefore, TRB is mostly performed for the diagnosis of uveal melanoma. Other diagnoses include metastasis, lymphoma, retinal vasoproliferative tumor (RVT), choroidal hemangioma, choroidal plasmacytoma,

choroidal neovascularization, and subretinal hemorrhage. The results of cyto/histopathology examination of TRB materials reported in the literature are presented in Table 1.

TRB-related complications reported in 354 cases included vitreous hemorrhage (n=151, 42.7%), retinal detachment (n=11, 3.1%), transient intraocular pressure increase (n=6, 1.7%), glaucoma (n=1, 0.3%), hyphema (n=1, 0.3%), macular hole (n=1, 0.3%), choroidal neovascularization (n=1, 0.3%), and phthisis bulbi (n=1, 0.3%).[22,24,26,27,28,30,31,32,33] Complications reported in previous studies on TRB are summarized in Table 2.

Table 1. Pathological examination results after transretinal biopsy via pars plana vitrectomy reported in the literature

Pathological examination method	Number of eyes	CM n (%)	Met n (%)	Lym n (%)	RVT n (%)	CH n (%)	RPE Ad n (%)	RAH n (%)	Deg n (%)	CP n (%)	CNV n (%)	SH n (%)	Mm n (%)	Gliosis n (%)	Sclerit n (%)	IS n (%)	Unspecified n (%)
Cyto[26,27,31]	75	58 (77.3)	5 (6.7)	2 (2.7)		1 (1.3)	1 (1.3)	1 (1.3)	4 (5.3)					1 (1.3)		2 (2.7)	
Histo[22,23,24,25,28,29]	222	164 (73.9)	14 (6.3)	10 (4.5)	2 (0.9)					1 (0.5)	1 (0.5)	3 (1.4)	2 (0.9)	1 (0.5)	2 (0.9)	6 (2.7)	16 (7.2)
Cyto/Histo[32]*	9	9 (100)															

Cyto: Cytopathology, Histo: Histopathology, CM: Choroidal melanoma, Met: Metastasis, Lym: Lymphoma, RVT: Retinal vasoproliferative tumor, CH: Choroidal hemangioma, RPE Ad: Retinal pigment epithelium adenoma, RAH: Retinal astrocytic hamartoma, Deg: Degeneration, CP: Choroidal plasmacytoma, CNV: Choroidal neovascularization, SH: Subretinal hemorrhage, Mm: Melanomacrophages, IS: Inadequate sample, *Diagnosis was confirmed by cytopathological examination in 7 cases and histopathological examination in 2 cases

Partial Lamellar Sclerouvectomy (PLSU, Exoresection)

PLSU can be performed for excision or biopsy of tumors involving the ciliary body and/or choroid. Although there are limitations with respect to tumor size for tumor excision, biopsy can be performed for any size tumor. The surgical methods used for ciliary/choroidal tumors with and without iris involvement are based on the same basic principle but differ in some respects. Therefore, these two procedure types will be discussed separately.

Iridocyclectomy and Iridociliochoroidectomy

Anesthesia

The procedure is performed under hypotensive anesthesia, with systolic blood pressure maintained at approximately 50-70 mmHg. If it is not possible for the patient to receive hypotensive anesthesia, systolic blood pressure should be kept as low as possible.

Surgical Indication and Technique

PLSU is recommended for ciliary body tumors involving at most 3 clock hours. The pupil should not be dilated in excisions of tumors involving the iris. Pupil dilation can be done in masses involving the ciliary body and/or choroid. PLSU is a difficult surgical technique with a pronounced learning curve (Figure 3a-e and Figure 4a-f). Following approximately 240-degree conjunctival peritomy, traction sutures are placed under 2-3 rectus muscles adjacent to the tumor using 3-0 or 4-0 silk sutures. Tumor location is determined by transillumination. If the tumor is under the muscle or at the insertion site, muscle disinsertion with 6-0 vicryl is necessary.

A limbus-based scleral flap is prepared. The flap should be 2-3 mm larger than the tumor on each side. An 80% to 90% thickness scleral flap is dissected up to the limbus. Then, 0.5 to 1 cc of core vitreous is aspirated. A vitrectomy ocutome should be used for this purpose. Following a pars plana sclerotomy 3.5-4 mm from the limbus, the ocutome probe is advanced up to 1 cm into the eye, core vitrectomy is performed, and the vitreous is aspirated with an injector connected to the ocutome. Wide-angle imaging systems are not used at this stage because the pupil is not dilated and no port is made for the endoilluminator. After vitrectomy is completed, the sclerotomy is sutured with 7-0 vicryl. In the past, vitreous aspiration was performed with a 20-22G needle advanced through the pars plana into the eye instead of an ocutome.[8,9,34] However, vitreous aspiration with a needle increases the risk of retinal traction.

After vitreous aspiration via vitrectomy, the eye pressure becomes hypotonus. The deep scleral fibers are excised to expose the intact ciliary body around the tumor. Bipolar cautery is applied to the healthy ciliary body surrounding the tumor. Then, a limbal incision is made to access the anterior chamber. The corneoscleral incision is enlarged with Westcott scissors. The tumor surrounded by cauterized ciliary body is excised using Vannas scissors starting at the ciliary body and continuing with the iris. Attempts are made to spare the pupil. The tumor is then excised by scraping off the unpigmented ciliary epithelium with a Weck-Cel sponge. Attention is paid not to rupture the

unpigmented ciliary epithelium, as this will result in vitreous loss. If vitreous loss occurs, vitrectomy should be performed at the wound edges with an ocutome. The scleral flap is then sutured in place using 8-0 or 9-0 nylon.[3,8,9,11] After closure, vitrectomy is repeated at the wound margins to ensure removal of remaining vitreous fibers.

The results of histopathological examination after exoresection reported in the literature are shown in Table 3. Iridocyclectomy is performed in tumors involving less than one-third of the ciliary body and angle region.[9,35,36] There is a risk of hypotony in tumors with greater involvement. In such tumors, treatment with plaque radiotherapy or proton beam radiotherapy instead of surgical excision may be more appropriate.[37,38]

Complications

The most important intraoperative problem in PLSU surgery is the risk of vitreous hemorrhage.[8,9,11,34,39]

Table 2. Summary of complications after transretinal biopsy via pars plana vitrectomy reported in the literature

Study, date of publication	Number of eyes	VH n (%)	New RD n (%)	Increase in existing RD n (%)	MH n (%)	Hyphema n (%)	IOP increase n (%)	Phthisis n (%)	CNV
Kvanta et al., 2005[28]	10	1 (10)	1 (10)	1 (10)				1 (10)	
Angi et al., 2008[33]	1*								1
Abi-Ayad et al., 2013[32]	9	8 (88.9)							
Seregard et al., 2013[24]	43			5 (11.6)			6 (14.0)		
Bagger et al., 2013[22]	85	82 (96.5)[†]	5 (5.9)						
Nagiel et al., 2017[27]	17	14 (82.4)[‡]							
Grewal et al., 2017[26]	18	13 (72.2)	2 (11.1)	2 (11.1)					
Angi et al., 2017[30]	131	17 (13.0)	2 (1.5)						
Gündüz et al., 2020[31]	40	16 (40.0)	1 (2.5)		1 (2.5)	1 (2.5)	1 (2.5)		

VH: Vitreous hemorrhage, RD: Retinal detachment, MH: Macular hole, IOP: Intraocular pressure, CNV: Choroidal neovascularization.
*Case report
[†]VH spontaneously regressed in 71 of 82 cases.
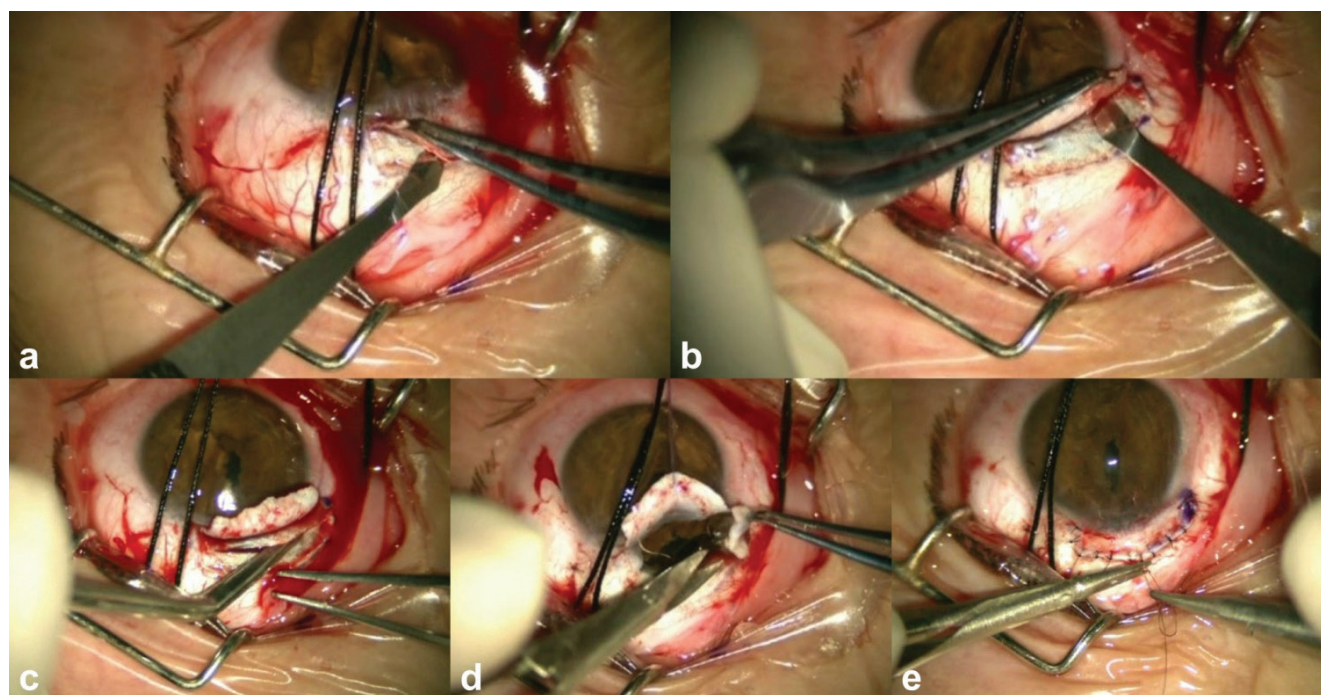[‡]Of 14 cases, 13 had focal and 1 had diffuse VH

Figure 3. Intraoperative images from a partial lamellar sclerouvectomy surgery. a) A scleral flap of approximately 80-90% thickness is prepared with a #57 beaver knife. b) The flap is dissected up to the corneoscleral limbus. c) A full-thickness incision is made to expose the underlying uveal tissue. d) Tumor excision is performed using Vannas scissors. e) The scleral flap is sutured in place
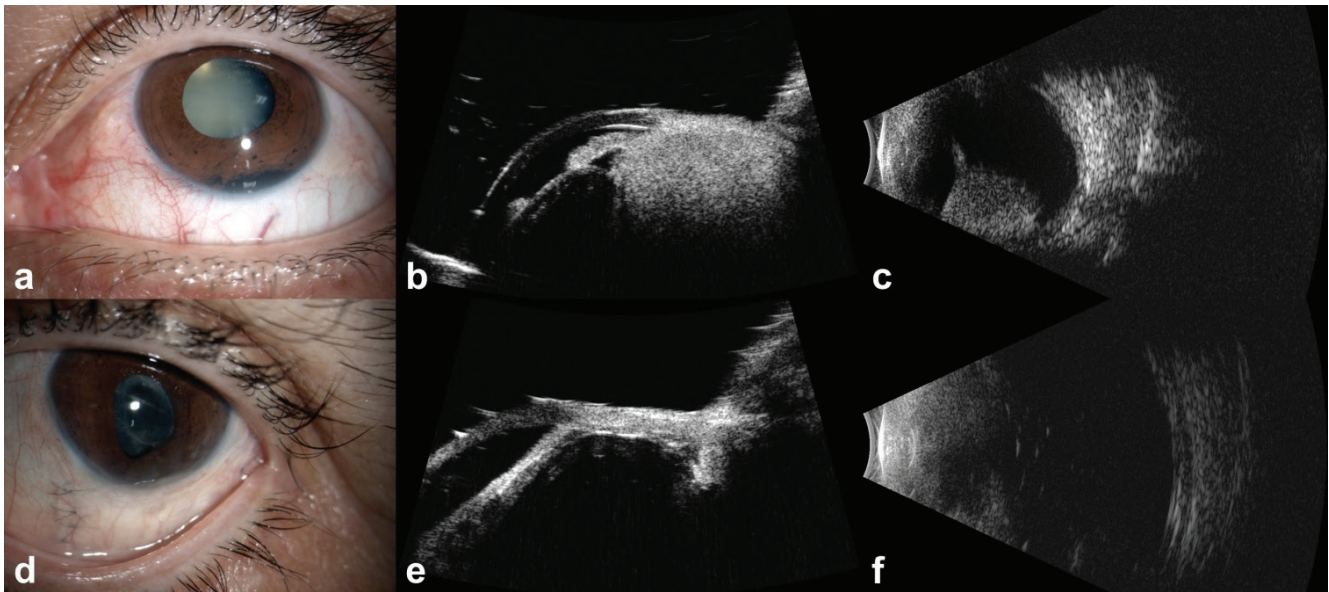
Figure 4. Photographs of a patient with melanoma with iridociliochoroidal involvement who underwent partial lamellar sclerouvectomy. a) Anterior segment image shows iridociliochoroidal melanoma in the left eye. The patient has mature cataract. b) Ultrasonic biomicroscopy shows a 4.1-mm thick acoustically hollow melanoma in the ciliary body region. c) B-mode ultrasonogram shows the choroidal component of the tumor. Choroidal tumor thickness is measured as 6.2 mm. d) In the postoperative anterior segment image, the inferior iridectomy after partial lamellar sclerouvectomy is not visible due to anterior synechia. Nylon sutures are seen in the sclera. e) No ciliary mass is observed in ultrasonic biomicroscopy at postoperative 6 months. f) No residual choroidal tumor or retinal detachment is observed in the silicone-filled eye on B-mode ultrasonogram at postoperative 6 months

Mild vitreous hemorrhage may occur while excising the tumor, but this hemorrhage resorbs spontaneously and is rarely a permanent problem. If vitreous loss occurs during tumor excision, vitrectomy should be performed with an ocutome to clear the wound margins from the vitreous.

Anteriorally located melanomas involving the iris and ciliary body compress the lens, causing notching and cataract. Cataract may also increase due to surgical trauma.[40,41] Postoperative hypotension may occur if the scleral flap is superficial or is of normal thickness but not well sutured. Excising more than one-third of the ciliary body carries the risk of hypotony. If the scleral flap is thinner than expected, anterior staphyloma may develop.[8,9,11,34,39]

Retinal detachment is not observed as long as the tumor is located anterior to the muscle insertions. The risk of retinal detachment is greater in choroidectomy procedures. Apart from these, hyphema, ptosis, corneal edema, and increased intraocular pressure may be seen in the early postoperative period.[8,9,11,34,39] The complications reported in previous publications related to exoresection are summarized in Table 4.

Cyclochoroidectomy or Choroidectomy

Surgical Indication and Technique

In tumors with posterior uveal involvement, the surgical technique differs slightly compared to iridociliary tumors. The hinge of the sclera flap is usually arranged to open posteriorly, toward the optic nerve. As there is no anterior chamber access or iris resection, the pupil can be dilated in this surgery and the ocutome probe's position in the vitreous cavity can be observed through the pupil during vitreous aspiration. The steps of the surgery are the same as those described for iridocyclectomy. The only difference here is that there is no entry into the anterior chamber. Firstly, the sclera flap is raised and vitrectomy is performed to make the eye pressure hypotonus. The deep scleral fibers are excised and bipolar cautery is applied to the ciliary body/choroid, followed by ciliary body/choroid excision and tumor removal by scraping from the underlying retina with a sponge. Retinal invasion may be present in mushroom-shaped tumors that rupture Bruch's membrane, and care must be taken to avoid retinal perforation. After the tumor is removed, the sclera flap is sutured in place with 8/0 or 9/0 nylon suture. In case of a retinal tear, PPV must be performed at the end of the procedure.

Peripheral choroidal, ciliary body, and ciliochoroidal tumors with a base diameter of <15 mm can be excised by this method. The risk of developing postoperative hypotony is high for iris and ciliary body tumors with more than 3 clock hours of involvement.[9,37,42] Although there is no clear consensus on the tumor thickness that can be removed with PLSU surgery, the accepted upper limit is 10 mm.[9,37,42] Enucleation is recommended for thicker tumors. In addition, it is preferable that the tumor does not extend more than 7 mm beyond the equatorial region of the eye. Scleral dissection and tumor excision become more difficult closer to the optic nerve.

Complications

Operative complications include retinal detachment and vitreous hemorrhage.[35,43] The risk of developing retinal detachment after excision is high, especially with tumors that

Study, date of publication	Number of eyes	MM n (%)	Mel n (%)	Fuchs' Ad n (%)	CPE Ad n (%)	Leiomyoma, n (%)	Med n (%)	Granuloma n (%)	Nevus n (%)	Met n (%)	SCC n (%)	FB n (%)	Cyst n (%)	LGC n (%)	Gliosis n (%)	Hemorrhage n (%)	Sch n (%)
Shields et al., 1991[9]	95	81 (85.3)	4 (4.2)	4 (4.2)	2 (2.1)	2 (2.1)	1 (1.0)	1 (1.0)									
Char et al., 2001[35]	145	125 (86.2)	5 (3.4)		1 (0.7)	2 (1.4)			7 (4.8)	2 (1.4)	2 (1.4)	1 (0.7)					
Kurt and Gündüz, 2010[39]	22	16 (72.7)	2 (9.1)						4 (18.2)								
Ramasubramanian et al., 2012[36]	37	19 (51.4)	3 (8.1)			1 (2.7)	4 (10.8)		1 (2.7)				5 (13.5)	2 (5.4)	1 (2.7)	1 (2.7)	
Lee et al., 2013[3]	27	19 (70.0)	2 (7.0)	2 (7.0)	1 (4.0)	1 (4.0)	1 (4.0)										1 (4.0)
Mirzayev et al., 2021[47]	56	30 (53.6)	4 (7.1)	2 (3.6)					13 (23.2)	1 (1.8)			6 (10.7)				

MM: Malignant melanoma, Mel: Melanocytoma, Ad: Adenoma, CPE Ad: Adenoma of the ciliary pigment epithelium, Med: Medulloepithelioma, Met: Metastatic tumor, SCC: Squamous cell carcinoma, FB: Foreign body; LGC: Lacrimal gland choristoma; Sch: Schwannoma

infiltrate the retina. In the event of problems such as retinal detachment and vitreous hemorrhage, early vitreoretinal surgery is recommended. The success rate of vitreoretinal surgery decreases after the development of proliferative vitreoretinopathy. In this respect, vitreoretinal surgery for the treatment of complications should be performed at the end of the surgery or in the first postoperative days.[43] Other complications such as subretinal fibrosis, posterior synechia, glaucoma, cataract, and expulsive hemorrhage may also occur.[3,9,34,39]

Tumor Recurrence, Visual Prognosis, and Life Expectancy After PLSU

According to the results of the Collaborative Ocular Melanoma Study (COMS), intrascleral tumor cells are present in 57% of enucleated choroidal melanomas.[44] In addition, there is the possibility of microscopic tumor cells remaining in the surrounding choroid after surgery. For this reason, some authors recommend administering Ruthenium-106 plaque radiotherapy to deliver a dose of 100 Gy radiotherapy to a depth of 1 mm, either at the end of the procedure or within the first postoperative month.[45,46,47] Postoperative plaque radiotherapy reduces the likelihood of recurrence due to intrascleral melanoma cells.

In their PLSU series including 112 cases, Damato[48] reported that the rate of eye preservation was 88% and the proportion of patients with vision of 0.1 or better was 58%. Tumor recurrence occurred in 11 eyes, 8 of which did not receive plaque radiotherapy after PLSU. Retinal detachment developed in 9 eyes with a mean tumor diameter of 15 mm and thickness of 9 mm. As these eyes would normally be treated by enucleation, the authors considered this complication rate acceptable.[48]

Bechrakis et al.[49] reported that larger tumor base diameter, older patient age, lack of adjuvant plaque radiotherapy, and preoperative retinal detachment were risk factors for tumor recurrence after PLSU. The visual prognosis after PLSU depends on tumor location. Visual prognosis is better with nasal tumors and tumors located more than 1 disc diameter from the optic disc and fovea.[50]

Bechrakis et al.[49] and Augsburger et al.[51] evaluated the effect of PLSU surgery on survival prognosis and found that life expectancy after PLSU was equivalent to that obtained by plaque radiotherapy. In other words, PLSU surgery is not disadvantageous in terms of life expectancy. The prevalence of metastasis was reported to be 7% (5 of 95 patients) in a series by Shields et al.[9] and 15% (52 of 332 patients) in a series by Damato et al.[52]

Endoresection Surgery

Endoresection techniques have recently been adopted in the treatment of choroidal melanomas (Figures 5a-f and 6a, b). Residual tumor after radiation causes toxic tumor syndrome through the release of various cytokines and neuromediators, resulting in complications such as neovascular glaucoma, retinopathy, exudation, and retinal detachment.[53] In addition, tumor necrosis leads to the dispersion of pigment and necrotic tumor fragments into the eye, which makes it difficult to observe the tumor by indirect ophthalmoscopy. Endoresection prevents these complications by removing the tumor debris.[12,13,54]

Table 4. Summary of complications after exoresection surgery reported in the literature

Study, date of publication	Number of eyes	VH n (%)	Hyp n (%)	Hem n (%)	RD n (%)	CD n (%)	Pto n (%)	Cat n (%)	CC n (%)	Sy n (%)	CME n (%)	IOP↑ n (%)	Fib n (%)	ST n (%)	ERM n (%)	VRT n (%)	Hypo n (%)	İN n (%)	ID n (%)	SO n (%)	ON n (%)
Shields et al., 1991[9]	95	79 (83.1)	32 (33.7)	33 (34.7)	26 (27.4)	23 (24.2)	12 (12.6)	32 (33.7)	8 (8.4)	20 (21.1)	13 (13.7)	8 (8.4)	25 (26.3)					2 (2.1)			
Damato, 1997[45]	163				49 (30.0)			25 (15.3)													
Char et al., 2001[35]	145				19 (13.1)							2 (1.4)									
Damato ve ark, 2002[43]	156				28 (17.9)																
Bechrakis et al., 2002[49]	36	*			*			14 (44.4)				2 (5.6)						2 (5.6)			
Kivelä et al., 2003[40]	49	**						**			1 (2.0)				4 (8.2)						
Puusaari et al., 2007[41]	33				14 (42.4)			30 (90.9)			3 (9.1)		7 (21.2)								3 (9,1)
Kurt et al., 2010[39]	22	2 (9.1)	2 (9.1)					11 (50.0)	1 (4.5)	1 (4.5)		2 (9.1)		4 (18.2)					1 (4.5)		
Ramasubramanian et al., 2012[36]	37	11 (29.7)	9 (24.3)		3 (8.1)			12 (32.4)	12 (32.4)			6 (16.2)				5 (13.5)	9 (24.3)				
Lee et al., 2013[3]	27	12 (44.4)	8 (29.6)	3 (11.1)	14 (51.9)	2 (7.4)		4 (14.8)	1 (3.7)			1 (3.7)			5 (18.5)					1 (3.7)	
Mirzayev et al., 2021[47]	56	15 (26.8)	6 (10.7)		1 (1.8)		2 (3.6)	21 (37.5)		6 (10.7)		6 (10.7)		10 (17.9)					1 (1.8)		

VH: Vitreous hemorrhage, Hyp: Hyphema, Hem: Intra/subretinal hemorrhage, RD: Retinal detachment, CD: Choroidal detachment, Pto: Ptosis, Cat: Cataract, CC: Corneal complications, Syn: Anterior or posterior synechia, CME: Cystoid macular edema, IOP: Intraocular pressure, Fib: Pre/subretinal fibrosis, ST: Scleral thinning, ERM: Epiretinal membrane, VRT: Vitreoretinal traction, Hypo: Hypotony, IN: Iris neovascularization, ID: Iridodialysis, SO: Sympathetic ophthalmia, ON: Optic neuropathy
* Rates of VH and RD were not reported, but vitreoretinal surgery was performed due to complications in 12 of 36 eyes (33.3%) that underwent exoresection.
**Cataract and VH was reported to develop in some patients after exoresection, but the exact rates were not been specified
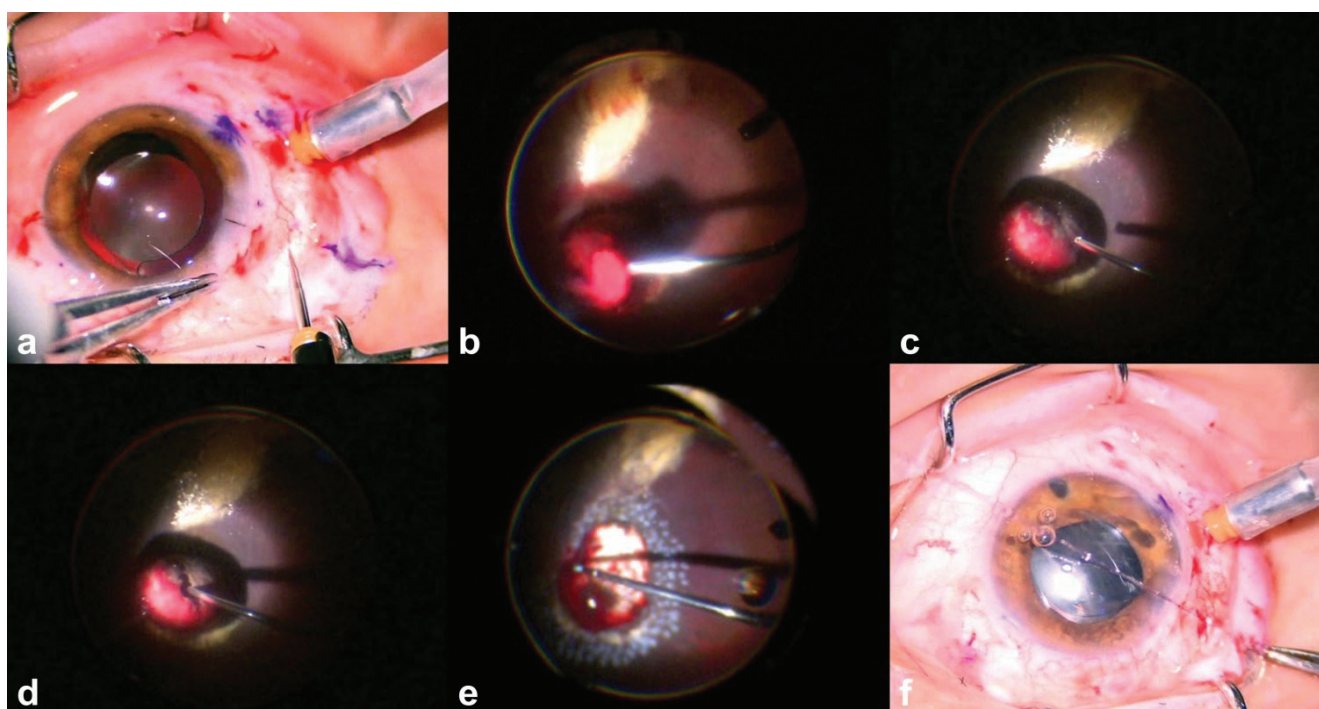
Figure 5. Intraoperative images from endoresection surgery. a) The trocar is advanced into the eye. b) The vitreous hemorrhage around the tumor is cleared using an ocutome. c) Fundus photograph of the choroidal melanoma before endoresection. d) The vitrector is inserted into the tumor during endoresection. e) After endoresection, the choroidal tumor has been resected to the bare sclera. Laser photocoagulation spots are seen around the resection area. f) The sclerotomy is sutured at the end of the procedure
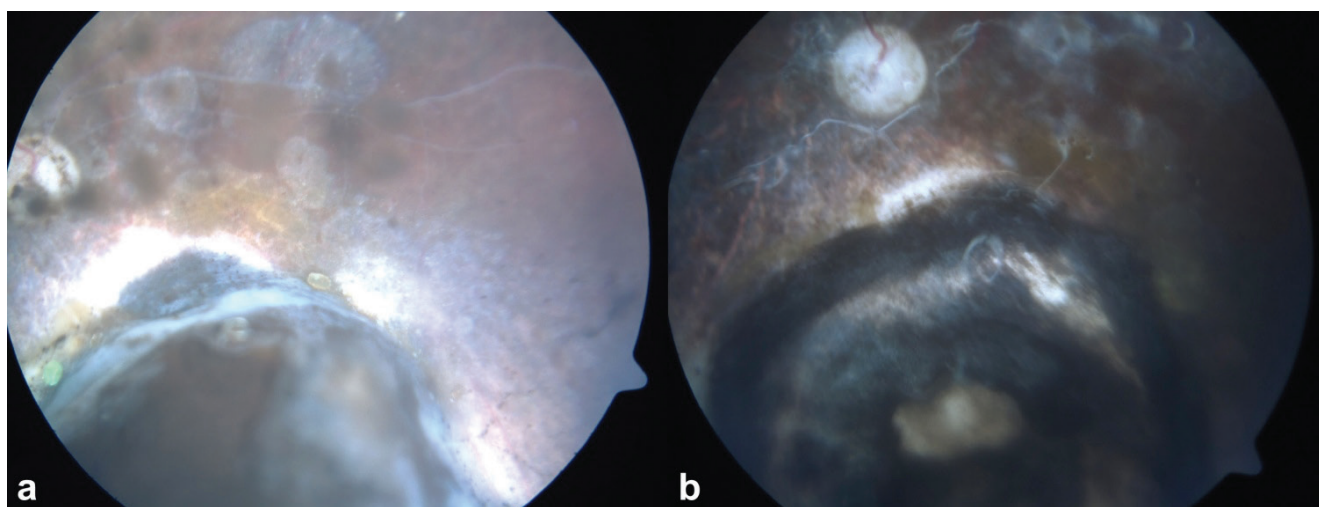

Figure 6. Preoperative and postoperative fundus photographs of a 44-year-old woman with choroidal melanoma who underwent secondary endoresection. a) After plaque radiotherapy and four sessions of transpupillary thermotherapy, the patient had diffuse radiation retinopathy, obliterated vessels, radiation maculopathy, optic atrophy, and vitreous spread from the necrotic tumor. Pigment granules are seen on the optic disc. b) After endoresection, no pigment granules are seen in the vitreous and the tumor is excised down to the bare sclera. The sclera shows areas of residual pigment

Performing endoresection after radiotherapy is recommended because of the risk of live tumor cells leaking out of the eye during the procedure. As radiotherapy kills the live tumor cells, this risk is eliminated.[13,54] However, Konstantinidis et al.[14] stated that preoperative radiotherapy was not necessary, reporting that there was no increased risk of metastasis after endoresection without radiotherapy in their series encompassing 71 cases. According to Konstantinidis et al.[14] and Damato et al.,[55] another advantage of endoresection, especially for tumors close to the optic disc, is the prevention of radiation papillopathy and radiation retinopathy because radiation is not applied. Although endoresection is usually performed for choroidal melanomas, it

can also be used to treat retinal hemangioblastoma, RVT, and (albeit controversial) retinoblastoma.[56,57,58,59,60,61,62,63,64,65,66]

According to generally accepted indications, endoresection should be used for tumors with a base diameter less than 15 mm and less than 3 clock hours contact with the optic disc.[13,54] The anterior border of the tumor is preferably at or posterior to the equator (towards the optic disc). Endoresection cannot be performed for tumors with ciliary body involvement because it is generally not possible to visualize the tumor in its entirety to ensure complete excision.

Endoresection surgery in a patient with cataract starts with phacoemulsification and in-the-bag intraocular lens implantation, followed by vitrectomy. Posterior hyaloid detachment, vitreous base removal, and clearing the vitreous over the tumor must be performed using wide-angle imaging systems. The ocutome is then introduced transretinally into the mass and the tumor is excised to the sclera. The retina is stabilized with perfluorocarbon, endolaser photocoagulation is applied to the excision margins, and intraocular silicone is administered. The intraocular silicone should be removed 3

months postoperatively. In some cases it may be necessary to leave the silicone in the eye for longer periods of time.

The main complications of endoresection surgery are retinal detachment and tumor recurrence.[55,67] Retinal detachment may occur for reasons such as proliferative vitreoretinopathy or retinal detachment at the edges of the retinotomy. Complications such as fibrosis in the scar base and macular ectopy may be observed. Tumor recurrence usually occurs at the margin of the coloboma resulting from tumor excision but may also arise in different, nonadjacent areas of the retina.[67]

Damato et al.[13] detected signs of subconjunctival, intraocular, and extraocular spread in less than 5% of the cases after endoresection surgery without radiotherapy. The authors noted that this was an acceptable risk in exchange for protection from other major complications associated with radiotherapy.

Complications such as increased intraocular pressure, vitreous hemorrhage, epiretinal membrane, phthisis bulbi, hypotonia, macular hole, choroidal neovascularization, proliferative vitreoretinopathy, and endophthalmitis may also occur after endoresection.[13,14,64,65,68,69,70,71,72,73,74,75] A summary of

Table 5. Summary of complications after endoresection reported in the literature

Study, date of publication	Number of eyes	RD n (%)	Cataract n (%)	OH n (%)	Phthisis n (%)	ERM n (%)	VH n (%)	Endo n (%)	CNV n (%)	MH n (%)	CC n (%)	Hypo n (%)	PVR n (%)
Damato et al., 1998[13]	52	17 (32.7)	28 (53.8)	14 (26.9)	1 (1.9)	1 (1.9)	2 (3.8)	1 (1.9)	1 (1.9)				
Bechrakis et al., 2006[70]	58	16 (27.6)	21 (36.2)	1 (1.7)	1 (1.7)	1 (1.7)				2 (3.4)			
Karkhaneh et al., 2007[75]	20	3 (15)	5 (25)				16* (80)				2** (10)		
Caminal et al., 2013[68]	27				1 (3.7)								
Konstantinidis et al., 2013[14]	71	16 (22.5)	60 (94***)	8 (11.3)		9 (12.7)	2 (2.8)						
McCannel, 2013[74]	5			1 (20)									
Garcia-Arumi et al., 2015[73]	41	11 (26.8)	39 (95.1)	14 (34.1)	5 (12.2)	5 (12.2)	1 (2.4)		2 (4.9)			3 (7.3)	
Sinyavskiy et al., 2016[71]	21	3 (14.3)		4 (19.0)									
Süsskind et al., 2016[72]	35	4 (11.4)		2 (5.7)		2 (5.7)				1 (2.9)	3‡ (8.6)	2 (5.7)	
Vidoris et al., 2017[69]	14	2 (14.2)		1 (7.1)									
Avci et al., 2017[64]	12									1 (8.3)	1 (8.3)		1 (8.3)
Karacorlu et al., 2018[65]	13		7 (53.8)	4 (30.8)									1 (7.7)

RD: Retinal detachment, OH: Ocular hypertension or glaucoma, ERM: Epiretinal membrane, VH: Vitreous hemorrhage, Endo: Endophthalmitis, CNV: Choroidal neovascularization, MH: Macular hole, CC: Corneal complications, PVR: Proliferative vitreoretinopathy
*Mild vitreous hemorrhage in 9 eyes, moderate in 2 eyes, and severe in 5 eyes.
**Silicone oil keratopathy (1 eye) and bullous keratopathy (1 eye).
***Percentage calculated from 64 phakic eyes.
‡Persistent corneal erosion (1 eye) and band keratopathy (2 eyes)

the complications reported in previous publications related to endoresection is shown in Table 5. Metastasis rates of 0-20% and mortality rates of 0-18.2% have been reported after endoresection of choroidal melanomas.[13,14,68,69,70,71,72,73,74,75,76,77,78]

Surgeries for Complications Secondary to Tumor Treatment

The main posterior segment complications resulting from the treatment of posterior segment tumors with radiotherapy and transpupillary thermotherapy (TTT) are vitreous hemorrhage, retinal detachment, and epiretinal membrane formation (Figure 7a,b). In uveal melanoma, vitreous hemorrhage is the most important posterior segment problem that develops after radiotherapy and requires surgical intervention. Vitreous hemorrhage occurs in 8-15% of cases following plaque radiotherapy at 5 years.[79] Vitreous hemorrhage develops as a result of posterior vitreous detachment and tumor necrosis in the early period, whereas after the first year it usually occurs due to proliferative radiation retinopathy.[79] In patients with vitreous hemorrhage and an attached retina on ultrasonography, a period of 3 months should be allowed for spontaneous resolution. Clearance of the vitreous hemorrhage is observed in approximately 48% of eyes after this period. PPV and other necessary vitreoretinal surgical interventions should be performed for vitreous hemorrhages that have not cleared by this time.[79] At this point, tumor endoresection can also be added to the treatment.

Bansal et al.[80] evaluated the outcomes of PPV surgery performed due to vitreous hemorrhage in 47 eyes with uveal melanoma and found that there was no intraocular or extraocular melanoma cell spread. The authors also reviewed literature reports of PPV performed due to uveal melanoma and concluded that PPV surgery can be used in the treatment of various complications such as retinal detachment and vitreous hemorrhage in patients with radiotherapy-treated uveal melanoma and does not increase the risk of tumor spread. The only exception to this may be cases undergoing PPV for vitreous hemorrhage where recurrent necrotic melanoma could not be detected preoperatively.[79]

PPV is applied for retinal detachment secondary to radiotherapy and TTT for the treatment of posterior segment tumors, the persistence of exudative retinal detachment present before treatment, the formation of iatrogenic retinal tears (especially with TTT), and the development of fibrovascular proliferation and tractional retinal detachment. Another common problem, especially in patients who undergo TTT, is the development of epiretinal membranes. Epiretinal membrane formation, especially in tumors close to the macula, is a serious problem in terms of vision prognosis. Epiretinal membrane peeling surgery should be performed after the tumor regresses if there is any hope of visual improvement. In case of macular ischemia, macular tumor involvement, and atrophy/massive cystoid edema due to treatment, there is no point in performing such procedures.

In addition to the posterior segment complications that develop after intraocular tumor surgery, tumor containing eyes may require cataract surgery for complicated cataract; trabeculectomy, diode laser cyclophotocoagulation or cyclocryotherapy for secondary glaucoma. Enucleation should be considered as a last option for a painful blind eye.
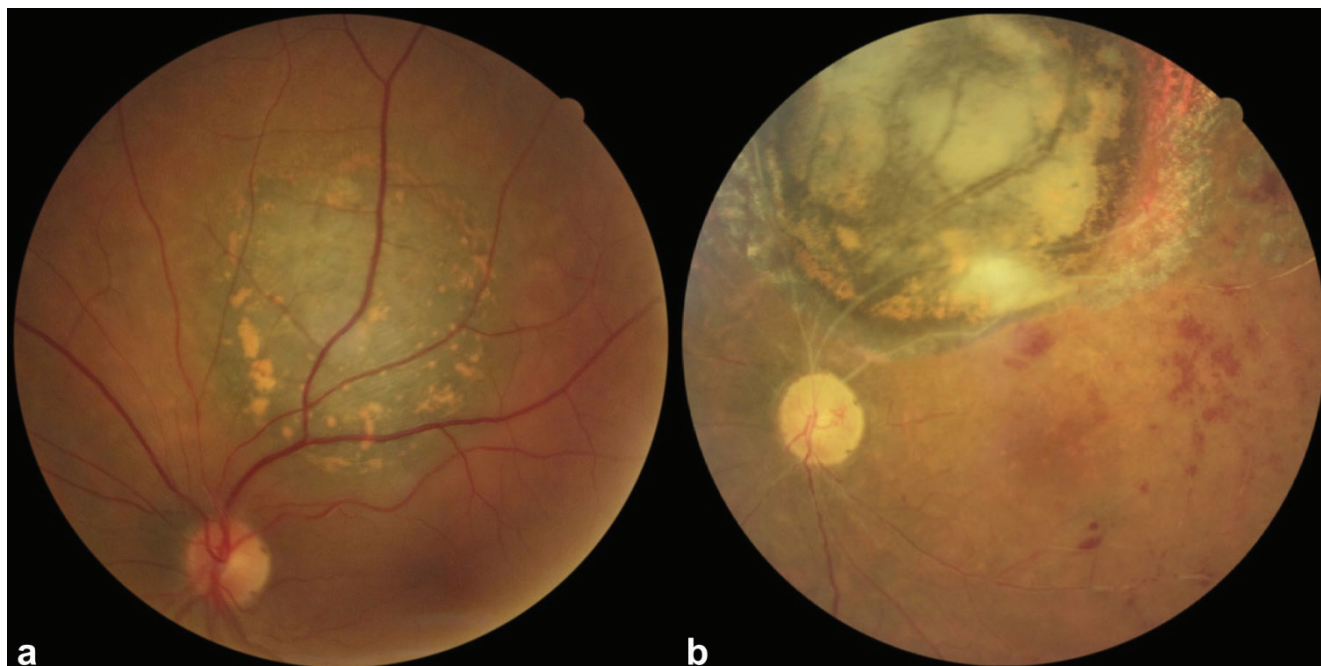

Figure 7. Fundus photographs of a 55-year-old woman who underwent pars plana vitrectomy for complications after plaque radiotherapy and transpupillary thermotherapy for choroidal melanoma. a) An 8 x 6 x 3.5 mm choroidal melanoma is seen in superotemporal of the optic disc. Vision was measured as 20/20. b) The patient underwent pars plana vitrectomy due to proliferative radiation retinopathy and vitreous hemorrhage after receiving plaque radiotherapy and three sessions of transpupillary thermotherapy. Postoperatively, vision was hand movements and optic atrophy, obliterated vessels, diffuse retinal hemorrhages, and macular edema are seen

Conclusions

In patients with intraocular tumors, surgery is performed for excision/biopsy and for the management of complications resulting from tumor treatment. FNAB and TRB are commonly used biopsy methods. Excision/biopsy by PLSU is performed for peripheral choroid and ciliary body/iris tumors. The procedure must be performed by experienced surgeons to ensure complete tumor excision and reduce or prevent complications. Endoresection surgery is a promising method for selected indications. Removing residual tumor after radiotherapy and thermotherapy is beneficial in preventing complications such as neovascular glaucoma, retinal exudation, retinal detachment, and subsequent vision loss. PPV surgery is performed for the management of complications such as vitreous hemorrhage, retinal detachment, and epiretinal membrane resulting from the treatment of posterior segment tumors. Before embarking on vitrectomy surgery for related complications, it should be made certain that there are no active tumor cells remaining in the eye.

In addition to posterior segment complications, the necessary surgical treatments should be performed in case of cataract and glaucoma development. Enucleation is necessary for painful blind eyes.

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