



# Study of intraocular tumours causing secondary Glaucoma : A Systematic review of 57 cases

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**Received:** February 15, 2026; **Published:** February 25, 2026

## Abstract

**Objective:** To identify intraocular or cerebral tumours responsible for secondary glaucoma.

**Materials and Methods:** A review was conducted on PubMed, Embase, Cochrane, Google Scholar, Pan African Journal, Ophthalmology Clinics and the French Society of Ophthalmology, covering the period 1996–2023. Fifty-seven studies meeting the inclusion criteria were selected

**Results:** The tumors most frequently associated with secondary glaucoma were retinoblastoma (23.6%), choroidal melanoma (10.9%), and medulloepithelioma (10.9%). These tumours develop within the iris, they affect the drainage angle, reducing the flow of fluid and causing high eye pressure. Medical imaging (CT scan, MRI) enabled accurate diagnosis in the majority of cases.

**Conclusion:** In cases of glaucoma resistant to treatment, a differential diagnosis including an intraocular tumor should be considered, with the use of medical imaging for appropriate management.

**Keywords :** Secondary glaucoma, Tumour, Radiology, Medical imaging.

## Introduction

Glaucoma is a progressive optic neuropathy affecting 0.5 to 1% of adults over 40 years of age in Europe and North America, affecting the optic nerve, which becomes damaged, and can occur at any age, but is more common in older people. It is a major cause of blindness worldwide (1). Although primary glaucoma is the most common, secondary glaucoma, often associated with identifiable etiologies, presents a diagnostic and therapeutic challenge. Among these etiologies, intraocular and cerebral tumors are often underdiagnosed due to their misleading clinical presentation, mimicking refractory glaucoma (2). Previous studies have shown a variable prevalence of secondary glaucoma, ranging from

The incidence of glaucoma ranges from 0.7% to 35% depending on the population, with a significant proportion linked to tumors (3–5). However, data on the specific tumors involved and their pathophysiological mechanisms remain scattered. This review aims to identify intraocular

and cerebral tumors responsible for secondary glaucoma and to evaluate the contribution of medical imaging to their early diagnosis.

## Materials and Methods

We conducted a comprehensive literature review on tumor-related secondary glaucoma, using several search engines, and limited the search to articles published in English, French, and Spanish spanning from 1996 to 2023 in order to have a range of etiological tumors.

### Electronic databases

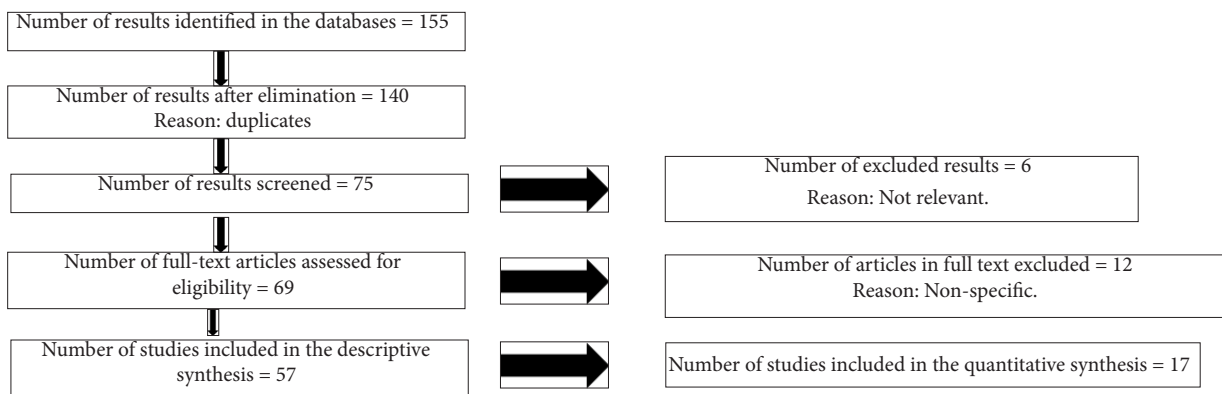
The articles of interest were chosen based on their relevance to the different types of tumors mimicking glaucoma. To this end, we searched PubMed, Embase, Cochrane, Google Scholar, the Pan African Journal (PAN), Ophthalmology Clinics, and the French Society of Ophthalmology (FSO).



**Other sources**

A manual search was conducted in the journal reference lists. In addition, we contacted experts in the field for other potentially eligible

studies that we might have missed. The selection of articles was made as shown in the Flow Chart below.



**Figure 1 :** Flowchart of relevant article selection.

**Selection criteria**

**Inclusion criteria**

We included all articles on secondary glaucomas diagnosed in patients of both sexes and all ages, whose diagnosis was made clinically and by any other means of investigation.

**Exclusion criteria**

Excluded from this study were any articles dealing with secondary glaucoma whose causes were not tumoral

**Ethical clearance**

Since previous studies had already received research authorization, it was not necessary to obtain another one for this study. Given the use of data from literature reviews, informed consent was required was not applicable in accordance with study quality regulations.

**Result**

The following results show the different studies presenting the types of intraocular tumors mimicking refractory glaucoma and their frequency in the population.

**Table I :** Summary of type of tumor and locations.

No's	Reference	Article Title	Year, Volume	Types of tumors
1	Nazih Tzili et al.	Congenital glaucoma and neurofibromatosis type 1	2015; 21:56	Neurofibromatosis type 1
2	Rodolfo López Rodríguez et al.	Choroid uveal melanoma masked like phacomorphic glaucoma	2021;22(1)	Choroid uveal melanoma
3	Anthony JH Hall	Clinical and experimental optometry: Secondary glaucoma	2000; 83: 3	Choroid melanoma, Irisciliary body melanoma,
4	Min Yang et al.	Eye Tumors Misdiagnosed as Glaucoma	2015; Volume 128: 2	Ciliary body medullaepit-helioma, Intraocular metastasis microgliaoma, Optic nerve sheath meningioma, Retinoblastoma, choroidal and ciliary body melanomas. Iris melanomas. Retinoblastoma. iris melanocytoma. juvenile xanthogranuloma.
5	<u>Arash Mansouri, and Leon W. Herndon.</u>	Glaucoma as the initial manifestation of ocular malignancy	<u>1999, Volume 12, 2,</u>	Lymphangioma. optic disk melanocytoma. ocular metastases. Leukemia. breast carcinoma. epithelial ingrowth non-Hodgkin's lymphoma.

6	Camp DA et al.	Glaucoma Associated with Intraocular Tumors	2019;30(2)	Choroidal melanoma Metastatic ring melanomas melanomas or melanocytomas melanomas, retinoblastomas (iris and ciliary body tumors) melanoma, metastasis, lymphoma.
7	Sonal P. Yadav	Glaucoma Related to Ocular and Orbital Tumors	April 27th, 2021	choroidal tumors (melanoma, metastasis), vitreo-retinal tumors (retinoblastoma, medulloepithelioma, vitreoretinal lymphoma) and orbital tumors (extra-scleral extension of choroidal melanoma or retinoblastoma, primary orbital tumors) ocular metastasis melanoma and melanocytoma. Iris heterochromia. ciliary body melanomas. Leukemia. Non-Hodgkin lymphoma.
8	<a href="#">Eric G. Feinstein</a> Et al.	Glaucoma Secondary to Intraocular Tumors	November 29, 2021.	Metastatic Tumors. Uveal Melanoma. Retinoblastoma Medulloepithelioma. Iris melanocytoma. Multiple Myeloma Juvenile Xanthogranuloma iris melanoma
9	<a href="#">David A Camp</a> et al.	Glaucoma secondary to intraocular tumors: mechanisms and management	2019;30(2)	iris metastasis, iris lymphoma, trabecular meshwork melanoma, choroidal melanoma, choroidal metastasis, retinoblastoma, and medulloepithelioma. intrasellar tumours. suprasellar tumours. parasellar tumors retrosellar tumour pituitary gland tumors. Meningiomas Craniopharyngiomas. chiasmal gliomas.
10	<a href="#">Yuanzhen Qu</a> et al.	Glaucoma-like optic neuropathy in patients with intracranial tumors	2011 Aug;89(5)	
11	<a href="#">De Gottrau, P;Holbach, L. M;Naumann, GO H</a>	Acute glaucoma: the first manifestation of a malignant melanoma of the choroid	1993, Vol 16, Num 4,	malignant melanoma
12	Manli Zhao, Yalin Mu1, Yalong Dang, Yu Zhu	Secondary glaucoma as initial manifestation of ringmelanoma: a case report and review of literature	2014;7(11)	choroid. Melanomas
13	Farida Zhumageldiyeva, Tynyskul Teleuova	Metastatic tumor of the ciliary body manifesting as phacomorphic glaucoma: A clinical case	2022; 19(3)	Metastatic ciliary body tumor
14	<a href="#">Ahmad Abdel-Aty</a> et al.	Necrotic Uveal Melanoma Mimics Orbital Cellulitis: A Review	2022 Feb;8(1)	Uveal Melanoma

				Uveal melanoma Uveal sarcoma Iris melanocytoma Iris pigment epithelium adenoma Iris malignant melanoma Ring melanoma Heterochromia Ciliary body medulloepithelioma Ciliary body melanocyte melanocytoma Ciliary body malignant melanoma Retinoblastoma Choroidal malignant melanoma Uveal metastasis Multiple myeloma Large-cell lymphoma Juvenile xanthogranuloma
15	<a href="#">Melissa G. Tonget al.</a>	Ocular Tumors and Glaucoma	<a href="#">January 2022</a>	
16	Anni E. Stadigh et al.	Incidence and Risk Factors for Secondary Glaucoma in Eyes with Uveal Melanoma	2023, Volume 6, Number 1,	Uveal Melanoma
17	John Mark S. de Leon et al.	Secondary glaucoma in retinoblastoma	2005 VOL. 30 • NO. 3	Retinoblastoma  uveal melanomas iris melanoma ciliary body melanoma choroidal melanoma uveal metastases iris metastases ciliary body metastases choroidal metastases retinoblastoma lymphoma, leukemia, medulloepithelioma, melanocytoma, and adenoma
18	<a href="#">CL Shieldset al.</a>	Prevalence and mechanisms of secondary intraocular pressure elevation in eyes with intraocular tumors	1987 Jul;94(7)	

**Table II :** Distribution of intraocular tumors from 15 articles.

Number	Different tumors	Tumor distribution	Percentage (%)
1	Neurofibromatosis	01	
2	Choroid melanoma	14	
3	Iris ciliary body melanoma	08	
4	Ciliary medulloepithelioma	06	
5	Intra-ocular metastasis	10	
6	Microglioma	01	
7	Optic nerve sheath meningioma	02	
8	Retinoblastoma	13	
9	Ciliary body metastasis	03	
10	Iris melanoma	02	
11	Iris melanocystoma juvenile	04	
12	Xanthgranuloma	03	
13	Lymphangyoma	02	
14	Optic disk melanocytoma	02	
15	Ocular metastasis	07	
16	Leukemia	03	
17	Non-Hodgkin lymphoma	03	

18	Ring melanoma	02
19	Lymphoma	04
20	Uveit melanoma	05
21	Multiple juvenile myeloma	02
22	Supra, intra, para, retroseller tumor	01
23	Pituitary gland tumor	01
24	Craniopharyngioma	01
25	Chiasmal glioma	01
26	Iris adenoma	02
27	Uveal sarcoma	01
28	Heterochioma	01

Number	Tumor class	Number	Distribution
1	Neurofrimatosi	1	(1.81%)
2	Melanoma	6	(10.90%)
3	Medulloepithelioma	6	(10.90%)
4	Metastasi	2	(3.63%)
5	Microglioma	1	(1.81%)
6	Meningioma	2	(3.63%)
7	Retinoblastoma	13	(23.63%)
8	Melanocytoma	2	(3.63%)
9	Xanthogranulocytoma	3	(5.45%)
10	Lymphangioma	2	(3.63%)
11	Metastasi	2	(3.63%)
12	Leukemia	3	(5.45%)
13	Lymphoma	4	(7.27%)
14	Multiple myeloma	2	(3.63%)
15	Craniopharyngioma	1	(1.81%)
16	Chiasmal glioma	1	(1.81%)
17	Adenoma	2	(3.63%)
18	Sarcoma	1	(1.81%)
19	Heterochromia	1	(1.81%)
<b>Total</b>		<b>55</b>	<b>100%</b>

Table III : Tumor class.

## Discussion

Glaucoma is a group of intraocular disorders exhibiting characteristics of optic neuropathy with associated visual loss, and manifesting as elevated intraocular pressure (4). In most cases, glaucoma is of the "primary" form, meaning there is no identifiable cause for high pressure or the development of glaucoma. A "secondary" glaucoma, on the other hand, occurs when there is an ophthalmic or medical condition that predisposes to the development of the high intra-ocular pressure (1). The etiologies of these secondary glaucomas are varied and numerous and include, among others: Pigment Dispersion Syndrome and Pseudoexfoliation, Iatrogenic and Drug-induced causes, Intraocular Inflammation (uveitic glaucoma), trauma, neovascularization, corneal damage and surgery, intraocular bleeding, and tumors (1).

Tumors developing in the iris affect the drainage angle, reducing drainage flow and causing elevated intraocular pressure. In the ciliary body, they can push the peripheral iris forward, closing the drainage angle. Large tumors in the posterior ocular region exert a mass effect on the lens, pushing it forward and thus closing the pupillary angle. These tumors can also cause neovascularization (1).

Although very few studies are reported worldwide on this particular entity, Quigley in 1996 established that 6 million people worldwide suffered from secondary glaucoma out of all glaucomatous people (7).

Partha Chakma in 2021 found 0.2% of secondary glaucoma among glaucomatous patients and established the following causes : traumatic (17.9%), neovascularization (10.4%), pseudoexfoliating glaucoma (2.8%), pigmentary glaucoma (1.9%), silicone oil-induced glaucoma (0.9%), and uveitis-glaucoma-hyphema syndrome (0.9%) (4). These results show that tumors were not found during this study, demonstrating the rarity of this entity, which is nevertheless a real cause of secondary glaucoma. Intraocular tumors can present with various clinical signs. They can be misdiagnosed as glaucoma due to jaundice, eye pain, headaches, elevated intraocular pressure (IOP), or even adhesions of the anterior chamber angle (4).

The most common symptoms encountered by Yang included decreased visual acuity, eyelid inflammation, jaundice, headache, nausea, vomiting, and increased intraocular pressure (IOP). Conjunctival and ciliary congestion, corneal edema, mydriasis, and iris neovascularization occur in some cases (9). Because these symptoms and clinical signs are similar to those of glaucoma, all of these clinical situations are most often misdiagnosed as primary or secondary glaucoma.

In a study by Shields et al., 58 out of 144 patients (40%) with iris melanoma were diagnosed with glaucoma at their initial consultation. However, specific clinical features, ophthalmological examination, and imaging technology helped to establish the most accurate diagnosis (8). Therefore, it is crucial to consider the possibility of tumor lesions in secondary glaucomas, especially when the clinical picture does not improve.

Among the tumors responsible for these situations, a review of the literature on secondary glaucoma identified retinoblastomas (23.63%), melanoma and medulloepithelioma (10.90%), lymphoma (7.27%), xanthogranulocytic leukemia and leukemia (5.4%), meningioma, lymphangioma, multiple myeloma, adenoma, and metastases (3.63%). Other tumors may also be encountered, such as neurofibromatosis, microglioma, craniopharyngioma, glioma, sarcoma, and heterochromia (8).

Intraocular tumors mimicking secondary glaucomas manifest through various mechanisms, as revealed in several literature studies. These mechanisms include direct invasion, infiltration, or seeding of aqueous-flow structures, as well as indirect processes such as angle closure and anterior segment neovascularization (2). They can be difficult to diagnose and are often refractory to treatment. Extensive literature shows that secondary glaucoma associated with intraocular tumors has been studied for many years. Just before the turn of the century, the first published series indicated elevated intraocular pressure in slightly more than half of the eyes enucleated for uveal melanoma (11).

Subsequent studies on choroidal and ciliary body melanomas in the 1960s already showed a frequency of secondary glaucoma ranging from

27% to 43%. When iris melanomas were included, as in a widely cited 1970 study, a lower rate of 20% was reported. In addition to numerous cases of association with malignant melanomas, secondary glaucoma has been reported in cases of retinoblastoma, iris melanocytoma, juvenile xanthogranuloma, lymphangioma, optic disc melanocytoma, and ocular metastases. Leukemia, breast carcinoma, and non-Hodgkin lymphoma are among the malignant lesions associated with secondary glaucoma (13).

## Conclusion

This review identifies retinoblastoma, choroidal melanoma, and medulloepithelioma as the intraocular tumors most frequently associated with refractory glaucoma. It confirms that medical imaging, particularly computed tomography (CT) and magnetic resonance imaging (MRI), is an essential diagnostic tool for unmasking the tumors in these glaucomas. Systematically including this etiology in the differential diagnosis and using imaging early helps avoid therapeutic errors and allows for the implementation of appropriate and potentially life-saving oncological management.

## Conflict of interest

None.

## Acknowledgements

To Professor Serge BILLONG

To the authors of articles,

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