SCARY OR NOT? BACK TO FRONT

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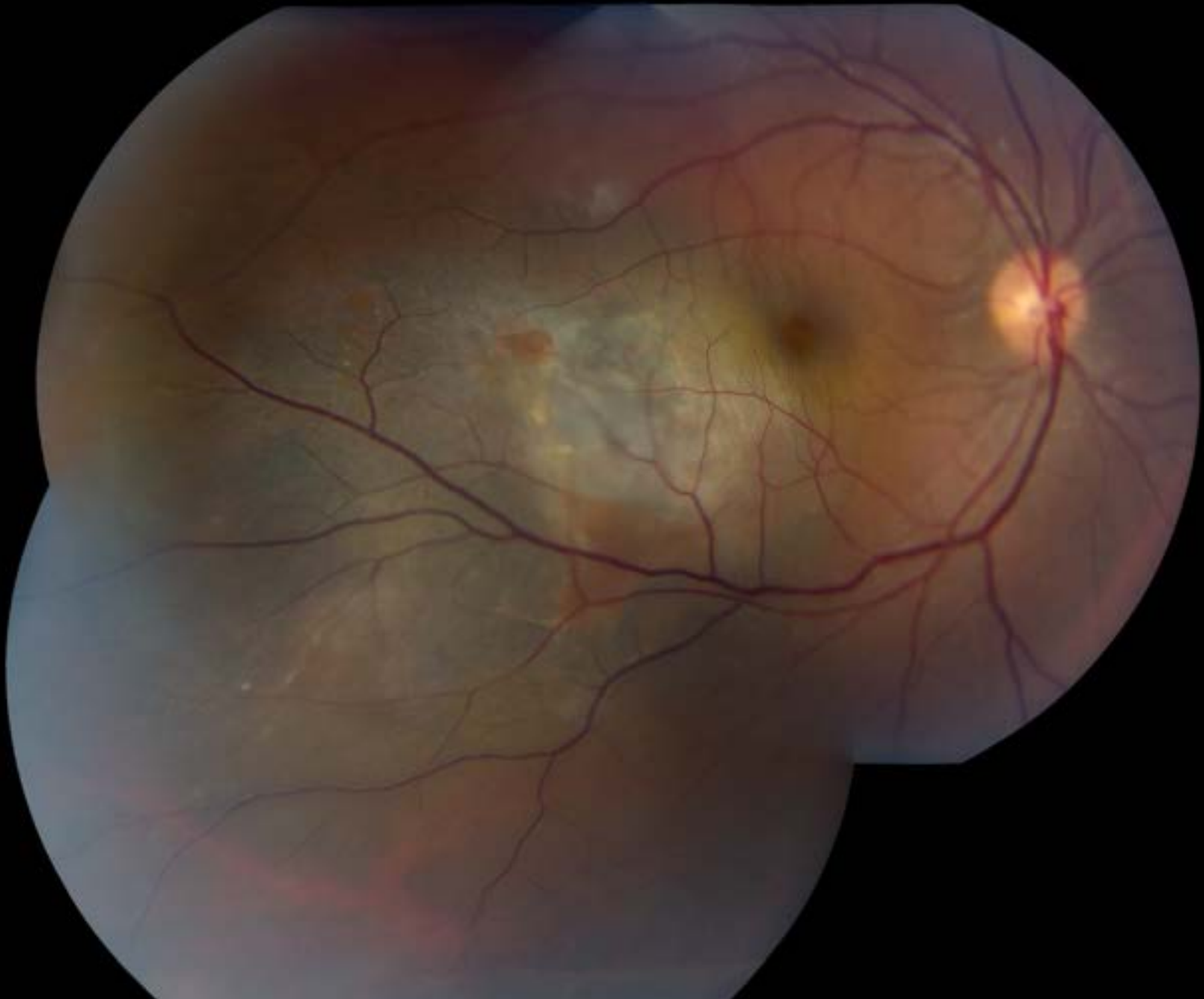
MURRAY
Ocular Oncology & Retina

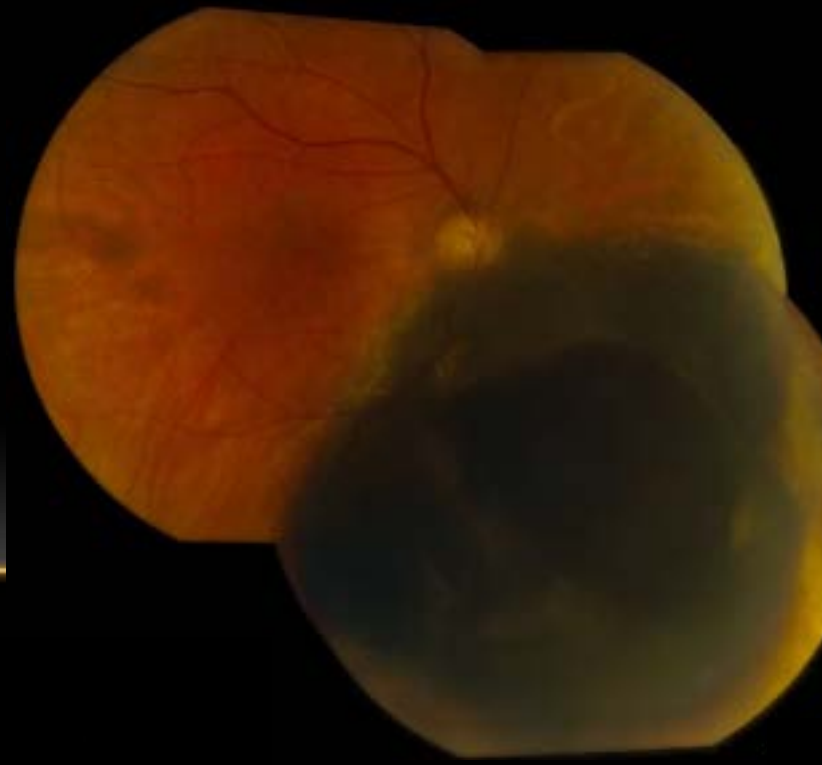
DISCLOSURE INFORMATION

- Dr. Gold:
  - No financial disclosures



CHOROIDAL MELANOMA

- Most common primary intraocular neoplasm in adults
- Incidence of ~4-6 per million per year in the US
- Risk factors include
  - Iris and Skin color
  - European ancestry
  - Age
  - Oculodermal Melanocytosis (Nevus of Ota)
  - Environmental factors (less understood)



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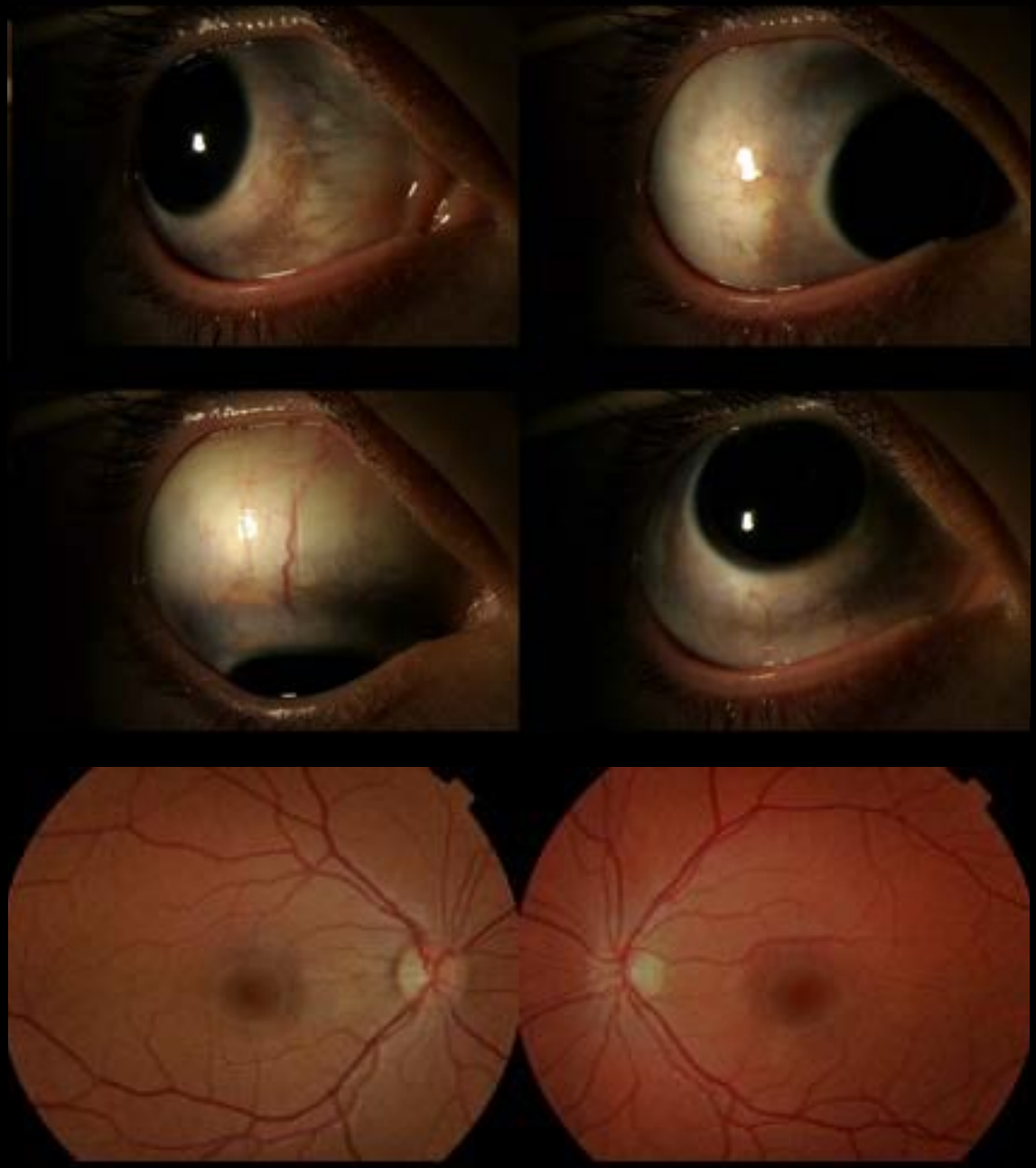
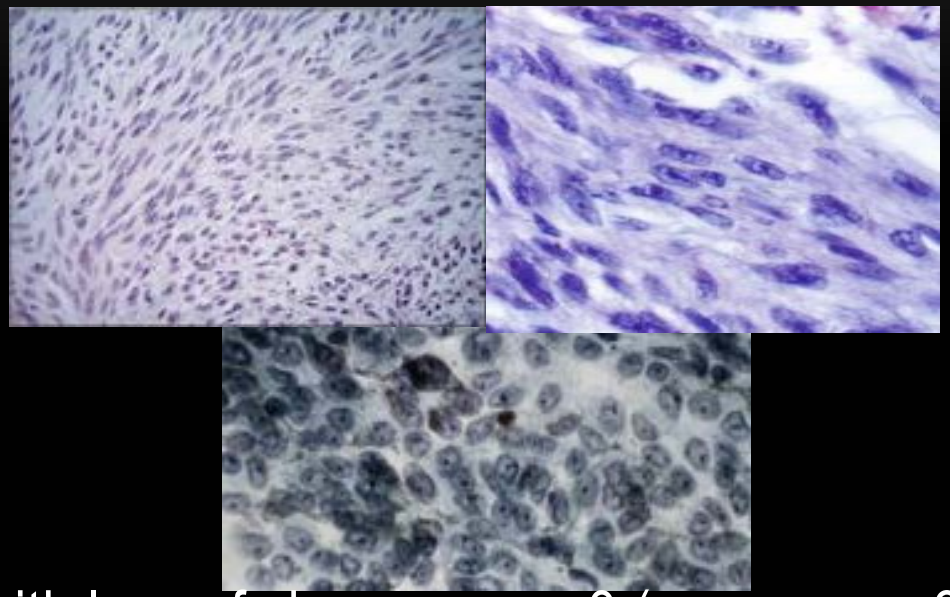


CHOROIDAL MELANOMA

- Histopathology
  - Spindle-cell (A,B)
  - Epithelioid-cell
  - Mixed-cell



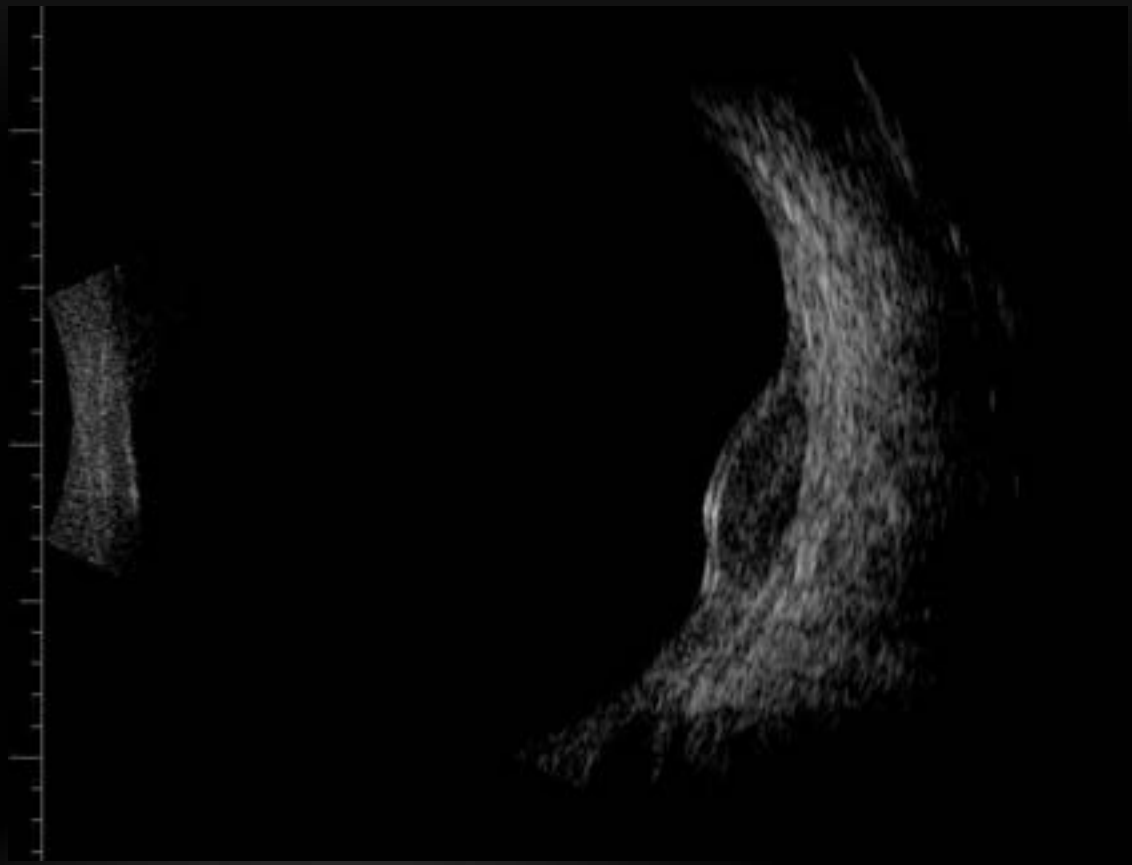
- Genetics
  - Strong association with loss of chromosome 3 (monosomy 3)
  - Mutations in chromosomes 6 and 8 have been reported

CHOROIDAL MELANOMA

- Typically present as elevated choroidal lesions that may be pigmented or amelanotic
- Favored metastatic sites are the liver and lungs
- Diagnosis is made primarily by physical exam
  - Indirect ophthalmoscopy
  - Echography
- FA may show dual circulation pattern

ECHOGRAPHY

- Acoustic hollowing
- Choroidal excavation
- Orbital Shadowing
- Collar-button configuration



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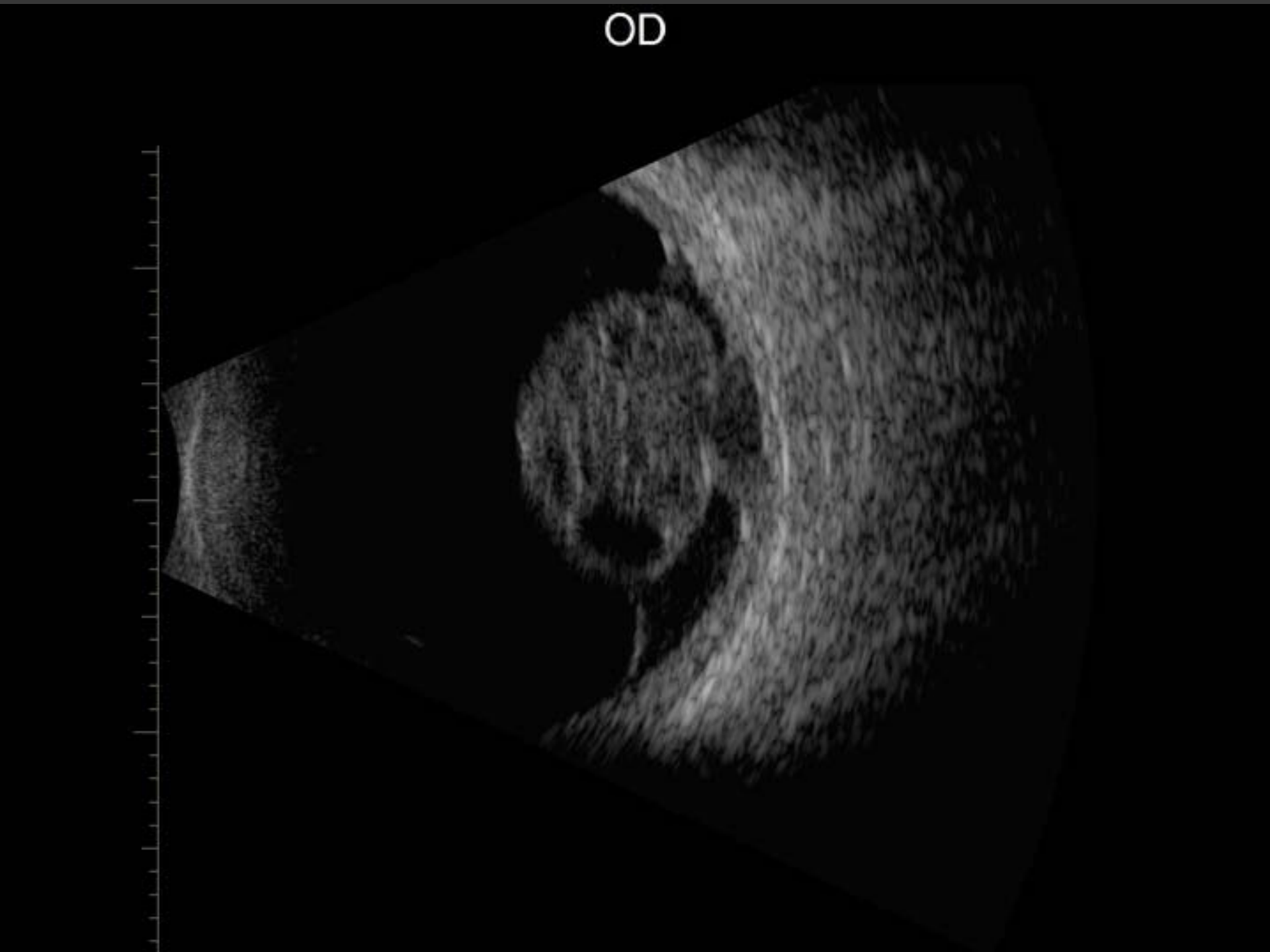
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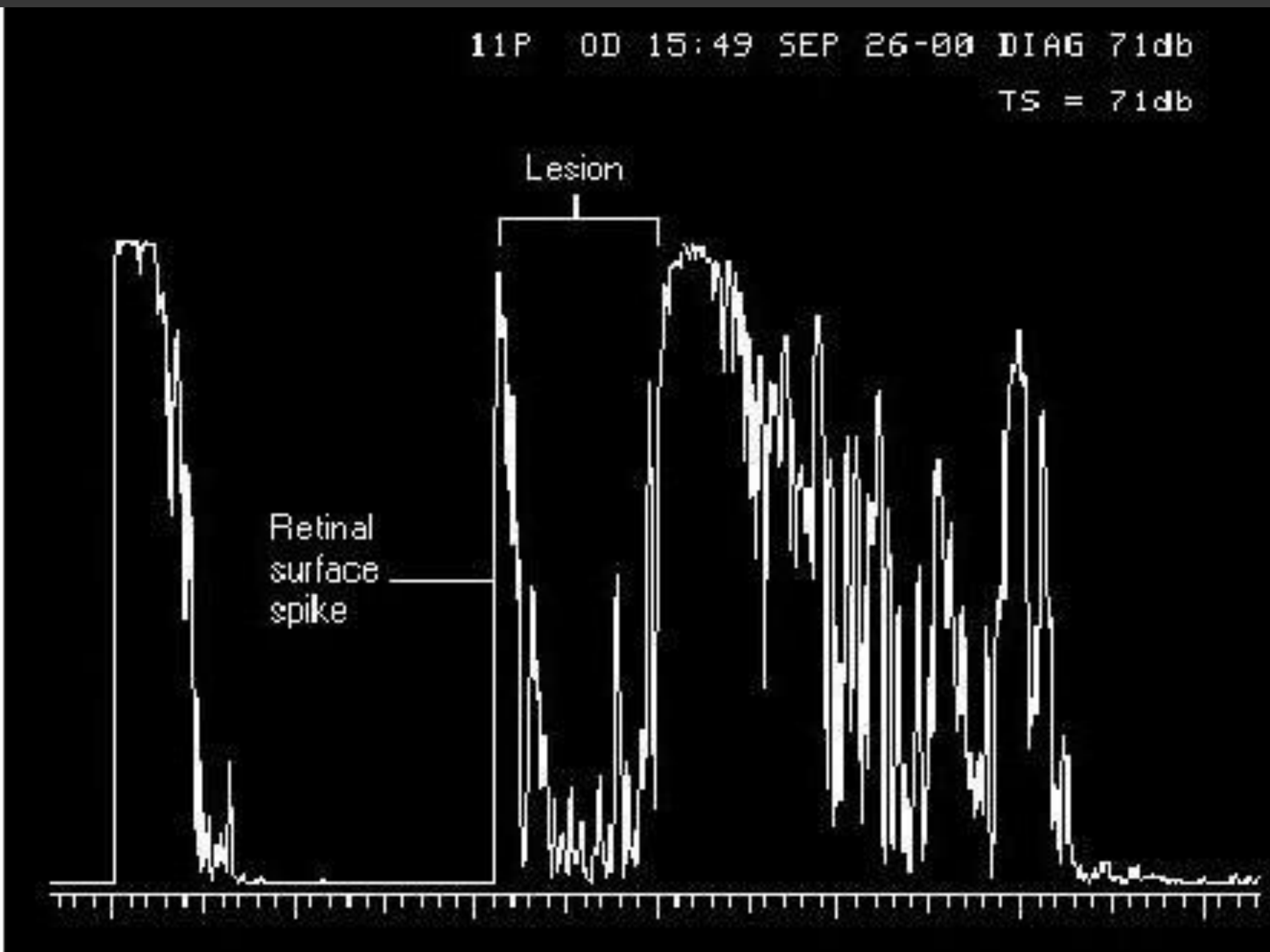
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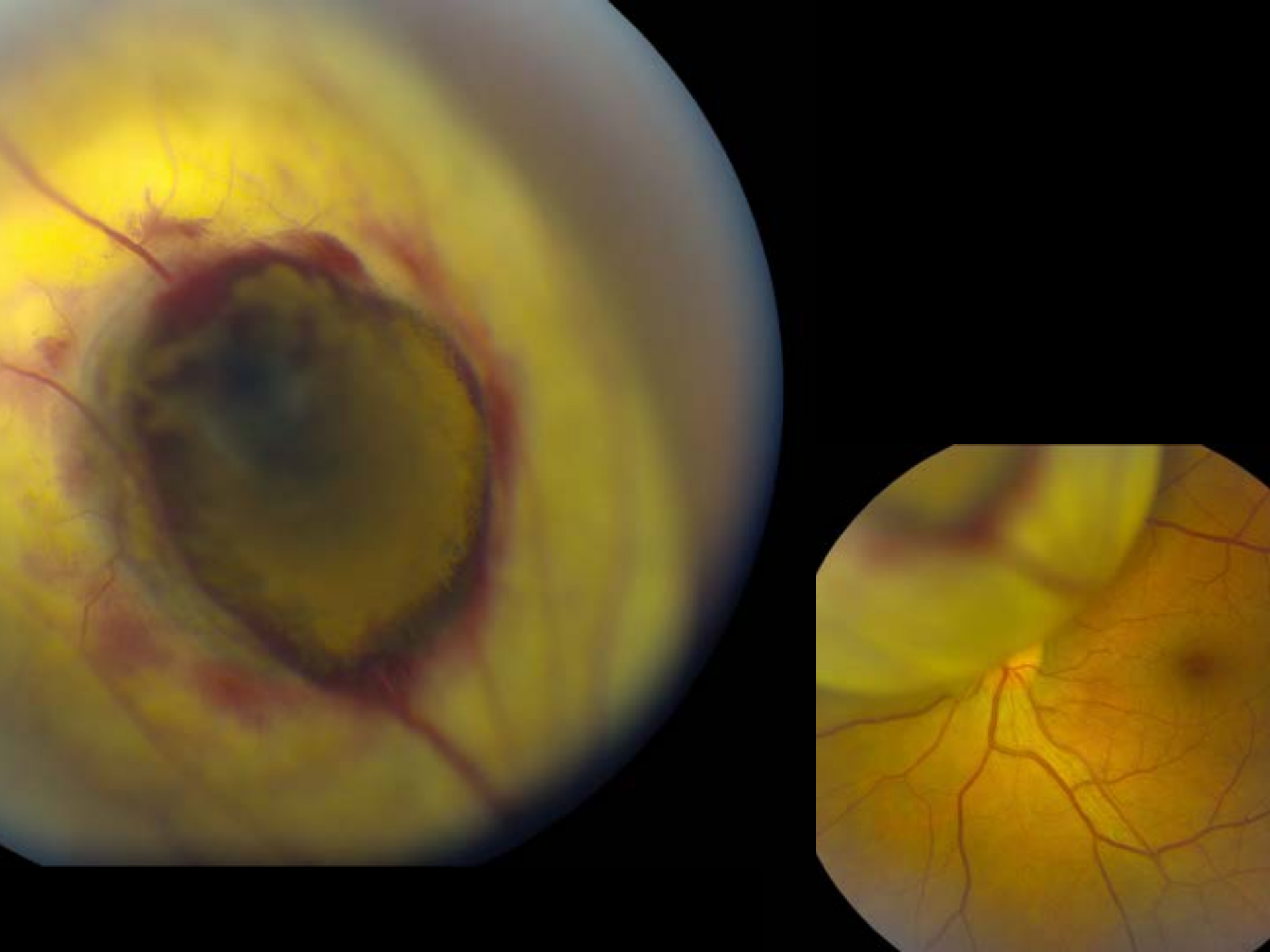
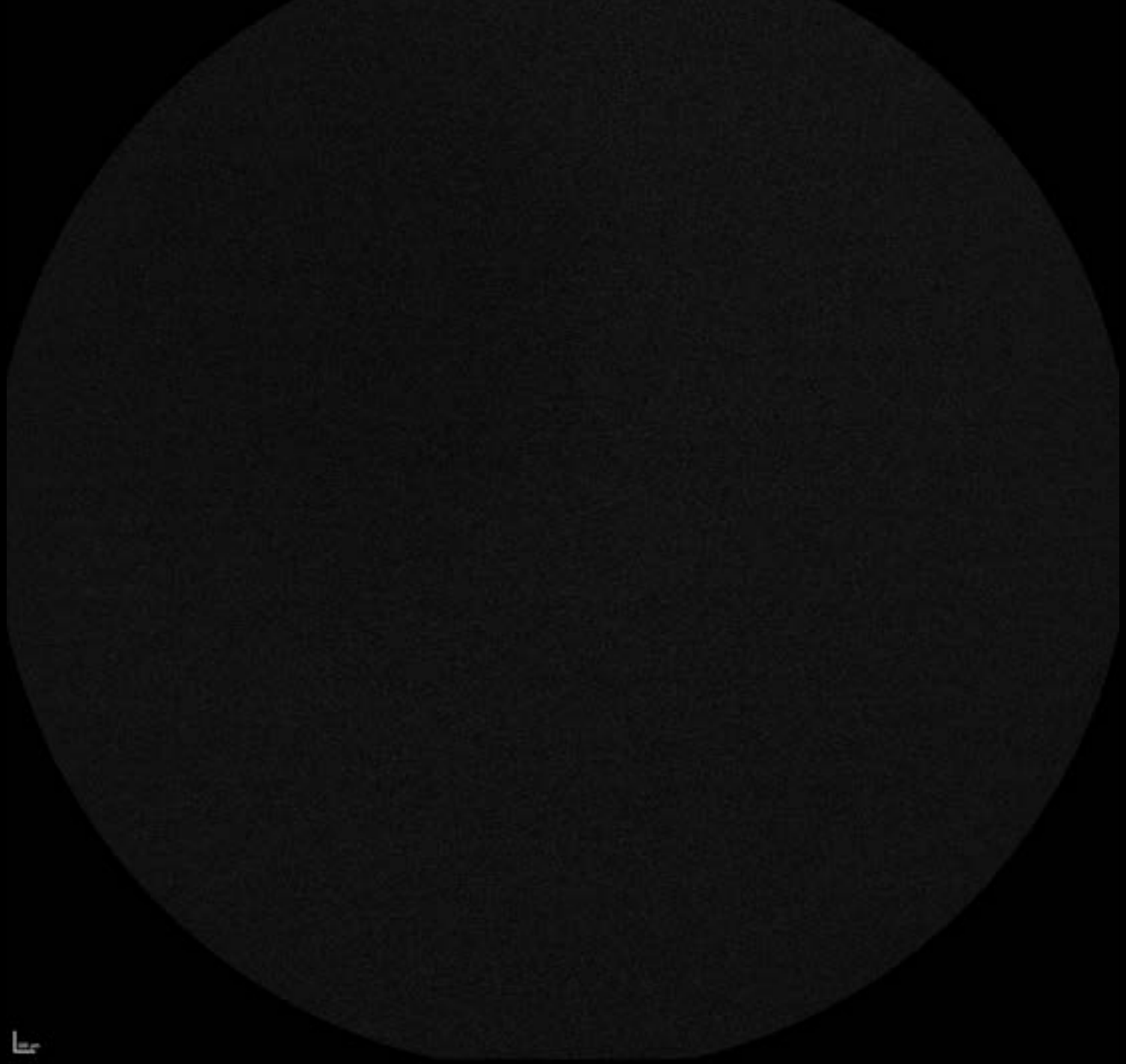
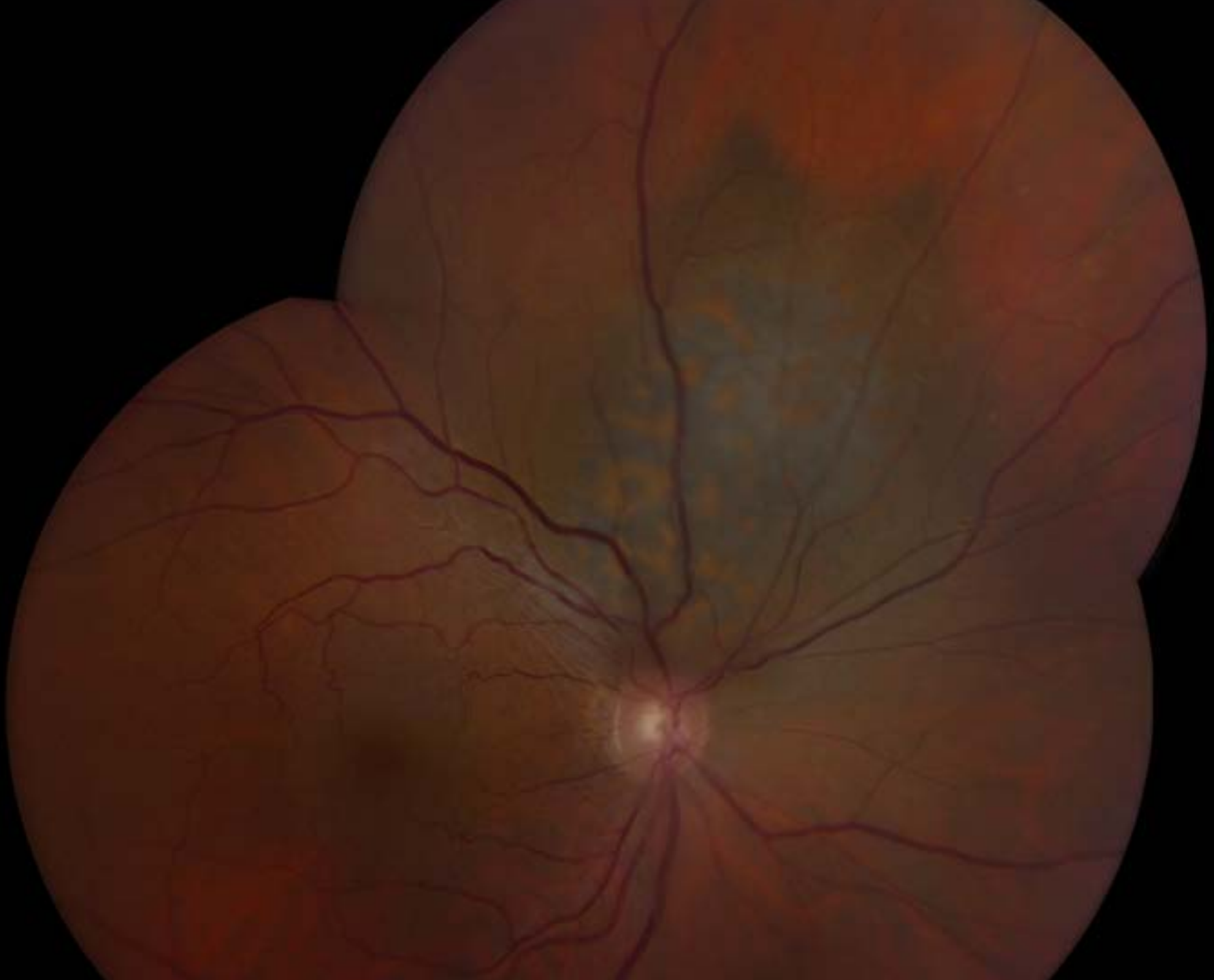
TS = 71db
Lesion
Retinal surface spike







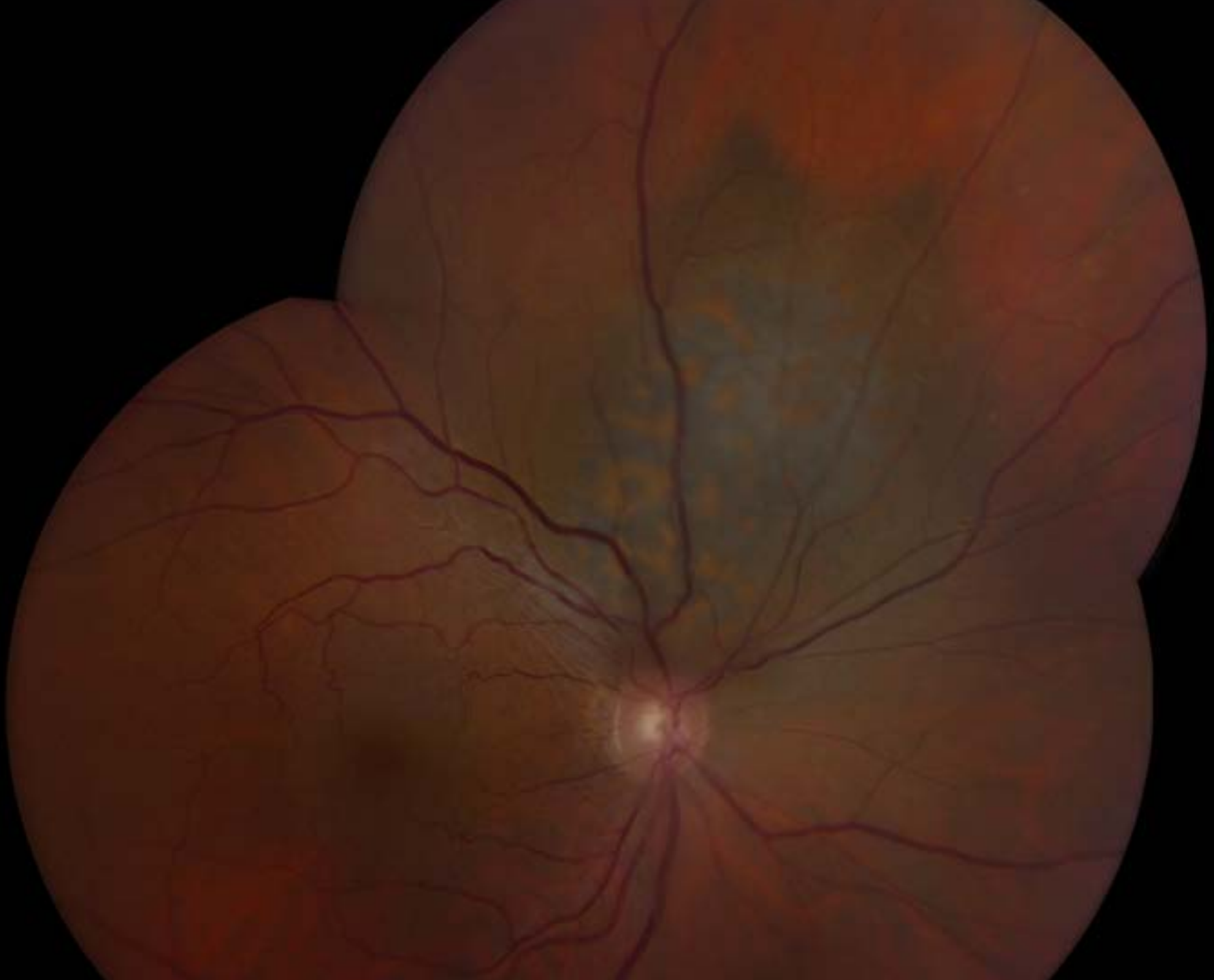
T F S O M-U H H D Acronym

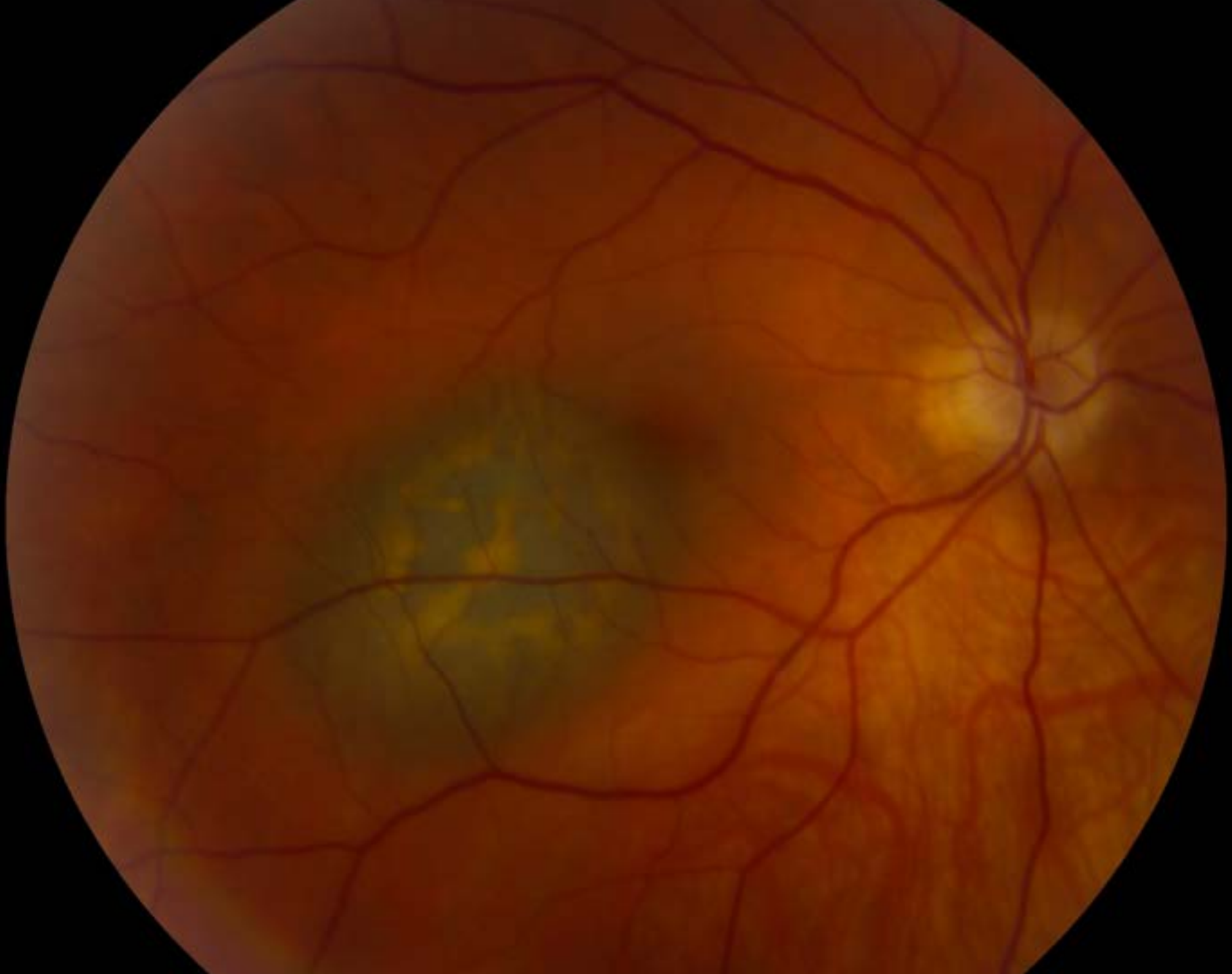
To	• Thickness • >2mm	For Small Melanoma Management
Find	• Fluid • Subretinal	
Small	• Symptomatic • Flashes/Floaters	
Ocular	• Orange Pigment	1 Risk Factor =38% chance of GROWTH
Melanoma	• Margin at Disc	
Using Helpful Hints	• Ultrasound Hollow • Halo Absent	2 Risk Factors ≥50% chance of GROWTH
Daily	• Drusen absent	

MOLES

- **M**ushroom shape
- **O**range pigment
- **L**arge size
  - Thickness: <1.0 mm vs 1.0-2.0 mm vs >2.00 mm
  - Diameter: <3DD vs 3-4DD vs >4DD
- **E**nlarging tumor
- **S**ubretinal fluid

- Scoring system: Absent = 0 points, Unsure/Borderline = 1 point, Present = 2 points
  - *total points of 3 or greater prompt urgent referral for probable melanoma





PRIMARY MELANOMA TREATMENT

- Enucleation
- Radiation Therapy
  - ^{125}I plaque brachytherapy
  - Proton beam therapy
  - Gamma Knife and other Stereotactic Radiosurgery
- Transpupillary Thermotherapy (with radiation)

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OTHER TREATMENTS EMPLOYED (WITH LESS SUCCESS)

- Microsurgical Resection
  - External Trans-Scleral Resection
  - Transvitreal Endoresection
- Laser Photocoagulation
- Photodynamic Therapy
- Hyperthermia
- Cryotherapy

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REVIEW: COLLABORATIVE OCULAR MELANOMA STUDY

- A set of prospective studies designed to compare survival after treatment
- Initiated in 1985 w/ 2 randomized arms
  - Medium Tumor Trial
    - Assessed lesions 2.5-10mm in apical height; <16mm in diameter
    - Episcleral I-125 plaque brachytherapy versus enucleation
  - Large Tumor Trial
    - Assessed lesions >10mm in apical height; >16mm in diameter
    - Enucleation Alone versus Pre-Enucleation Radiotherapy (PERT)

  - Small Tumor trial included later (observational study)

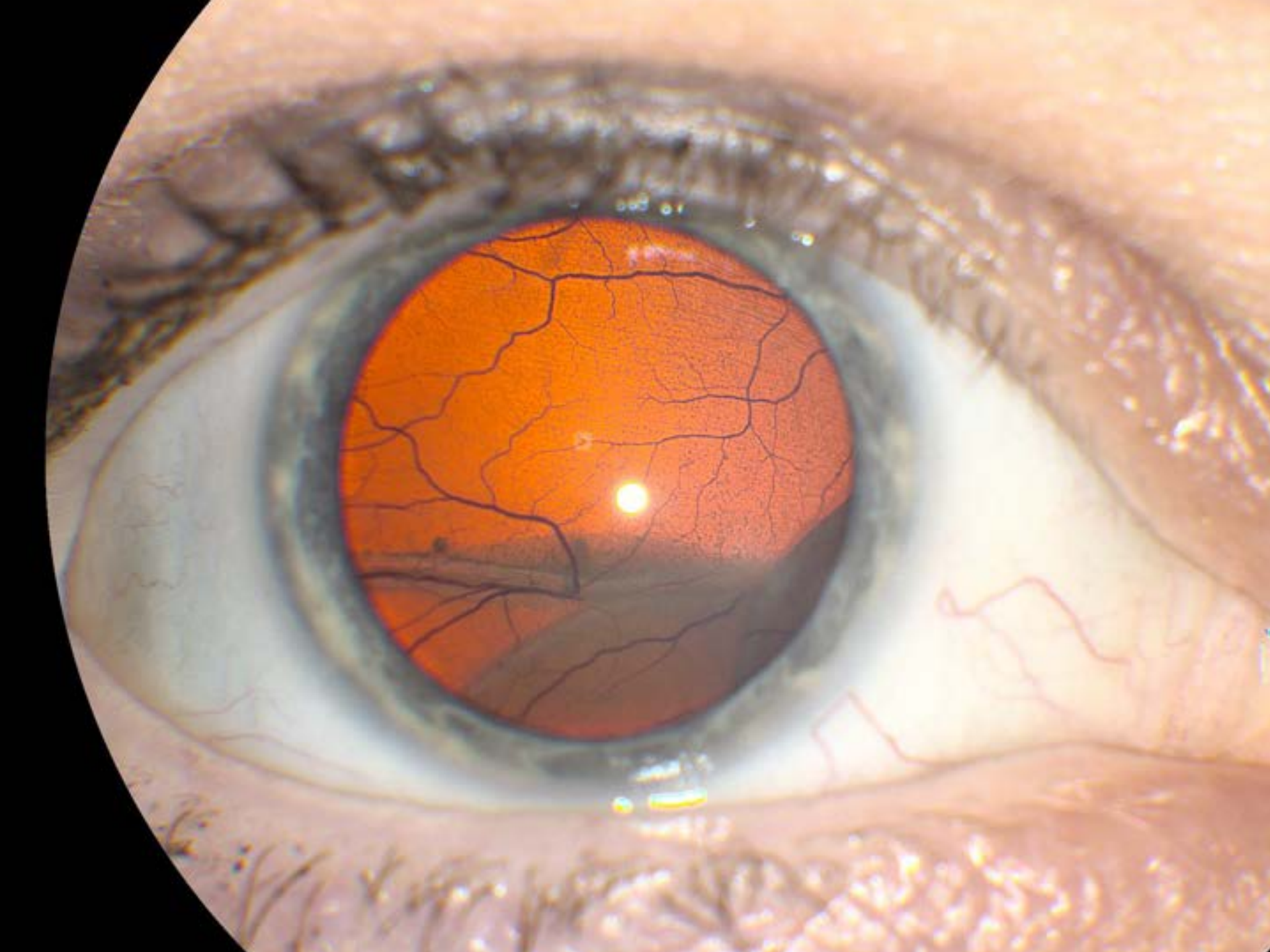
COMS MEDIUM TUMOR TRIAL

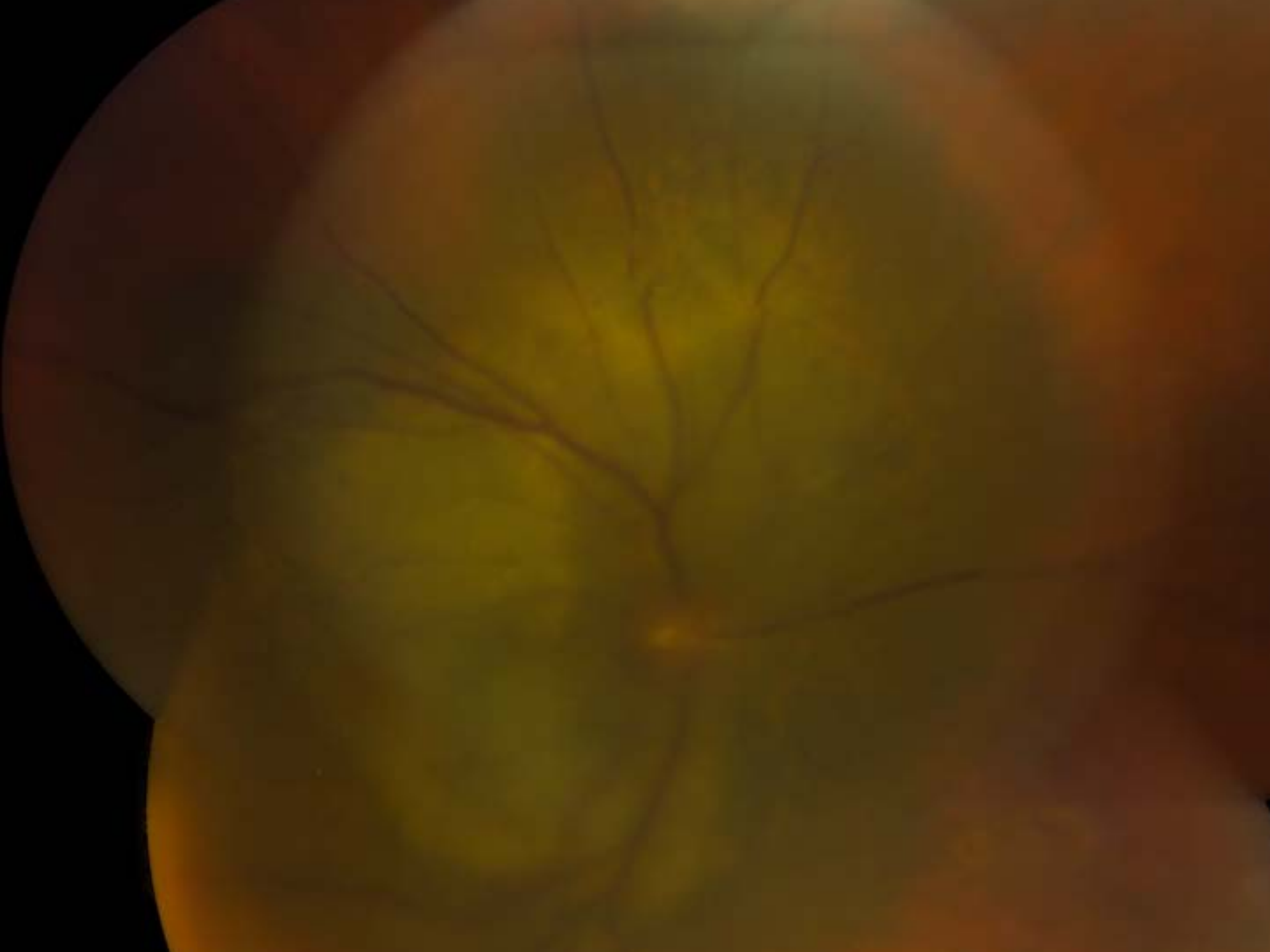
5 Year Data 1072 pts (81%)	**Enucleation**	**I-125** 85Gy at 43-105 cGy/hr
All-cause mortality	19%	18.5%
Death with histologically confirmed melanoma metastases	11%	9%

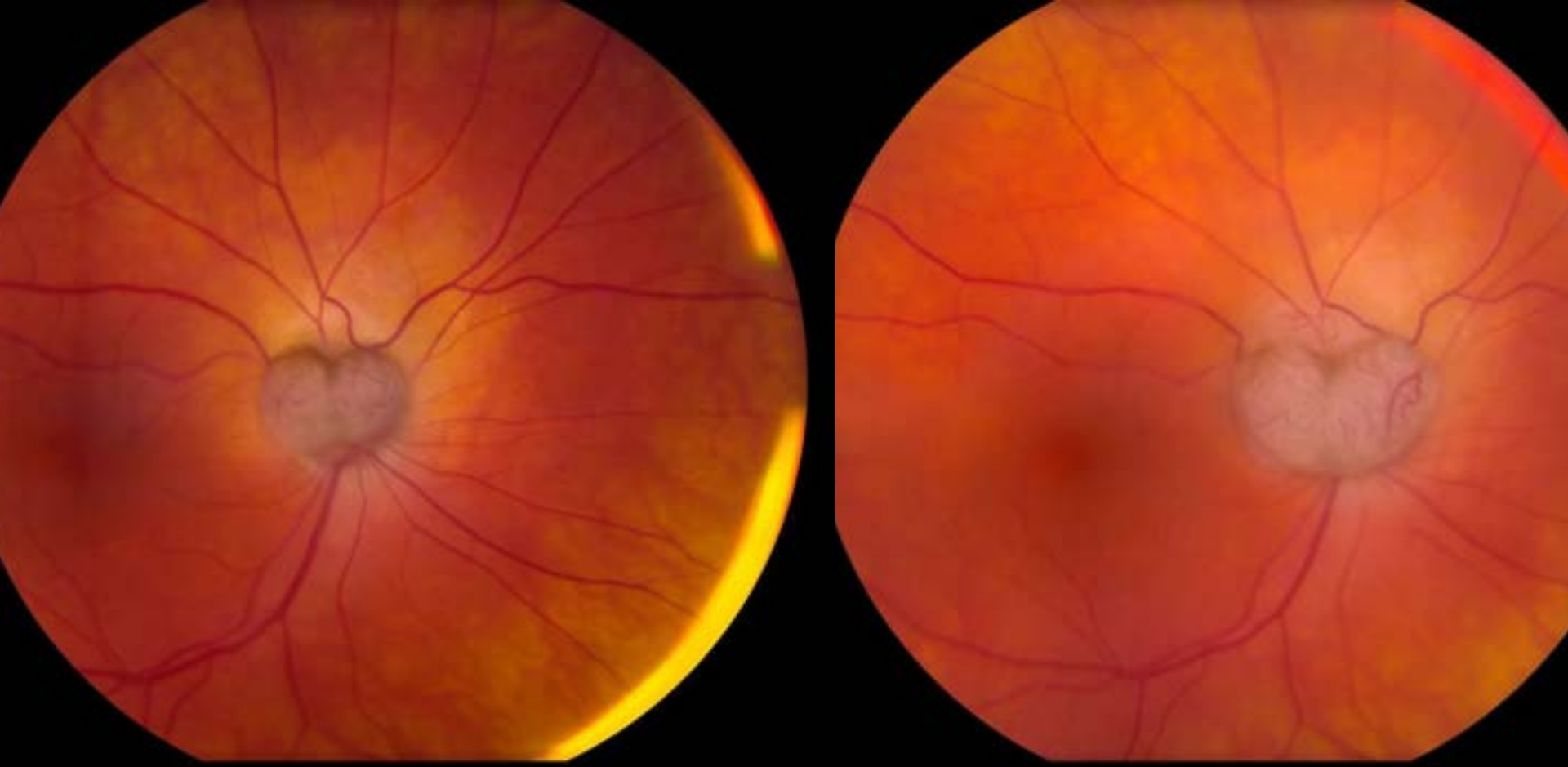
COMS LARGE TUMOR TRIAL

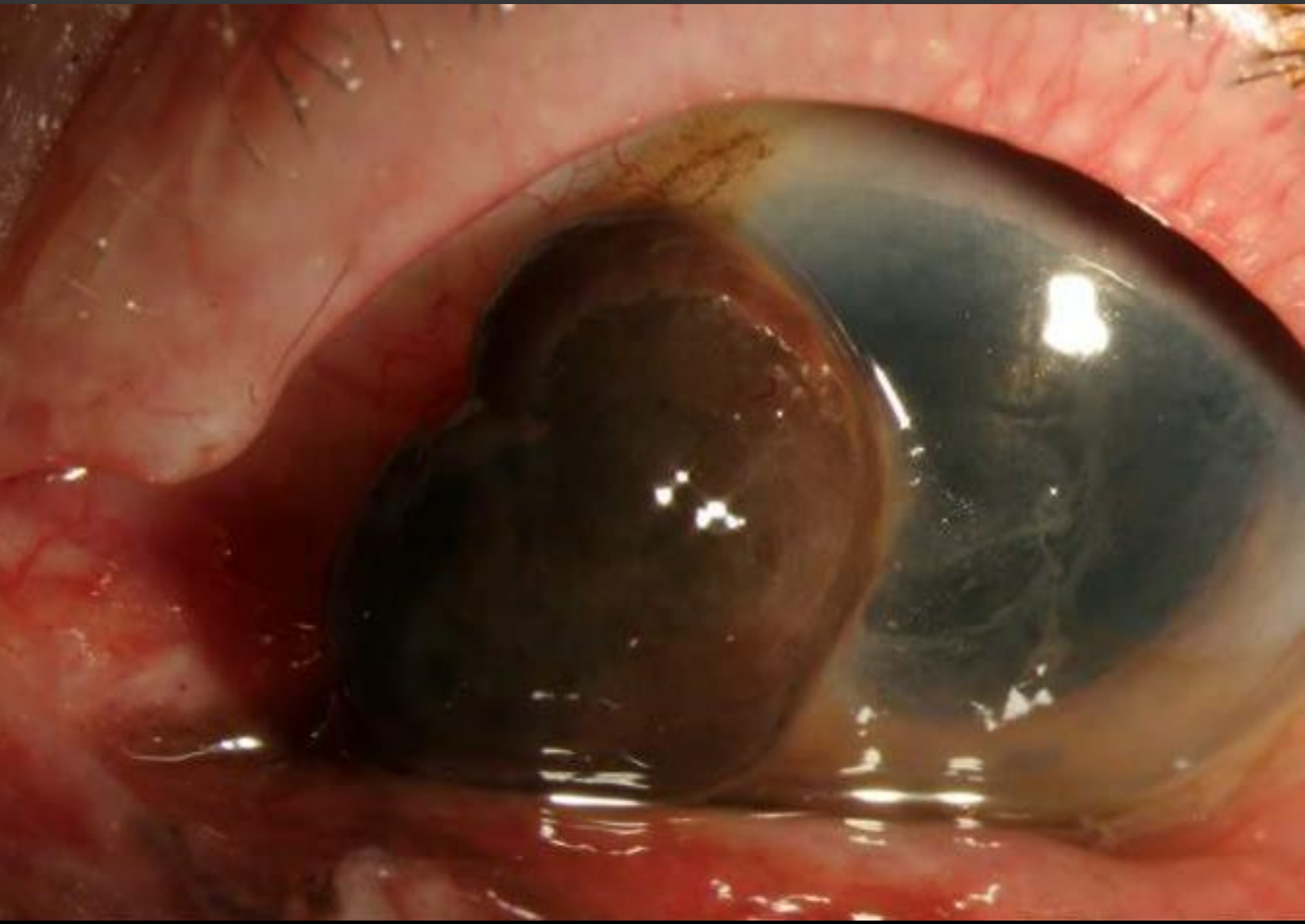
- Does pre-treatment of large melanomas with external beam radiotherapy (PERT) before enucleation impact the rate of metastases?

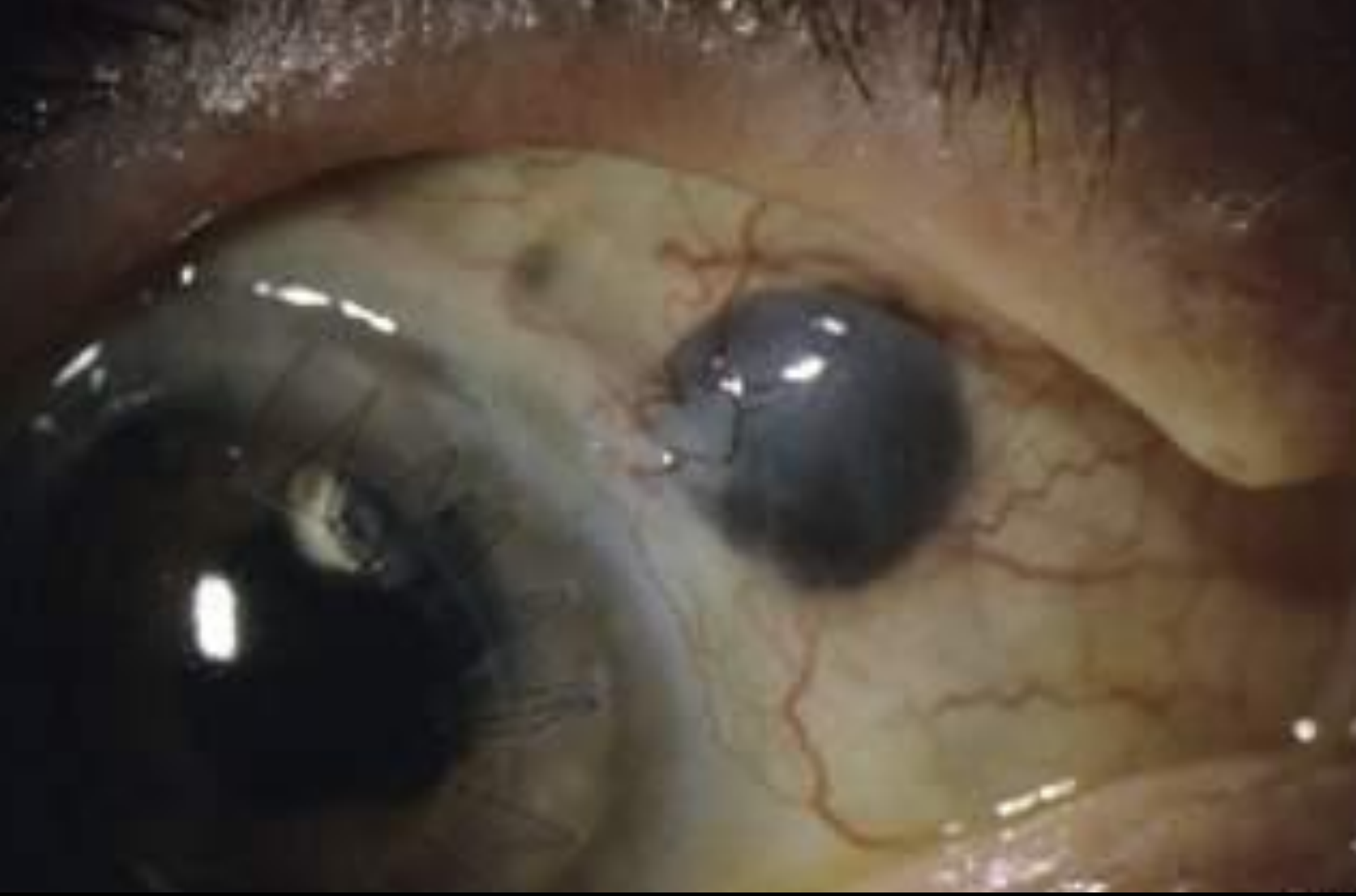
- No statistically significant difference in all-cause mortality or melanoma specific mortality over 10 years

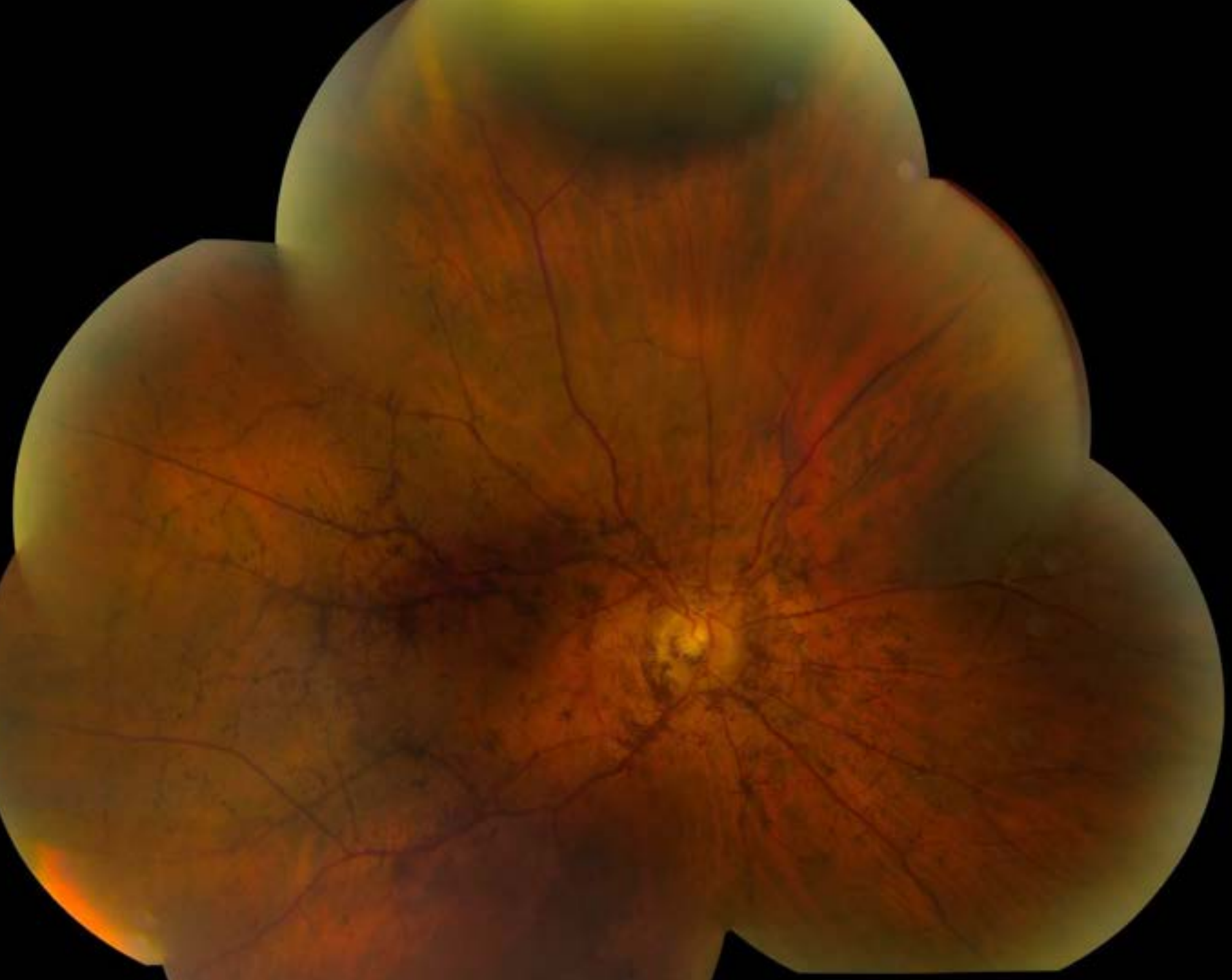












^{125}I PLAQUE BRACHYTHERAPY

- Currently most widely used treatment for choroidal melanoma
- Small "rice-sized" radioactive seeds are attached within a gold bowl – the plaque
- Plaque sewn onto sclera using intraoperative echography to guide positioning
- Patient remains in the hospital for four days
- Day 3, plaque is removed
- Day 4, patient goes home

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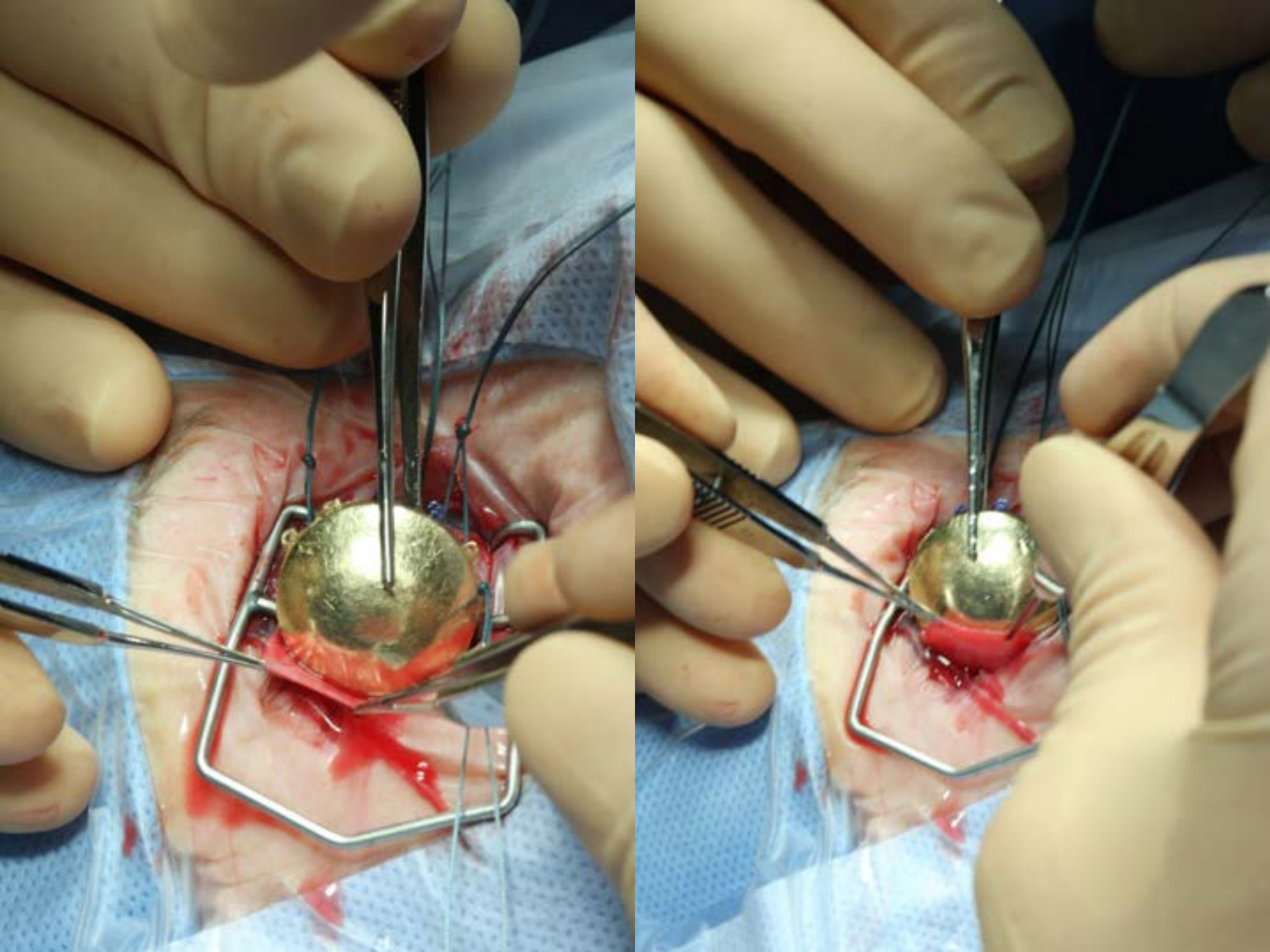

PLAQUE INSERTION

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^{125}I PLAQUE BRACHYTHERAPY COMPLICATIONS

- Radiation retinopathy
- Radiation papillopathy (or radiation optic neuropathy)
- Cataract
- Vitreous hemorrhage
- Exudative RD
- Neovascular Glaucoma

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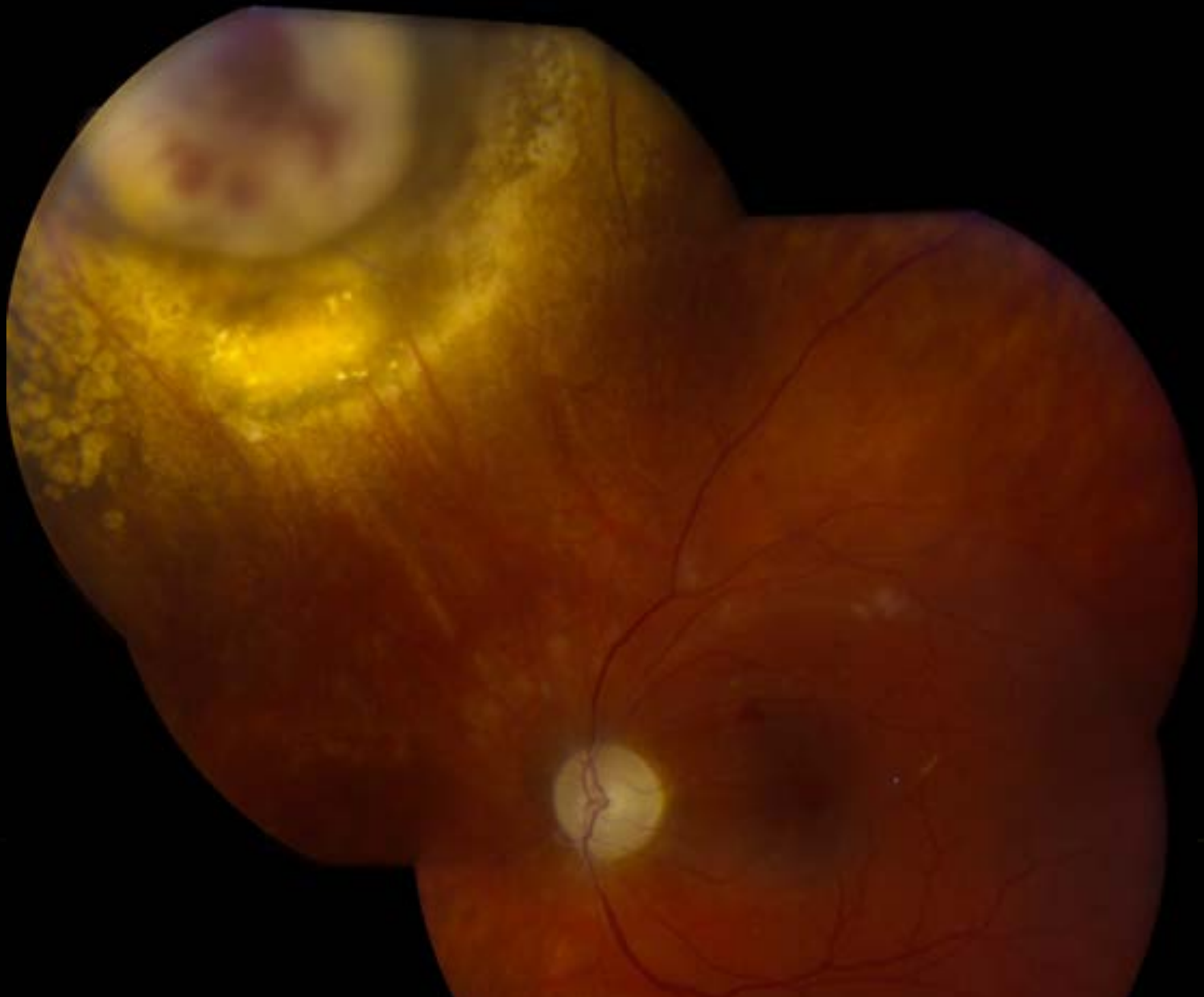
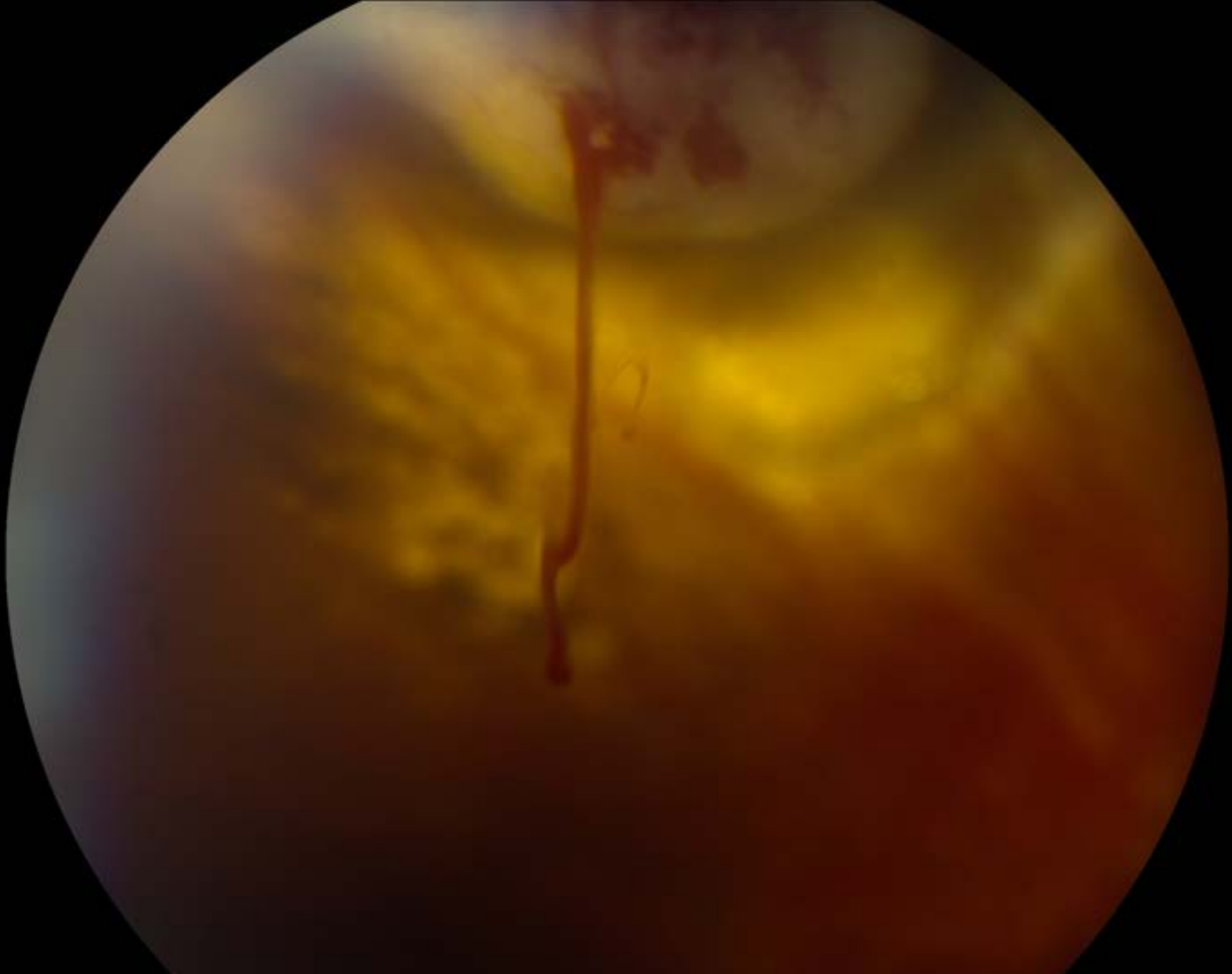
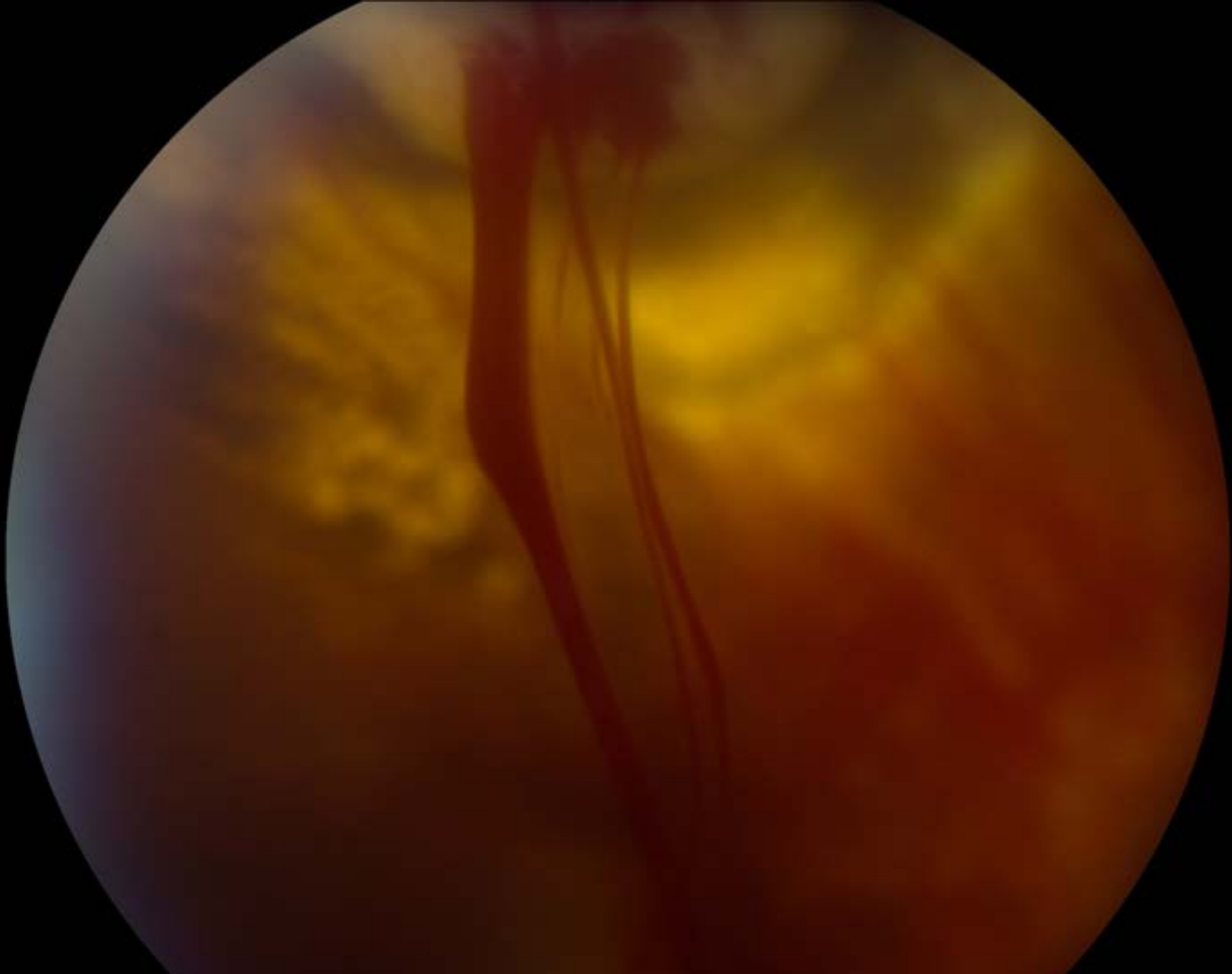
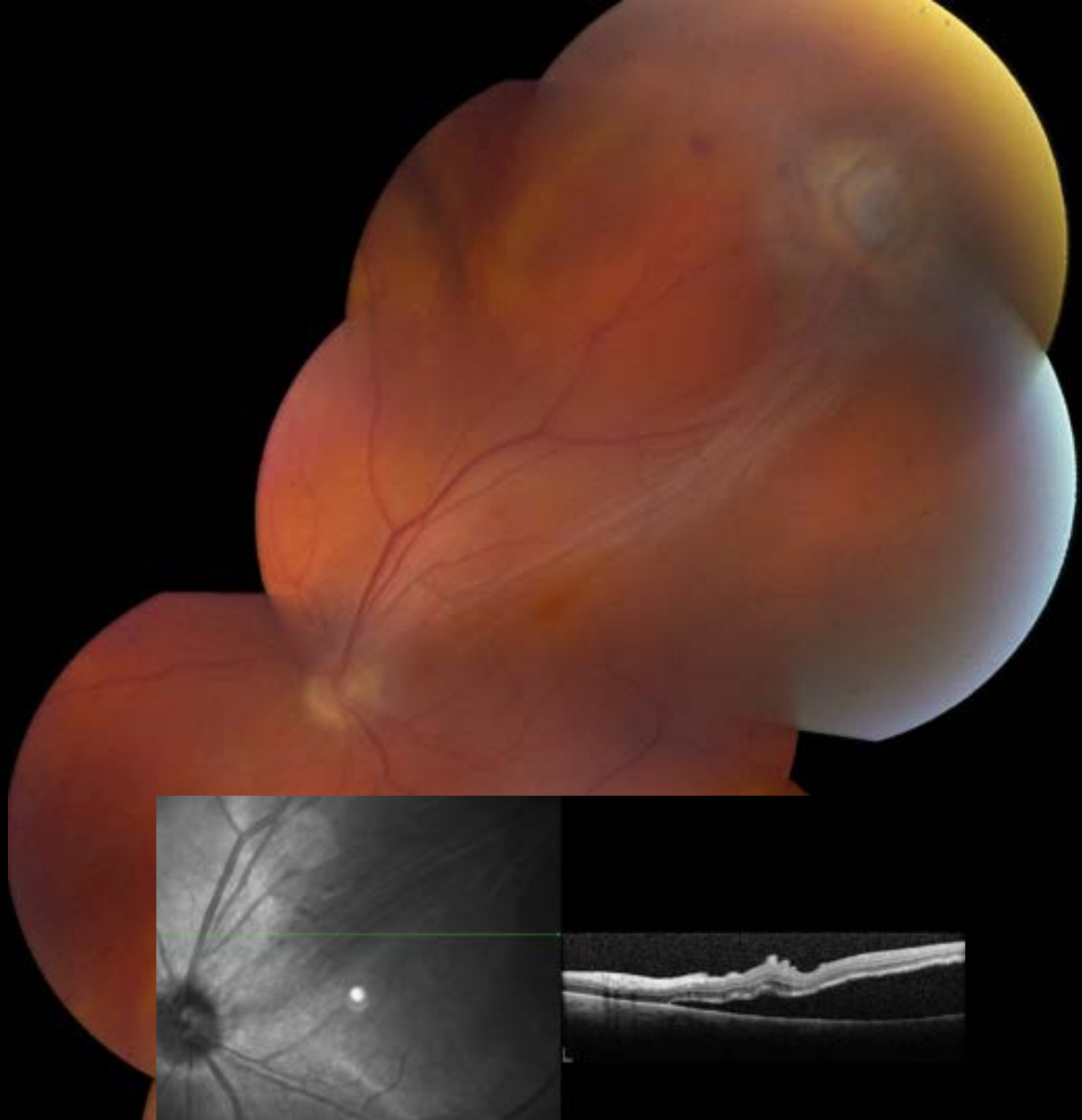
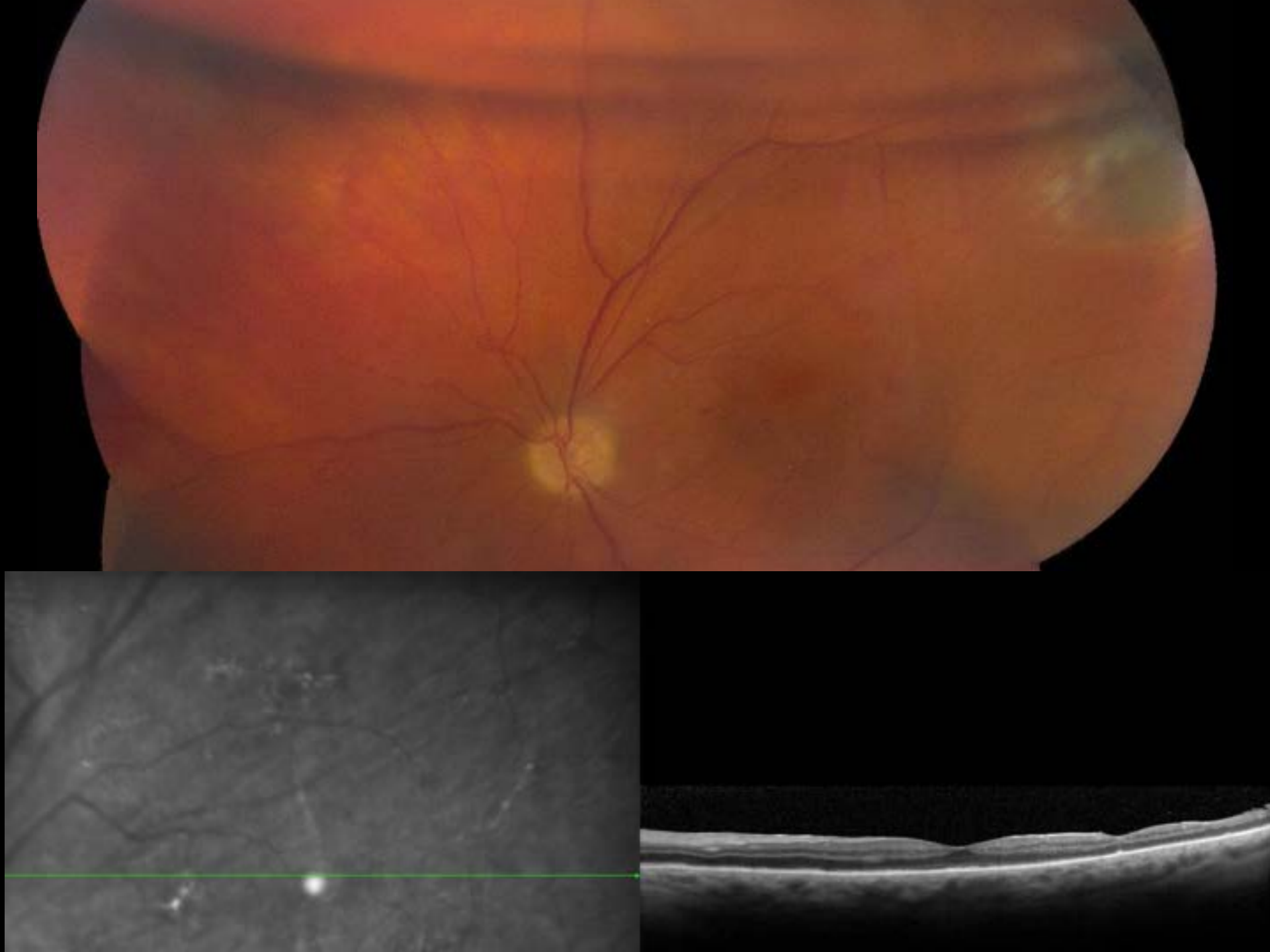
RADIATION RETINOPATHY











RADIATION RETINOPATHY/OPTIC NEUROPATHY
CLINICAL NATURAL HISTORY/SDOCT

Incidence/prevalence	Photographic	sdOCT
12 months	9%	78%
24 months	24%	98%
36 months	39%	99%
60 months	47%	99%

- Risk Factors: Increased tumor thickness, proximity to optic nerve/fovea, associated vascular disease
- COMS VA 20/200 3 years post-brachytherapy

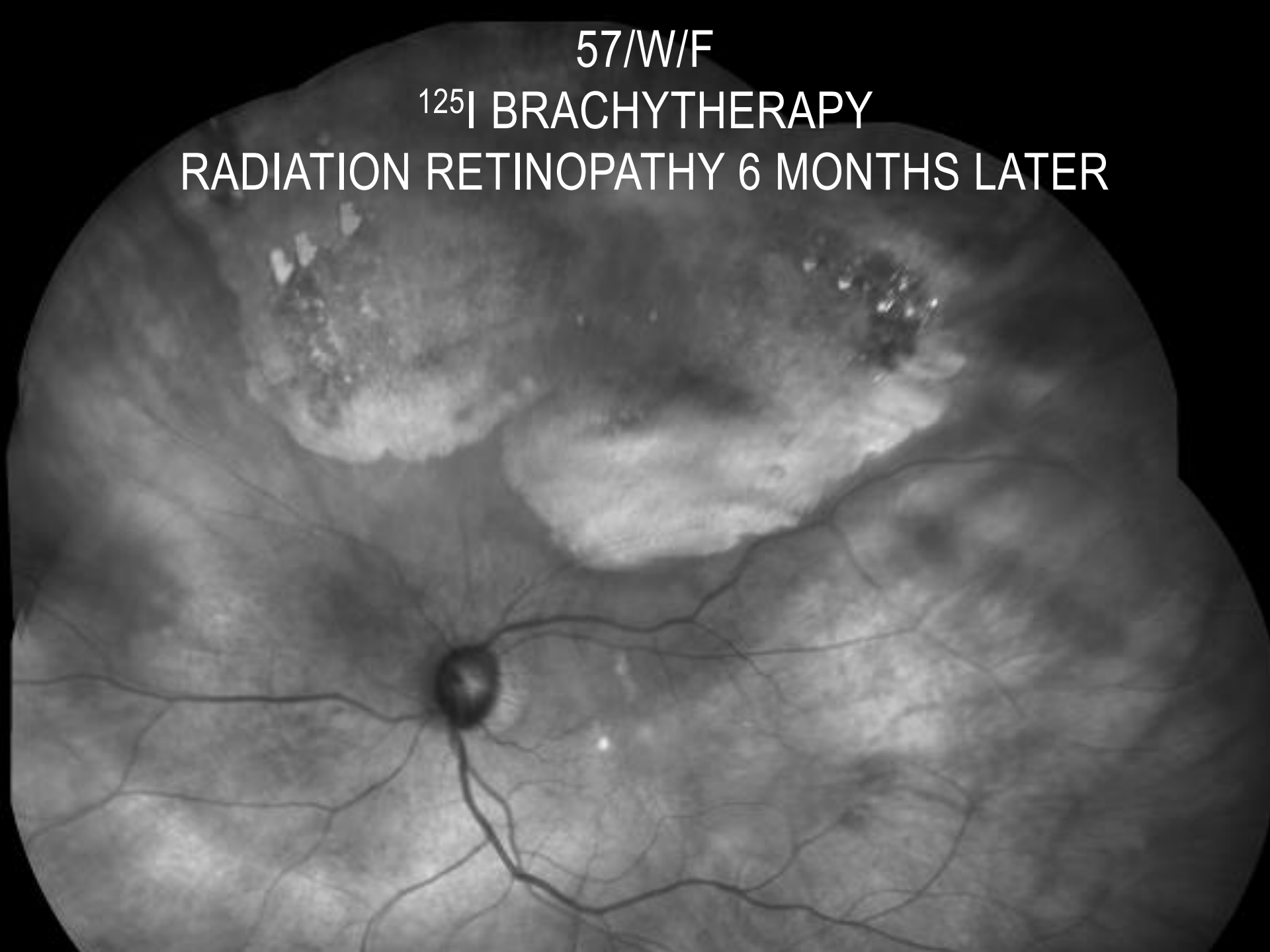
CURRENT MANAGEMENT OF RADIATION RETINOPATHY

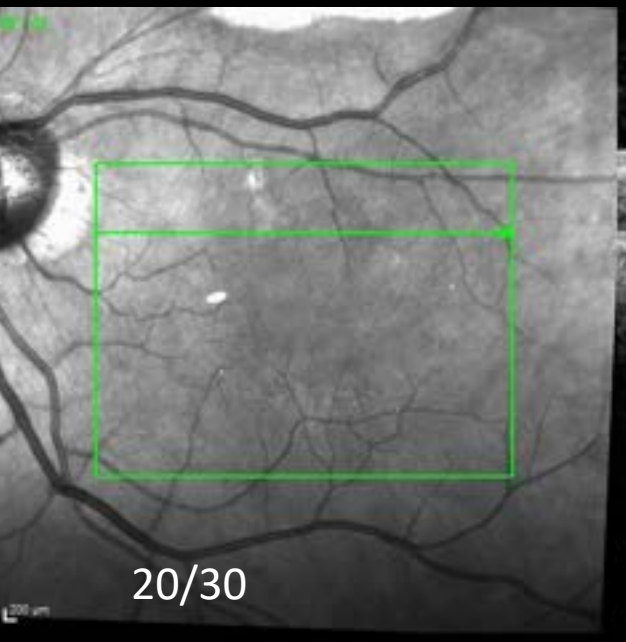
Intravitreal Injection therapy has become the first line of defense

-Bevacizumab

-Triamcinolone acetonide

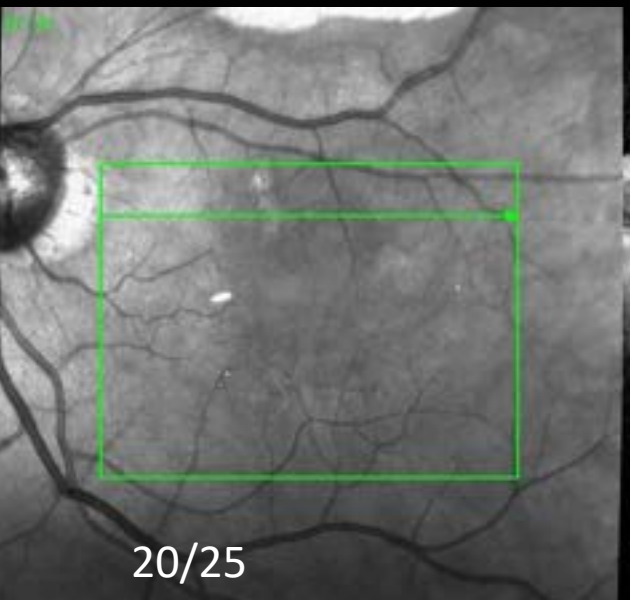
-Aflibercept


57/W/F
^{125}I BRACHYTHERAPY
RADIATION RETINOPATHY 6 MONTHS LATER

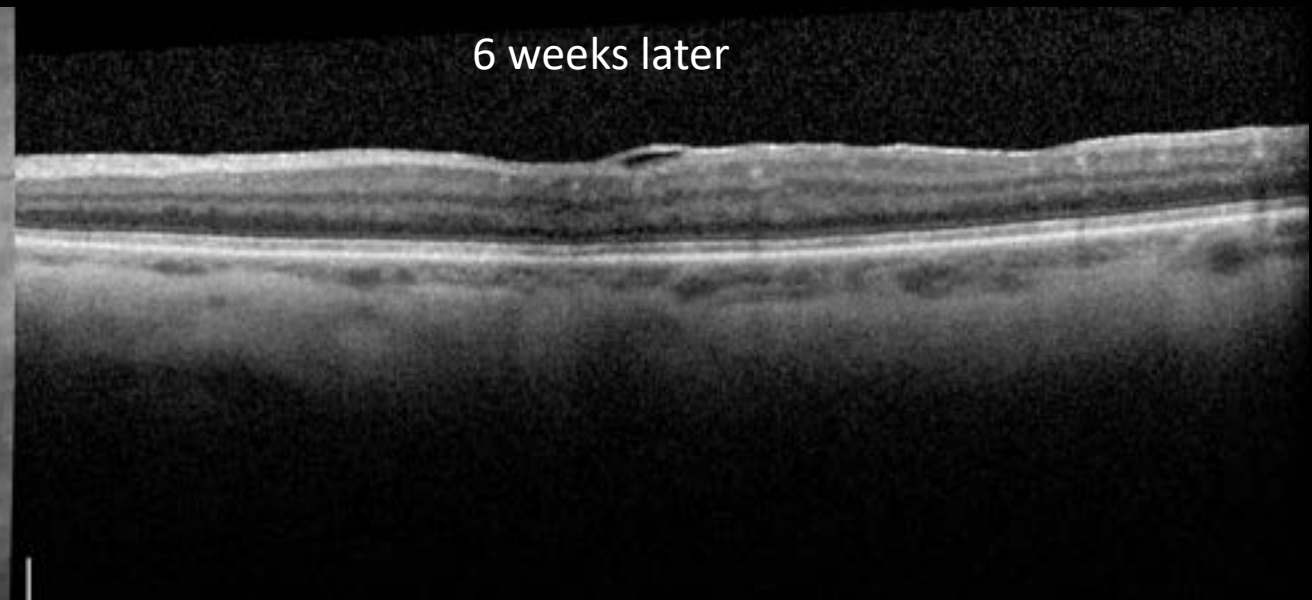


20/30

bevacizumab administered



20/25

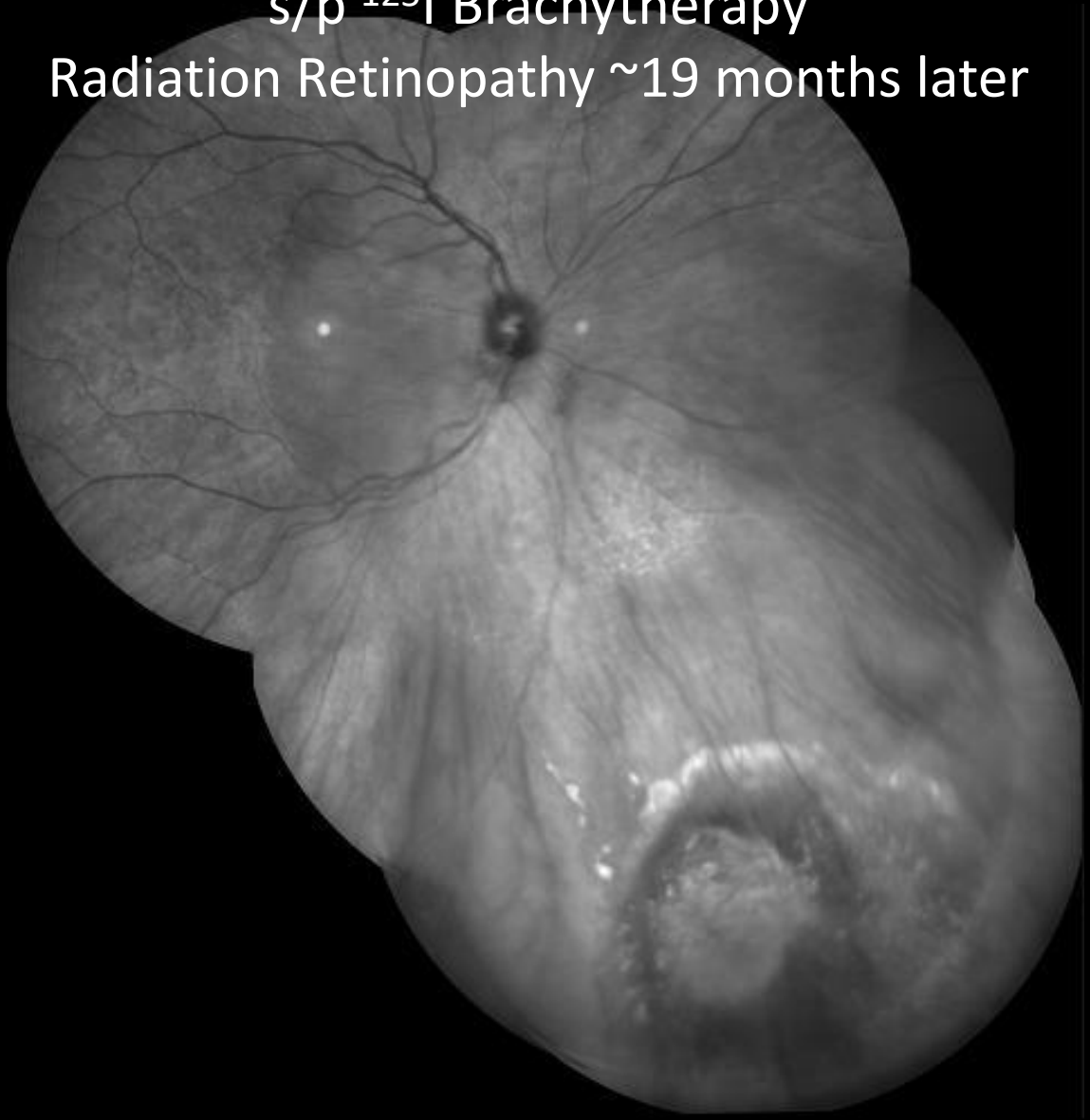


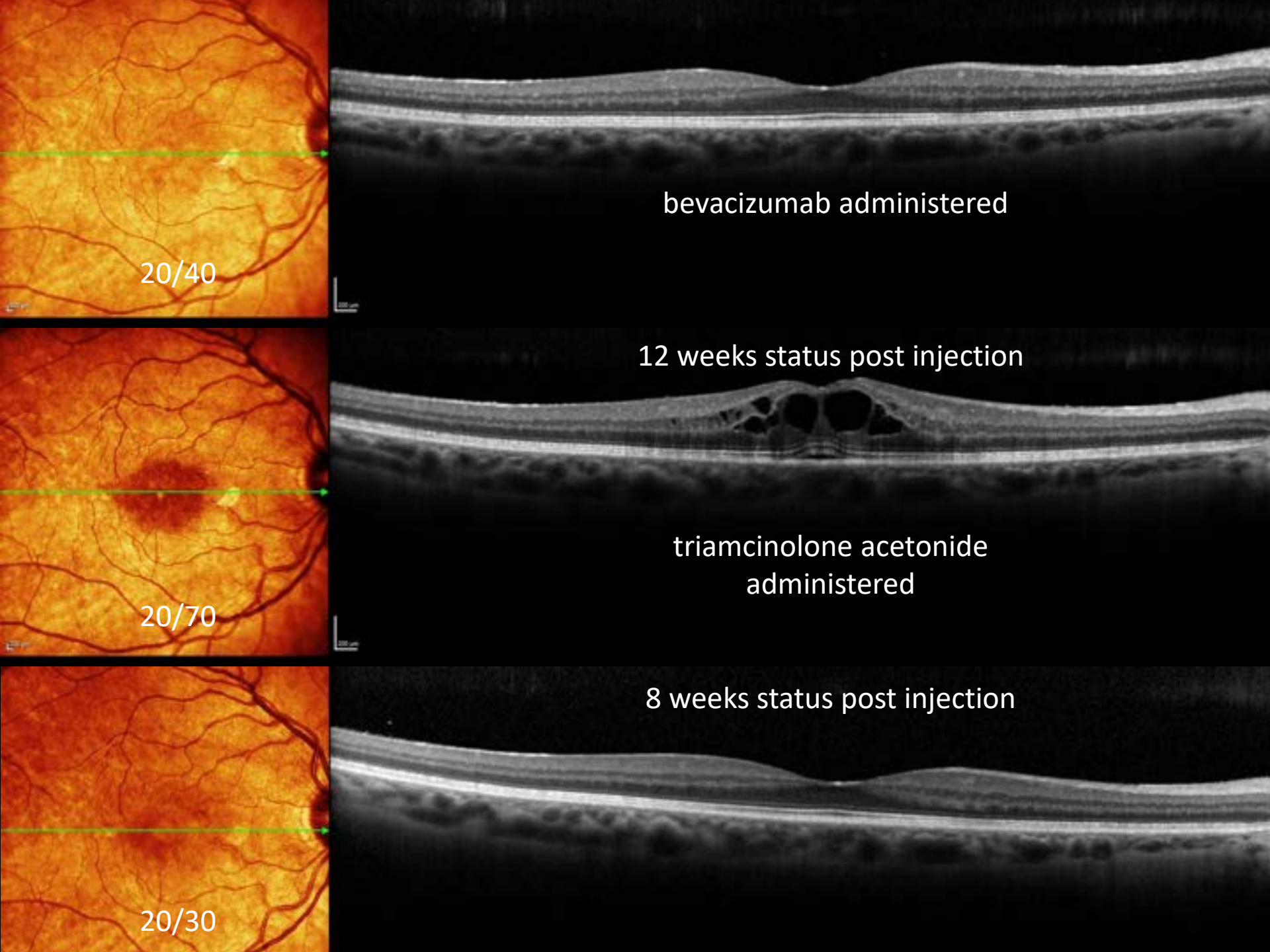
6 weeks later

70/W/F

s/p ^{125}I Brachytherapy

Radiation Retinopathy ~19 months later




20/40
bevacizumab administered
12 weeks status post injection
20/70
triamcinolone acetonide
administered
8 weeks status post injection
20/30

METASTATIC SCREENING WITH UVEAL MELANOMA

- **Abdominal MRI**
  - With liver function panel
- Chest X-ray
- CBC with differential
- SMA-20

- **Genomic testing**
  - Suppression subtractive hybridization (SSH)
  - Multiplex ligation-dependent probe amplification (MLPA)
  - Gene Expression Profiling

GENOMICS AS PREDICTORS OF METASTASIS

- Gene Expression Profiling
  - Assesses 15 genes located on chromosomes 3 and 8q
  - Two distinct molecular genetic signatures for uveal melanoma
    - Class 1
      - Associated with less aggressive melanoma
      - Further divided into subclasses 1A and 1B
    - Class 2
      - Associated with more aggressive melanoma
      - Associated with monosomy 3

GENE EXPRESSION PROFILING

- Castle Biosciences – Validated, CLIA approved
- RT-PCR 15 Genes (3 control genes)
  - CDH1,ECM1, EIF1B, FXR1, HTR2B, ID2, LMCD1, LTA4H, MTUS1, RAB31, ROBO1, and SATB1
- Predicted classification and discriminant value

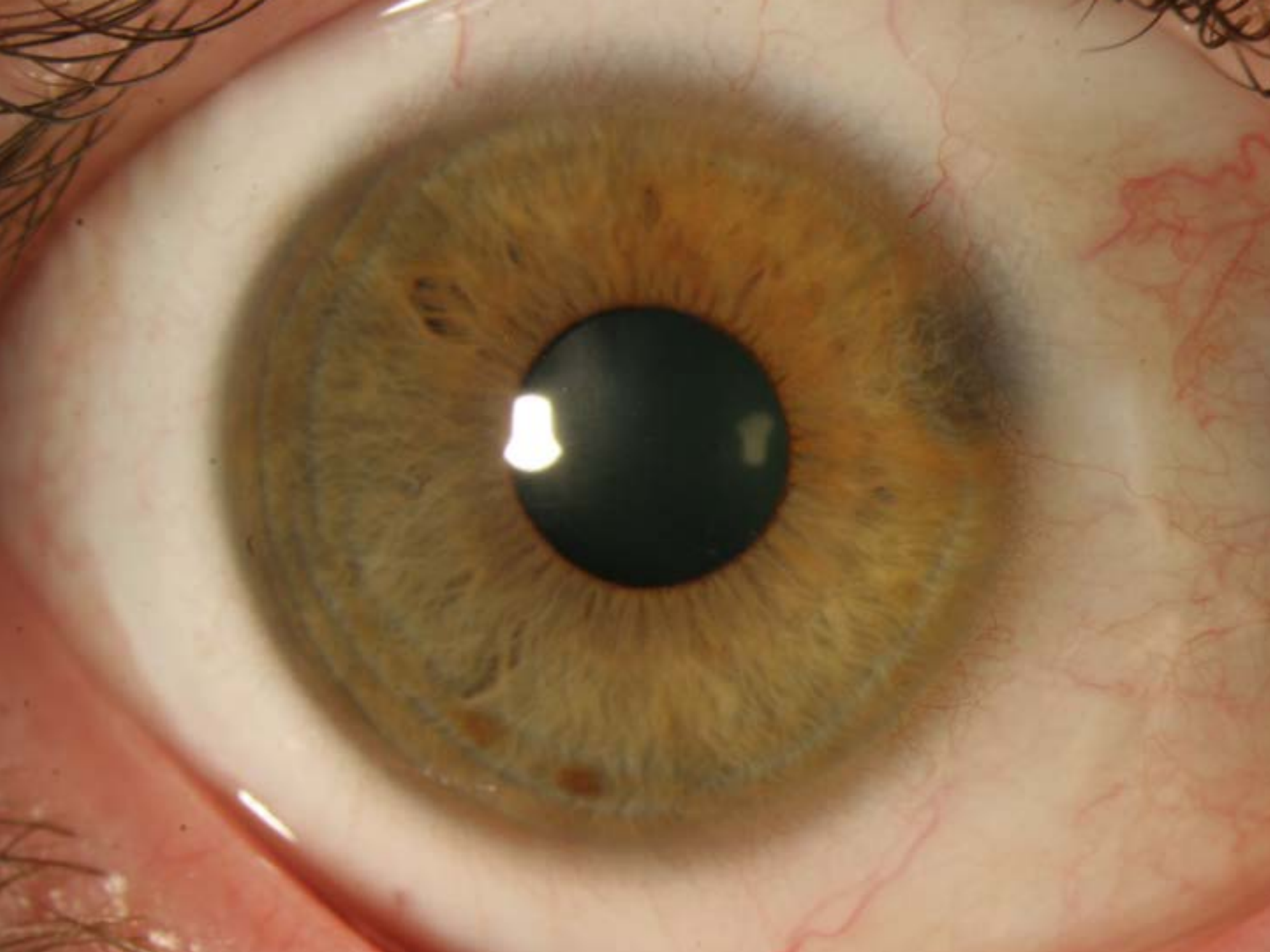
MOLECULAR SIGNATURE CLASS METASTASIS FREE

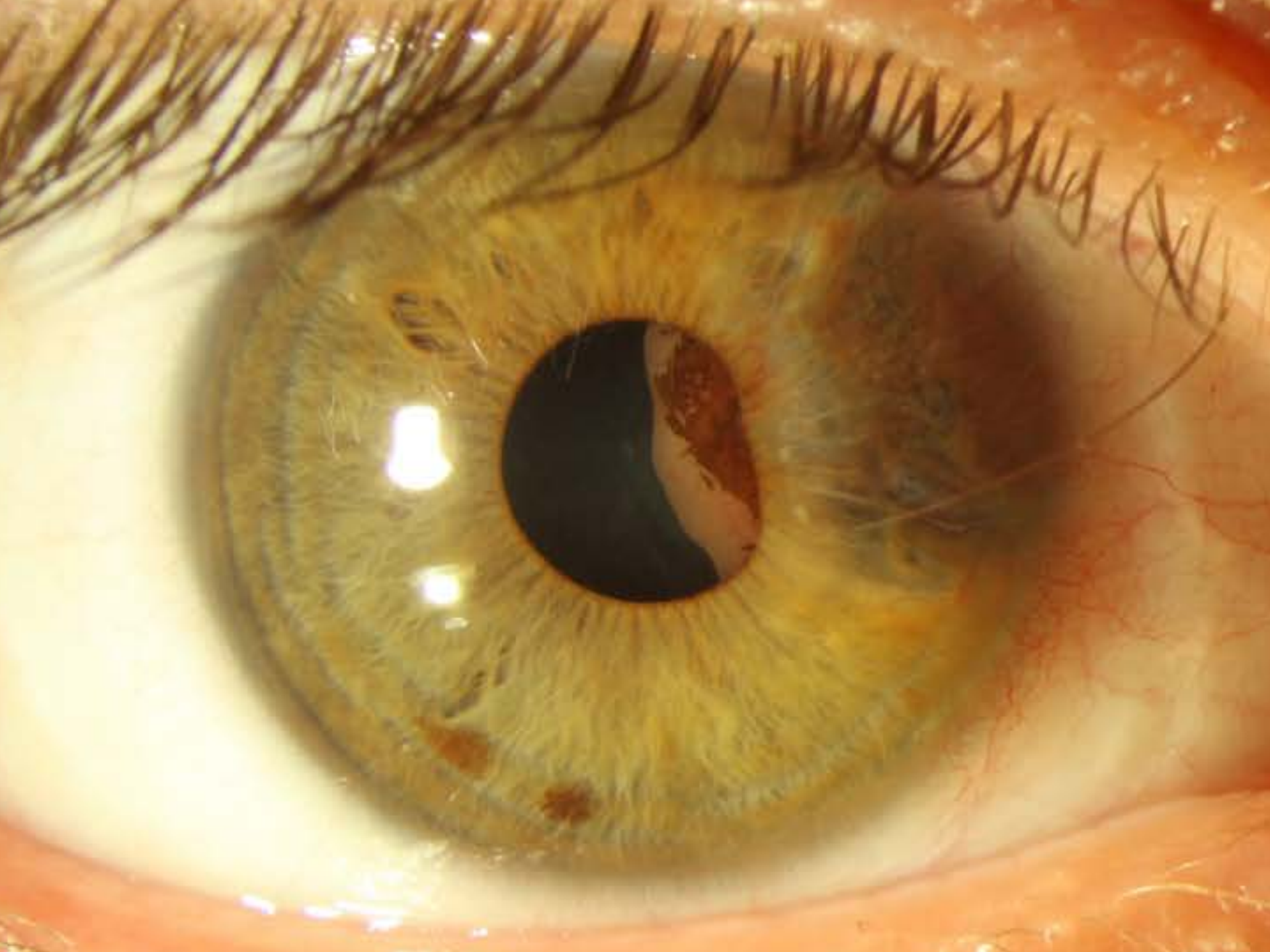
Class	3 year	5 year
Class 1A	98%	98%
Class 1B	93%	79%
Class 2	50%	28%

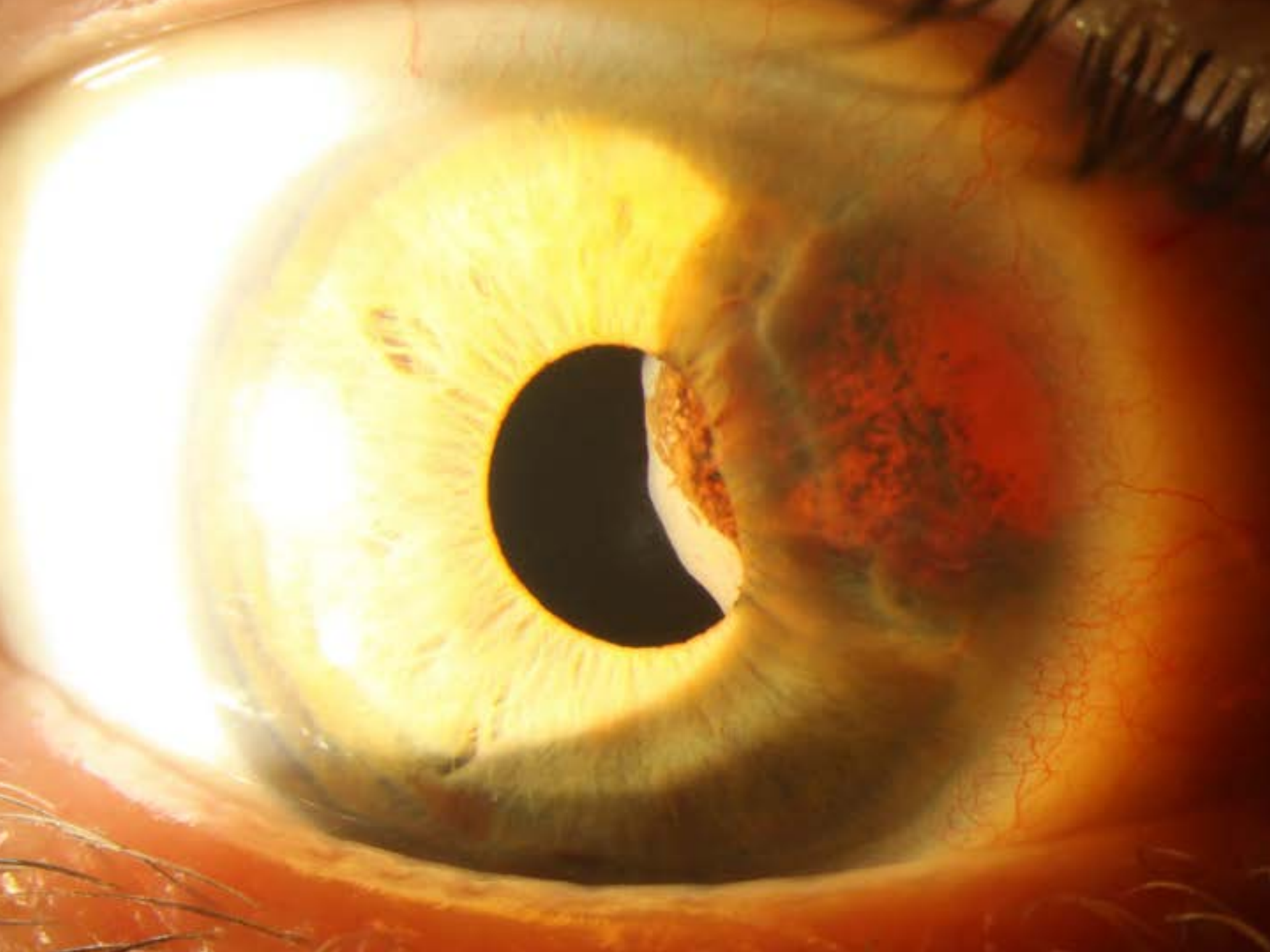
CENSORED DATA 6/9/2011 514 PATIENTS P<.0001

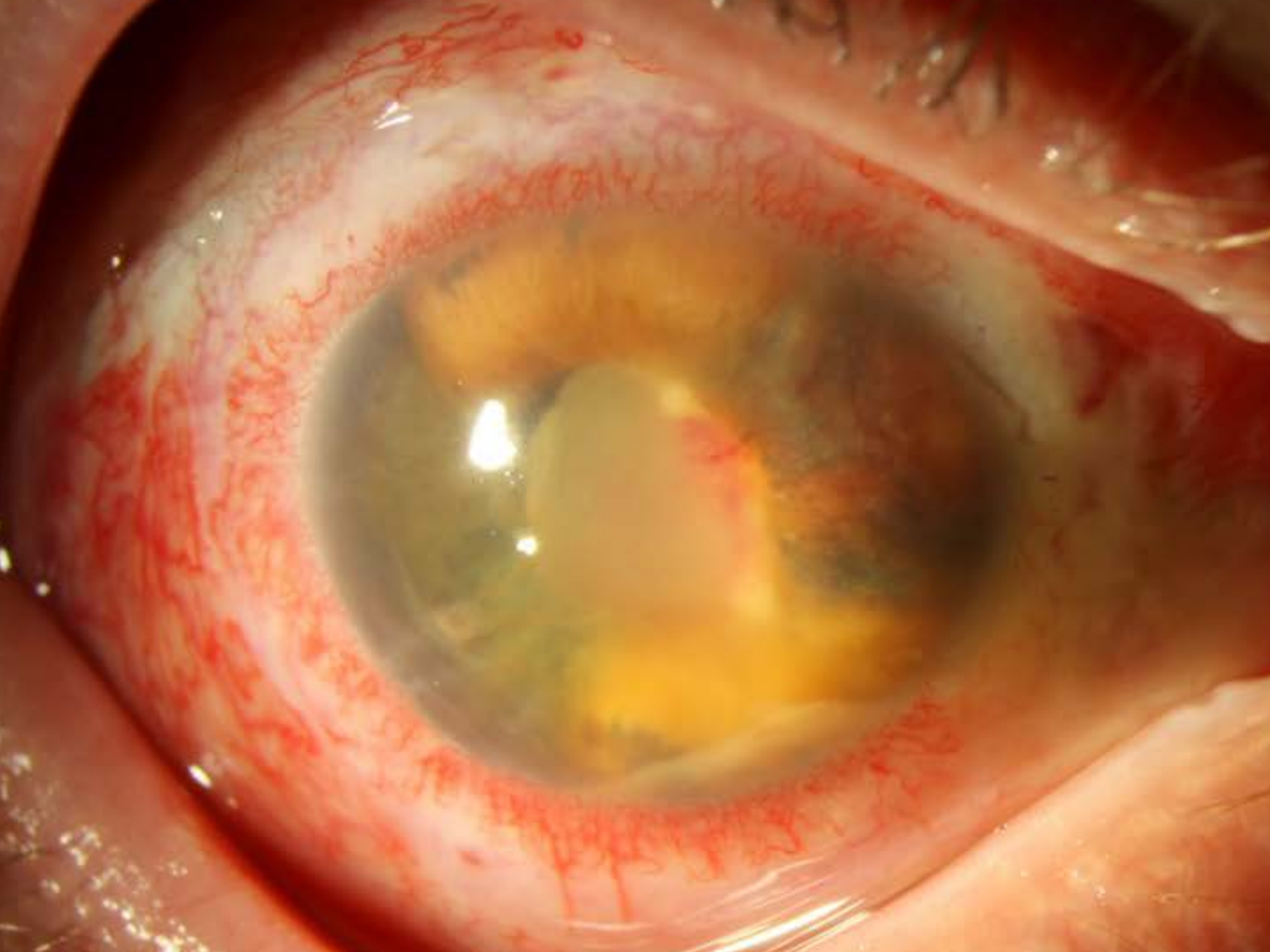
BENEFIT OF GENOMIC PREDICTOR

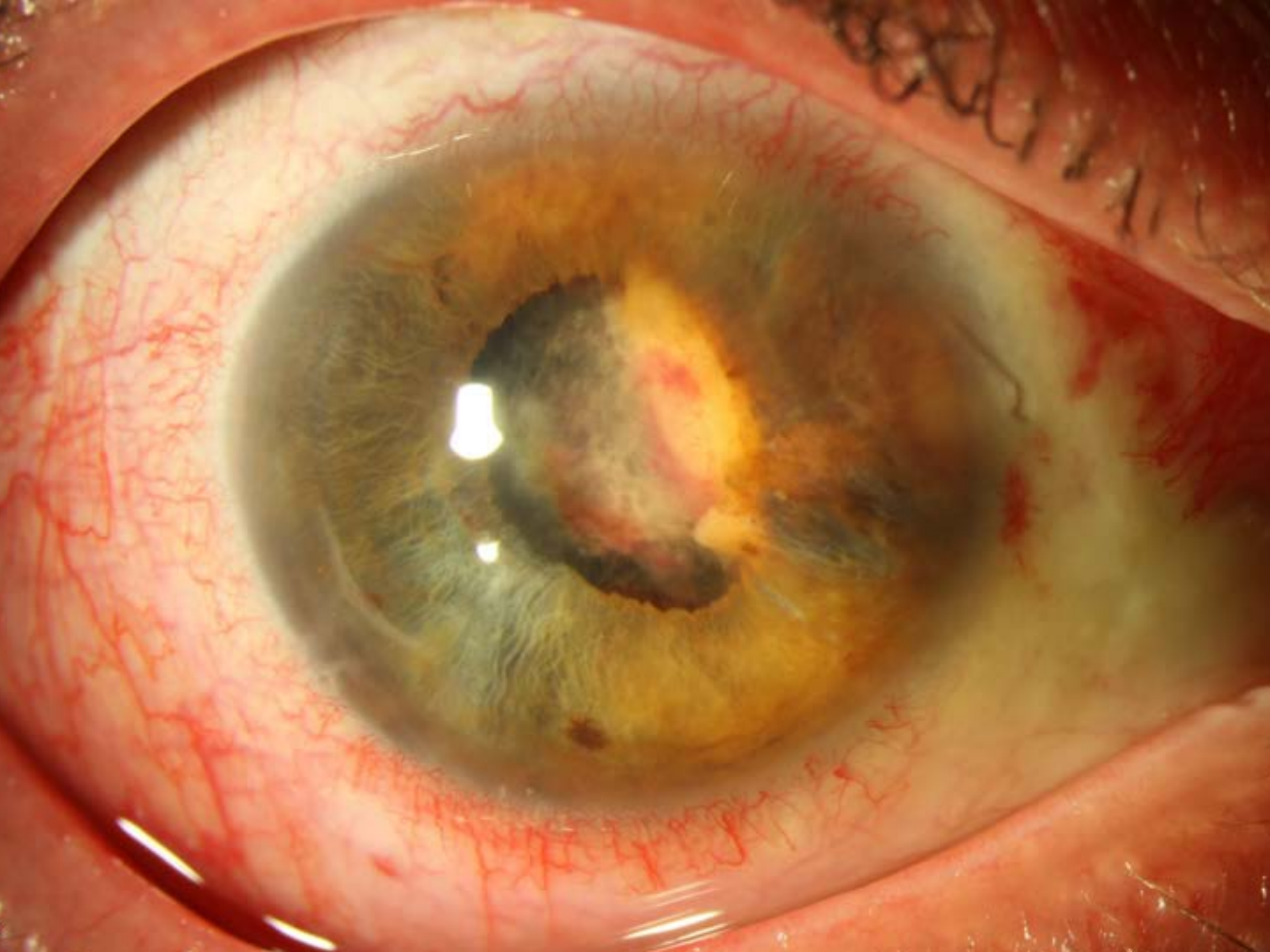
- Utility of genomic profiling in our practice
  - Class 2 patients undergo enhanced metastatic screening
  - Class 2 patients offered adjunctive systemic therapy
    - DEPAKENE (valproic acid)
    - YERVOY® (ipilimumab)/OPDIVO® (nivolumab)
    - KIMMTRAK® (tebentafusp-tebn)
    - Class 1 patients still followed with standard of care

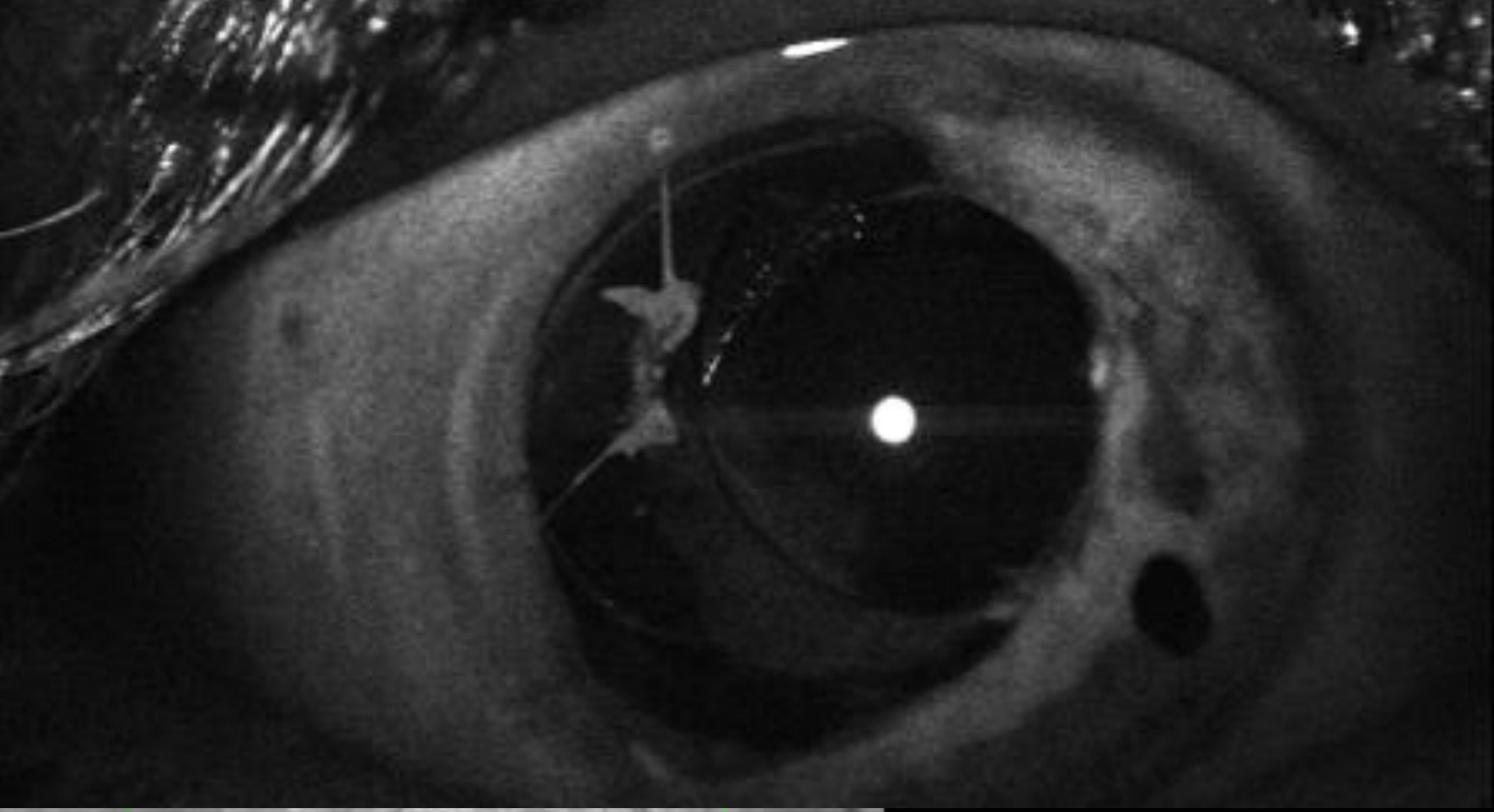


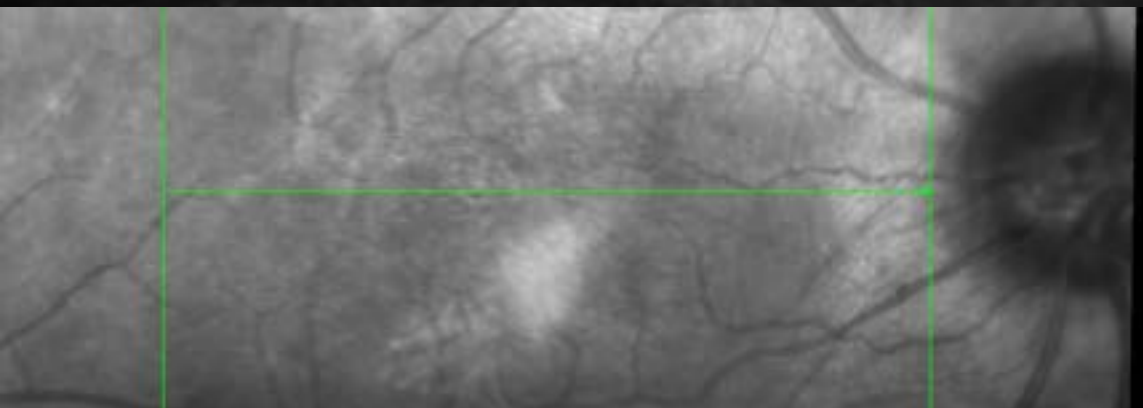


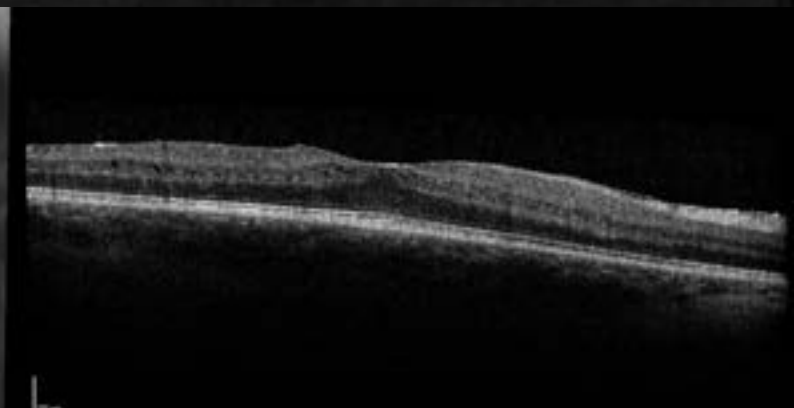


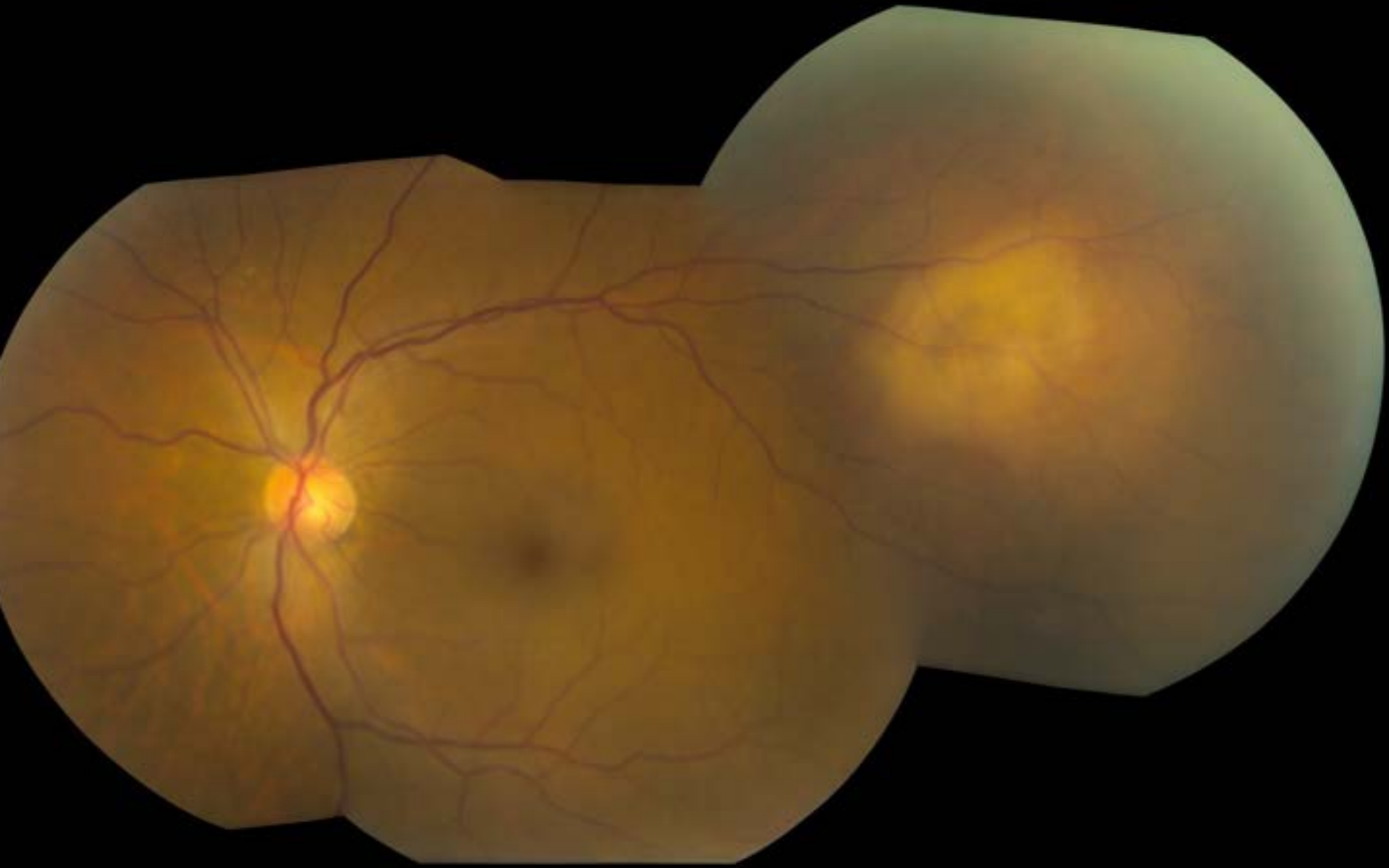


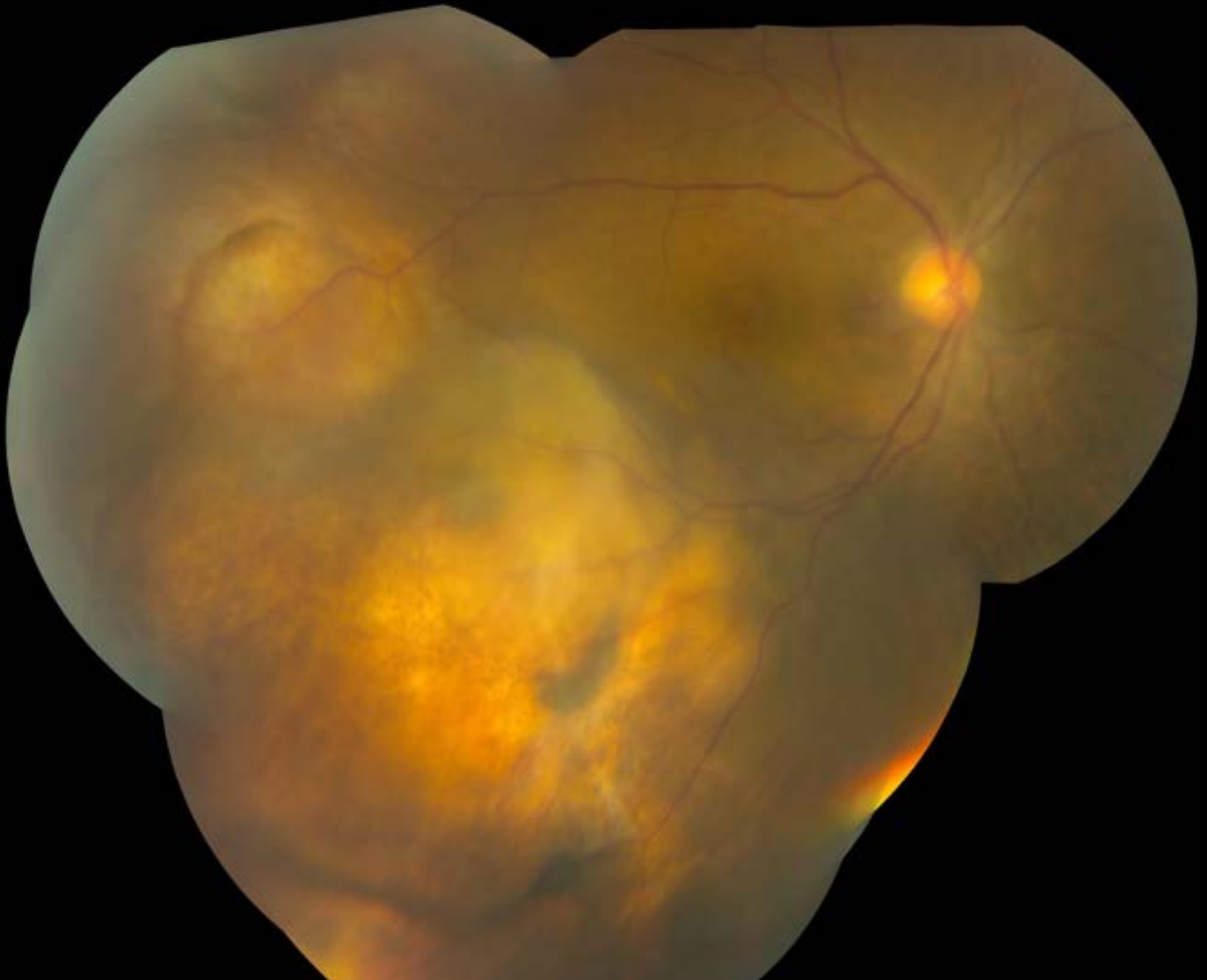












CHOROIDAL METASTASIS

- Most common intraocular malignancy
- 88% of uveal metastases involved the choroid
- Moderate to high reflectivity on ultrasound
- Primary neoplasms have been reported from:
  - Breast (39–49% of all uveal metastases), Lung, Kidney, Gastrointestinal, Cutaneous, Prostate, Thyroid, Contralateral uveal melanoma, Pancreas, and Bile duct.

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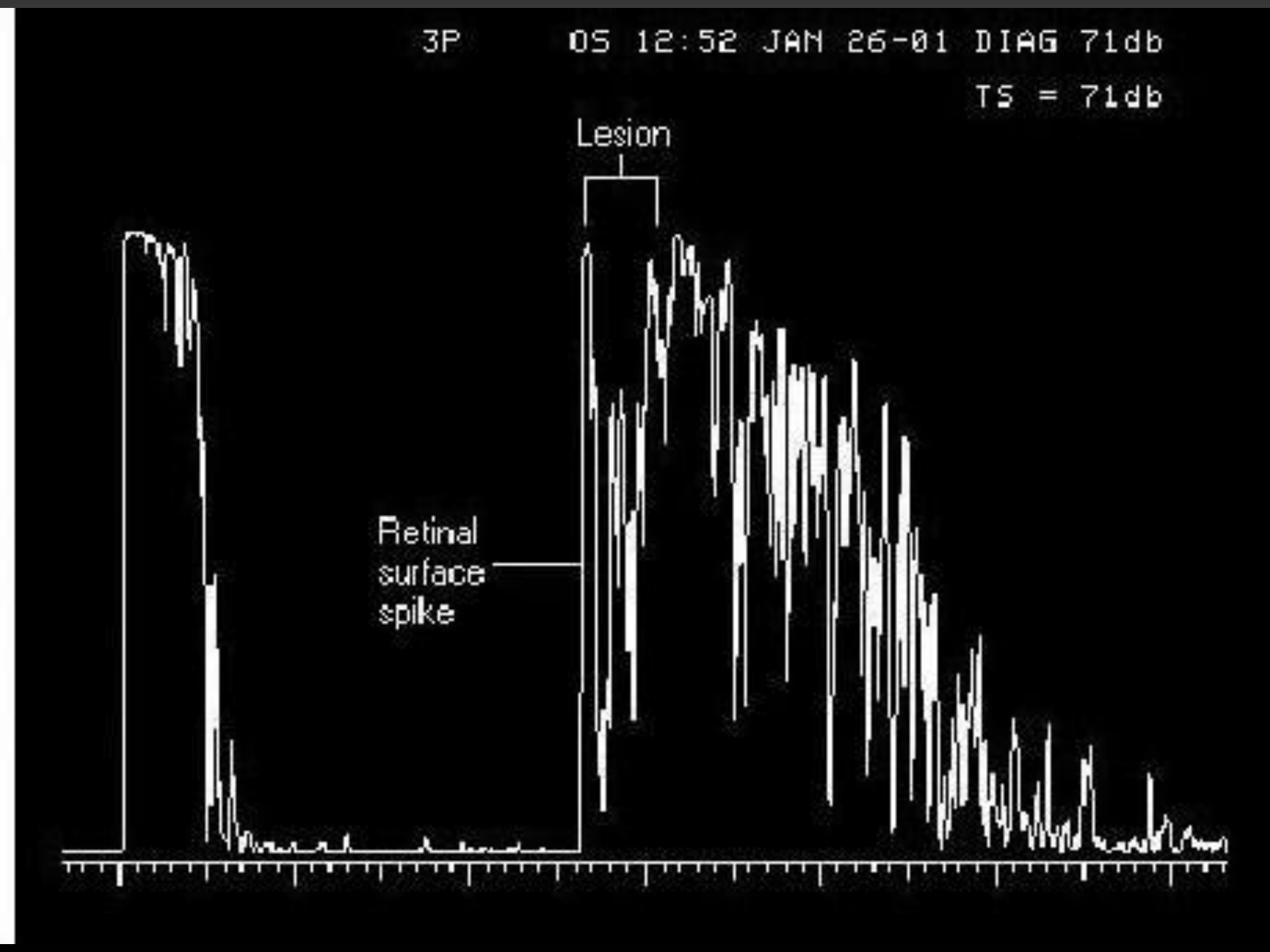
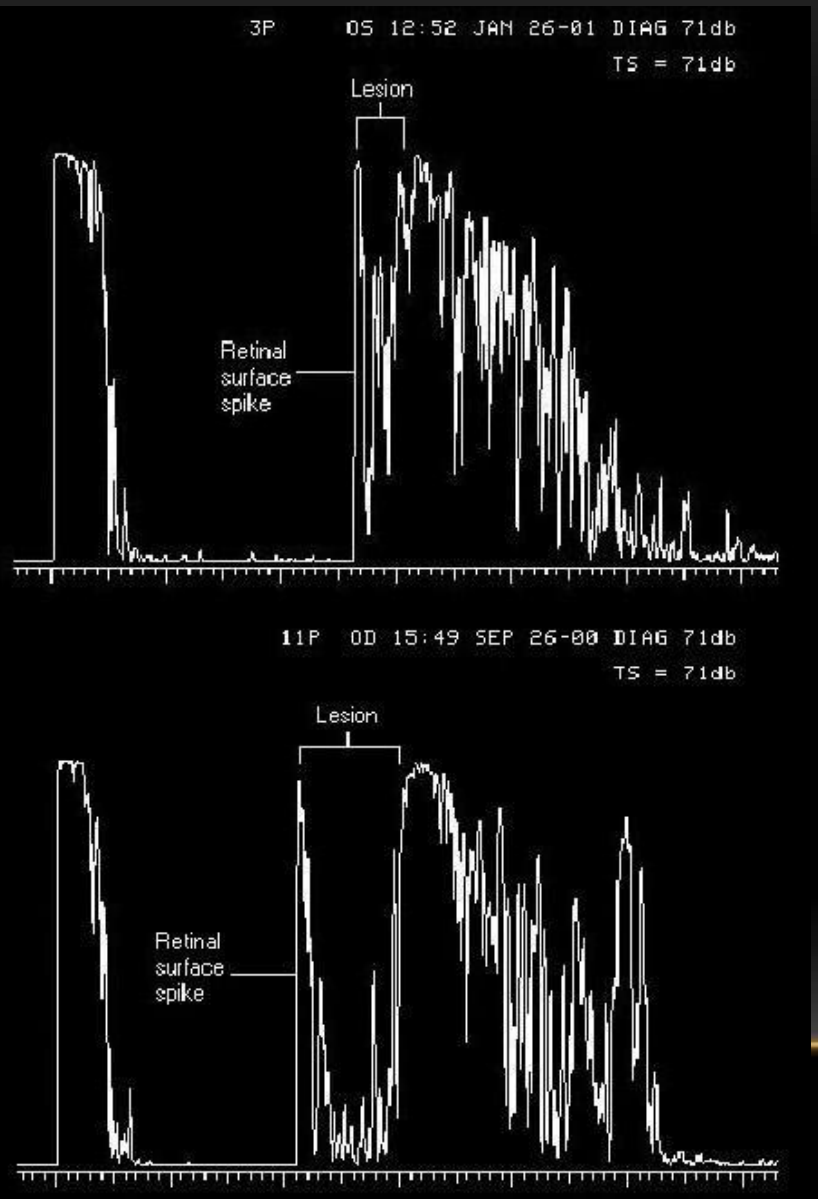

3P OS 12:52 JAN 26-01 DIAG 71db
TS = 71db
Lesion
Retinal surface spike

A-SCAN OF MET VS CM



- A-Scan Ultrasound of a metastatic choroidal mass. Notice the moderate-high reflectivity and internal disorganization.

- A-Scan Ultrasound of a primary choroidal melanoma. Notice the low-moderate reflectivity and greater internal organization of the lesion.

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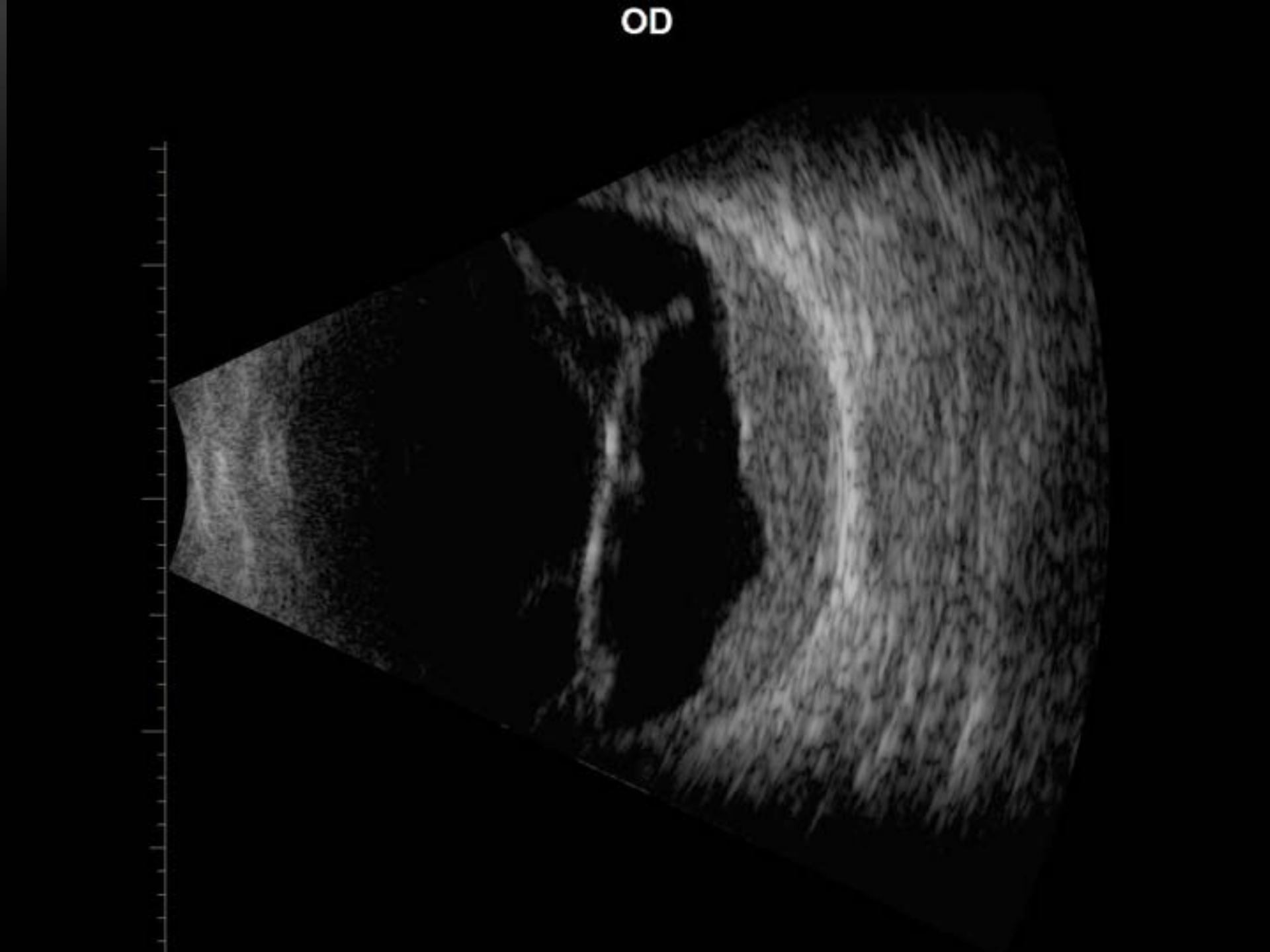
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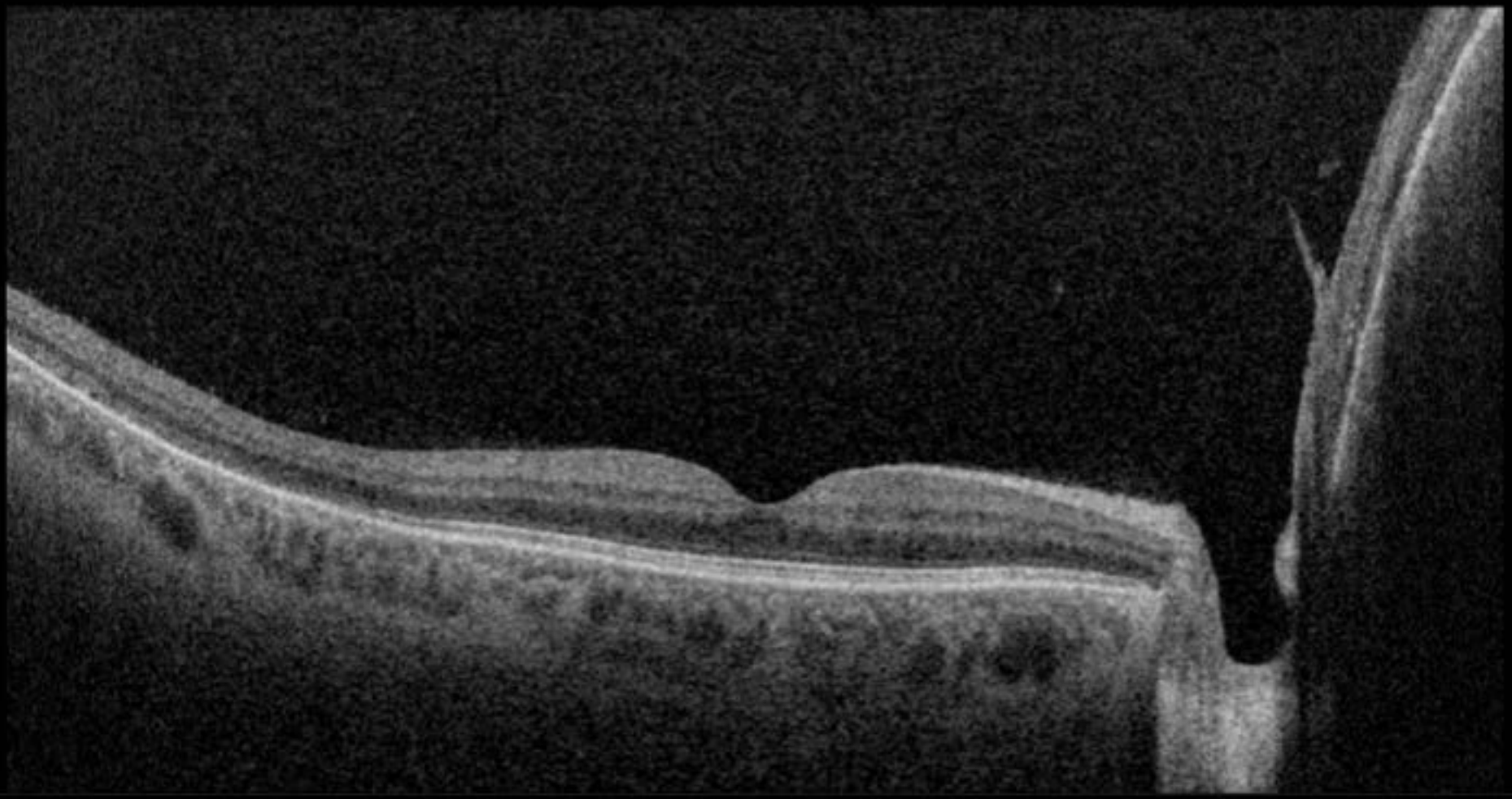
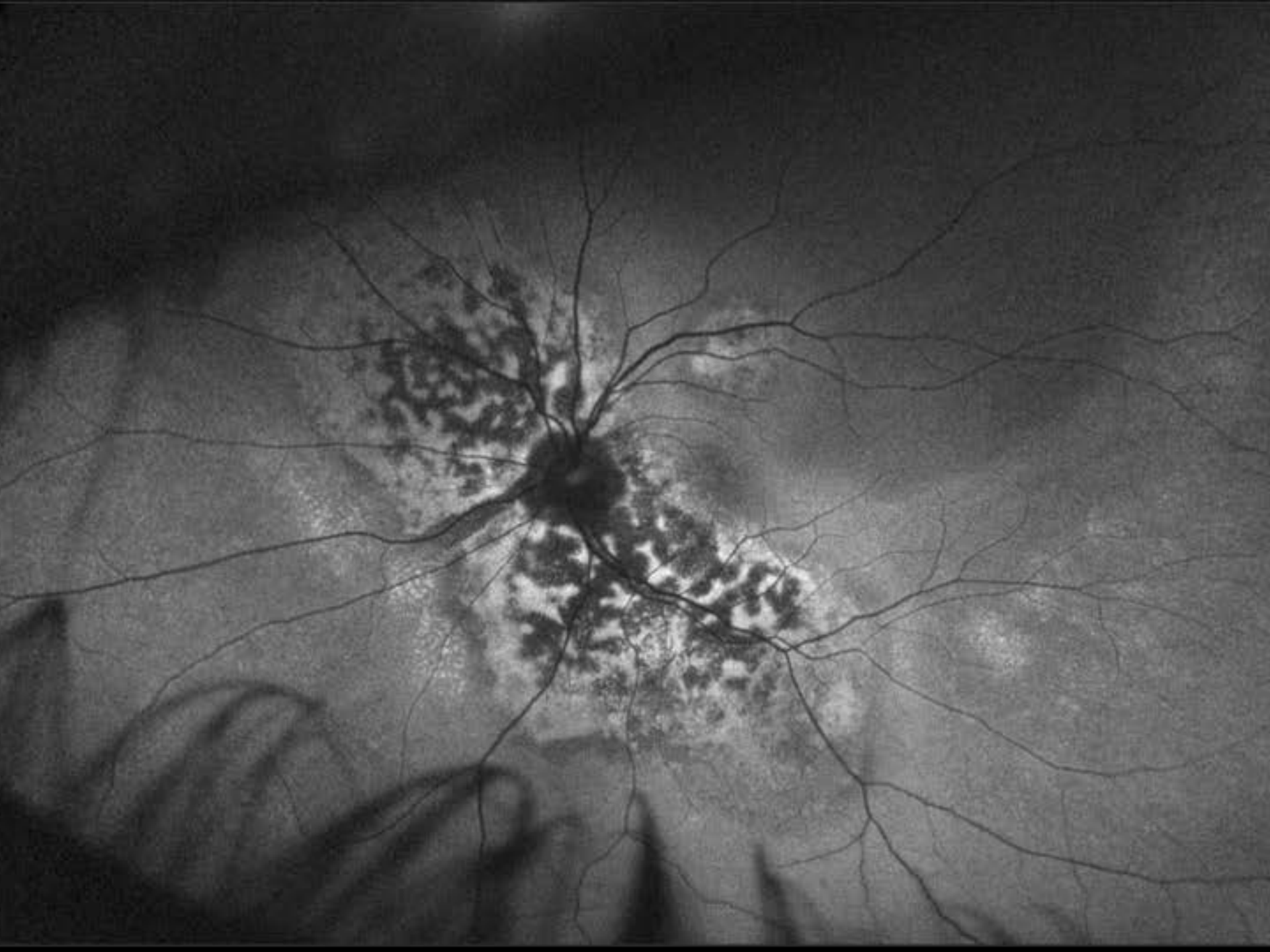
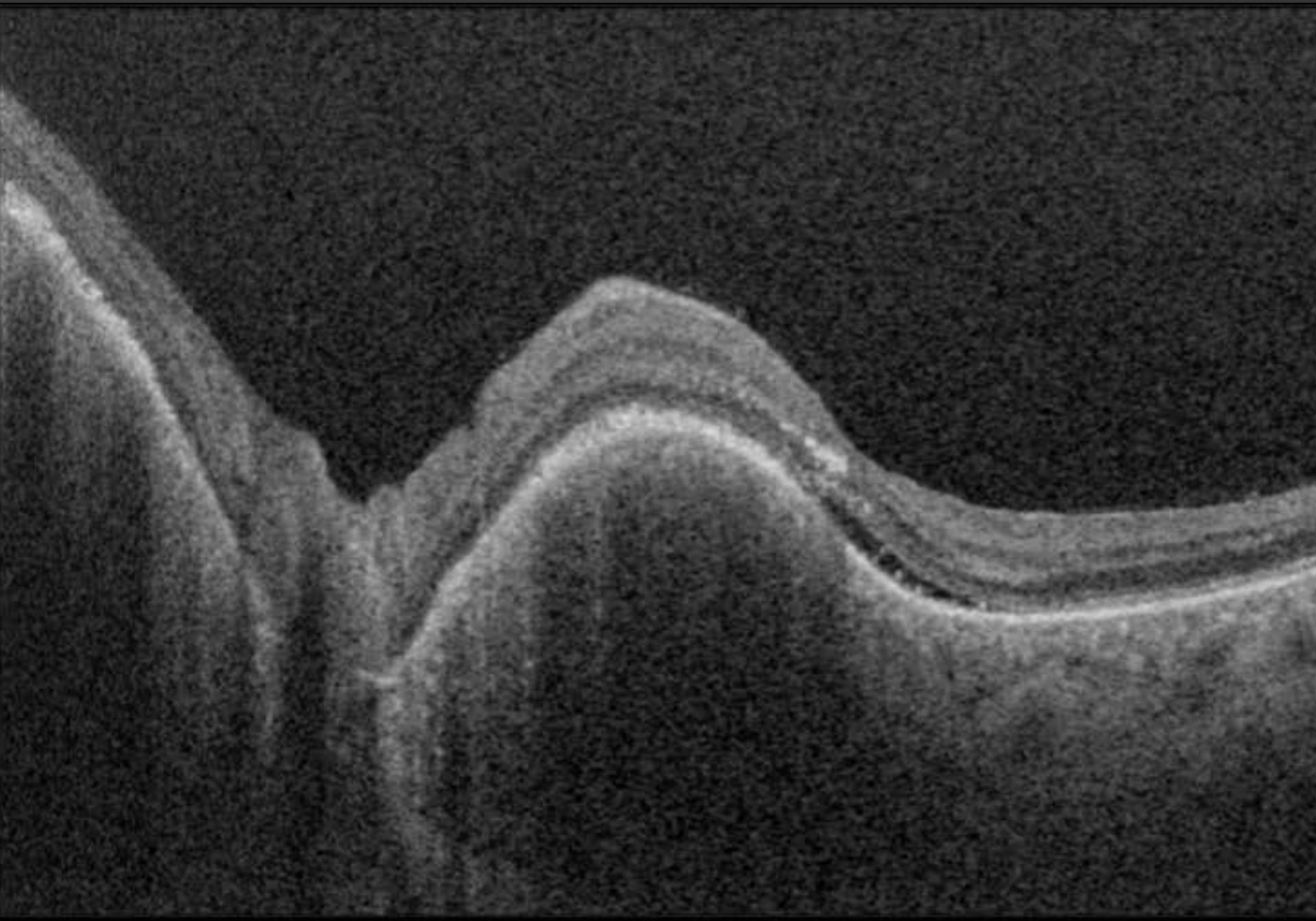
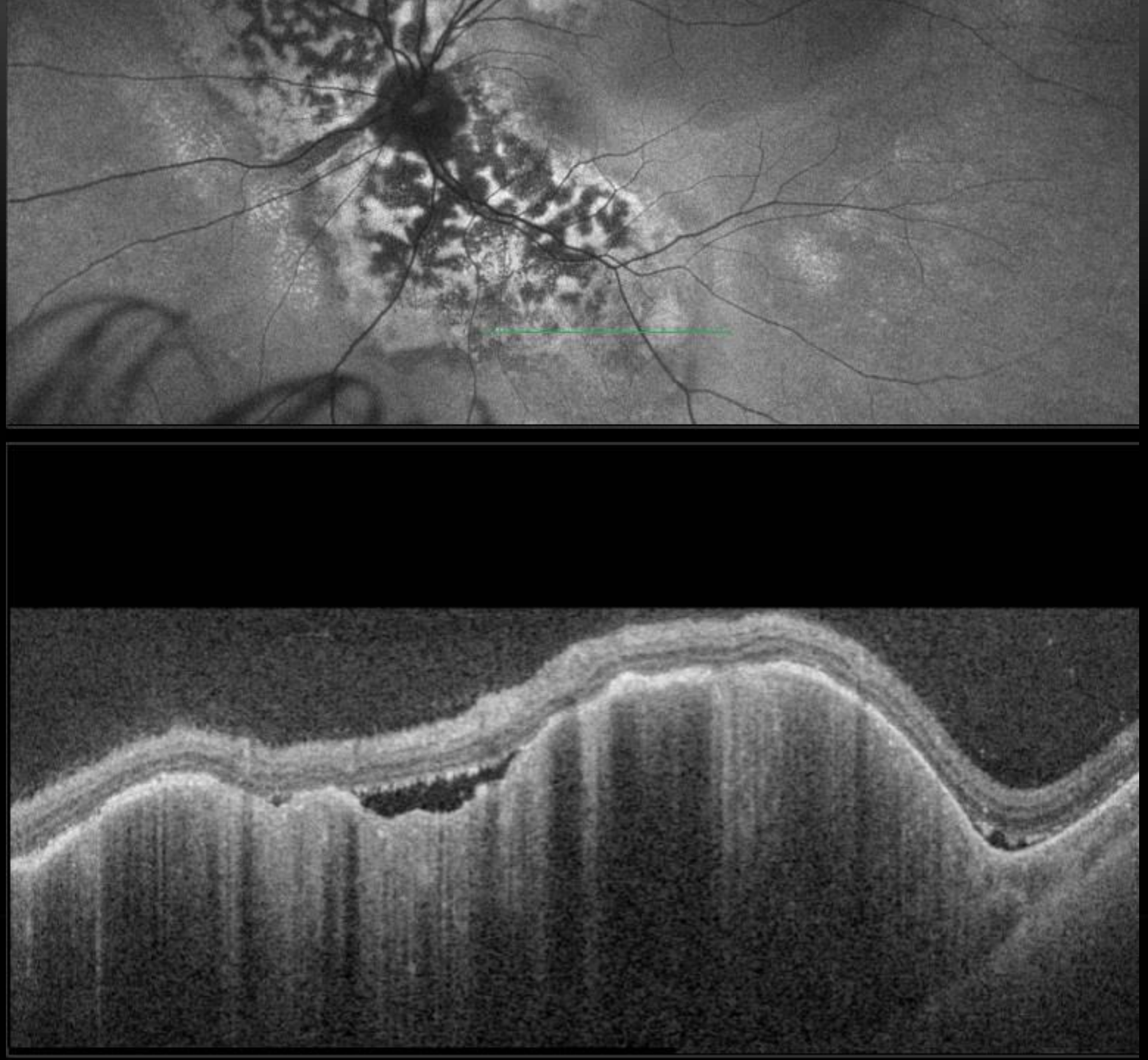






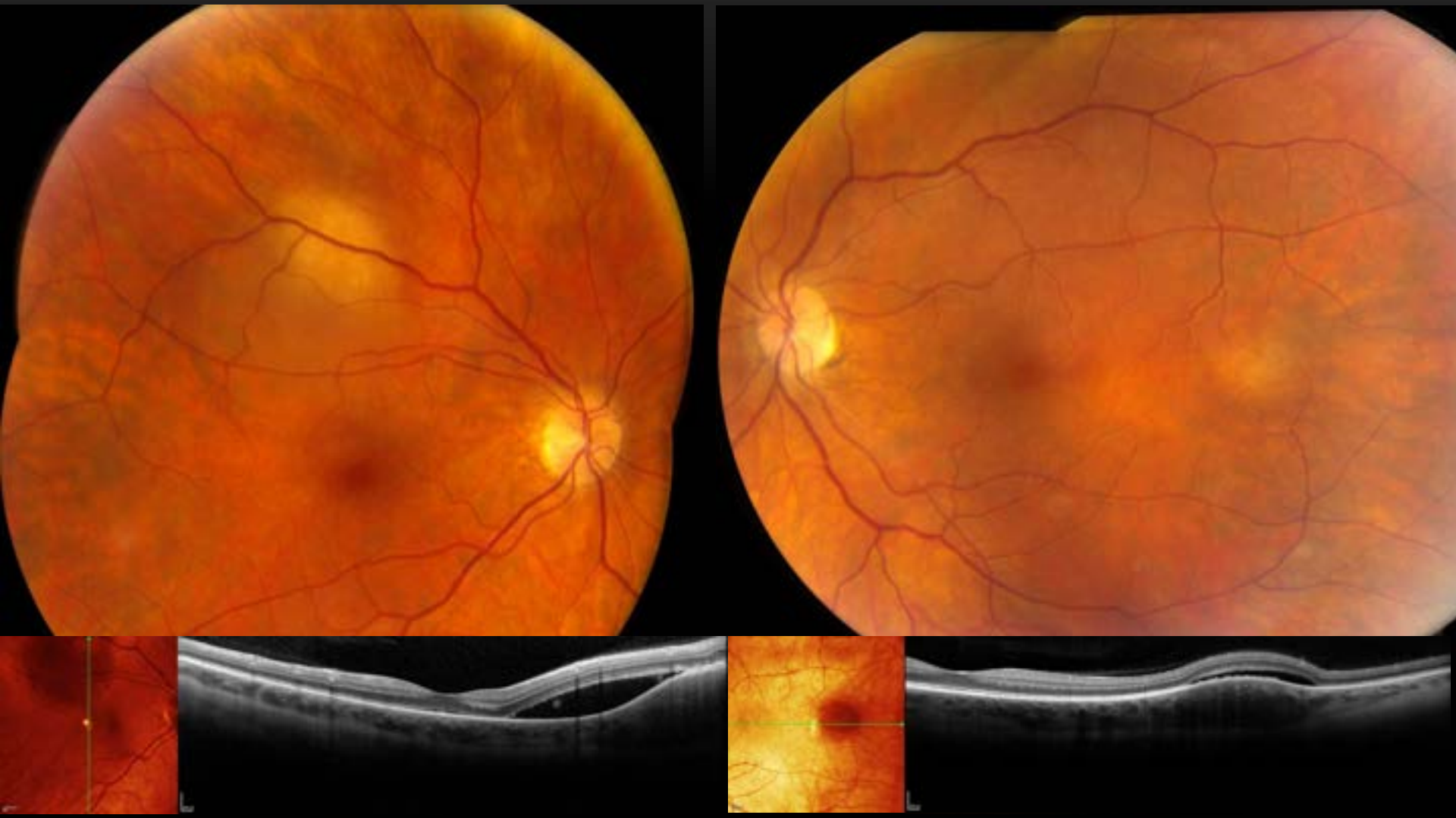


TREATMENT

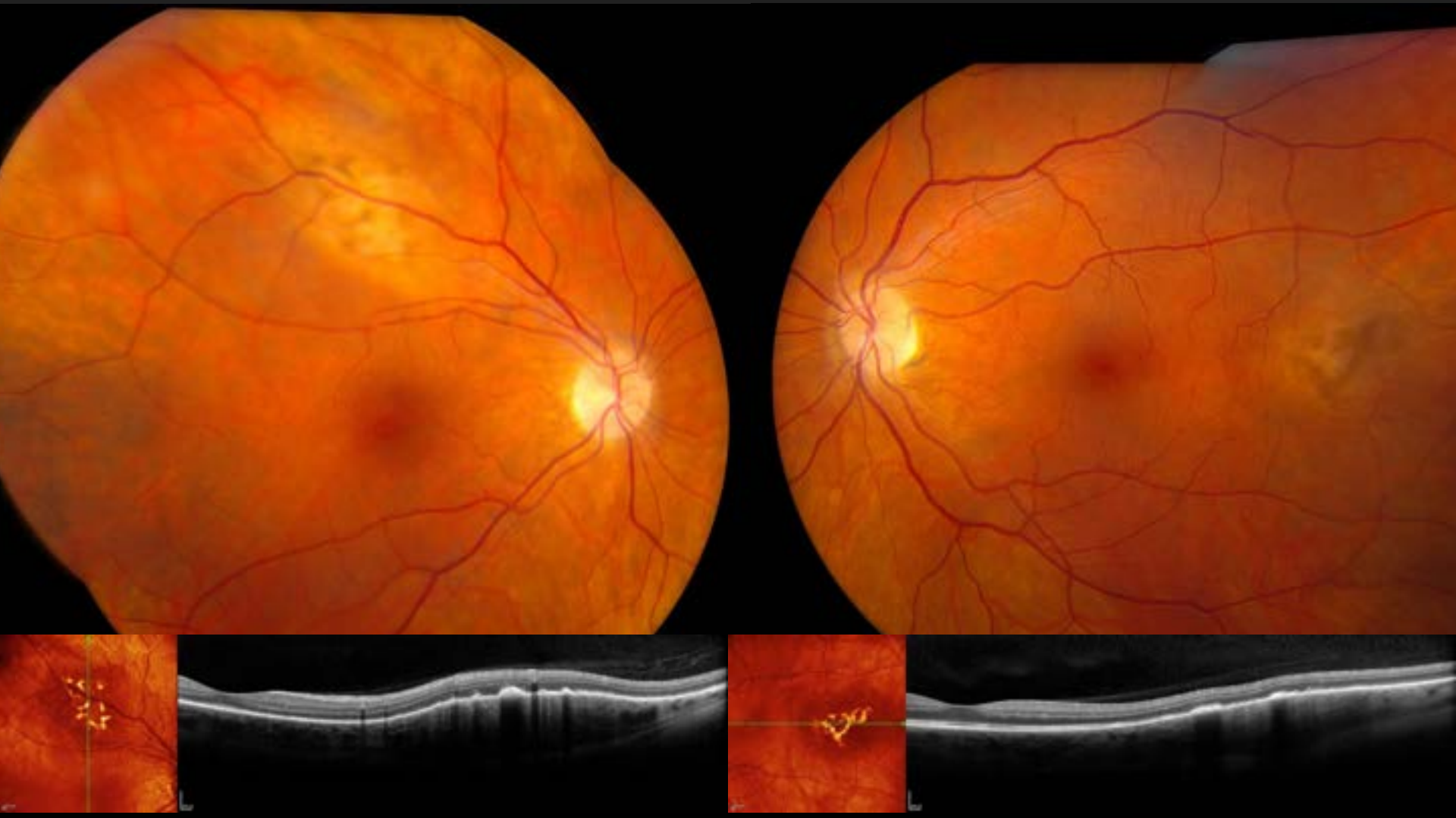
- Radiotherapy
  - EBRT
  - plaque brachytherapy
- Transpupillary thermotherapy
- Observation
  - Reserved for asymptomatic patients with widespread metastatic disease or occasionally patients receiving systemic chemotherapy
- Chemotherapy
- Enucleation
  - Reserved for the blind, painful eyes.

MURRAY
Ocular Oncology & Retina

INITIAL PRESENTATION



AFTER EBRT



CIRCUMSCRIBED CHOROIDAL HEMANGIOMA

- Rare, benign, intraocular tumors of the choroid
- Often mistaken for choroidal metastases and melanomas
- Characteristic appearance consists of an indistinct round-to-oval, orange-pink swelling at the posterior pole, often involving the optic disc, macula, or both
- Likely congenital -- macular hemangiomas are usually associated with amblyopia, most likely occurring as a result of hyperopia

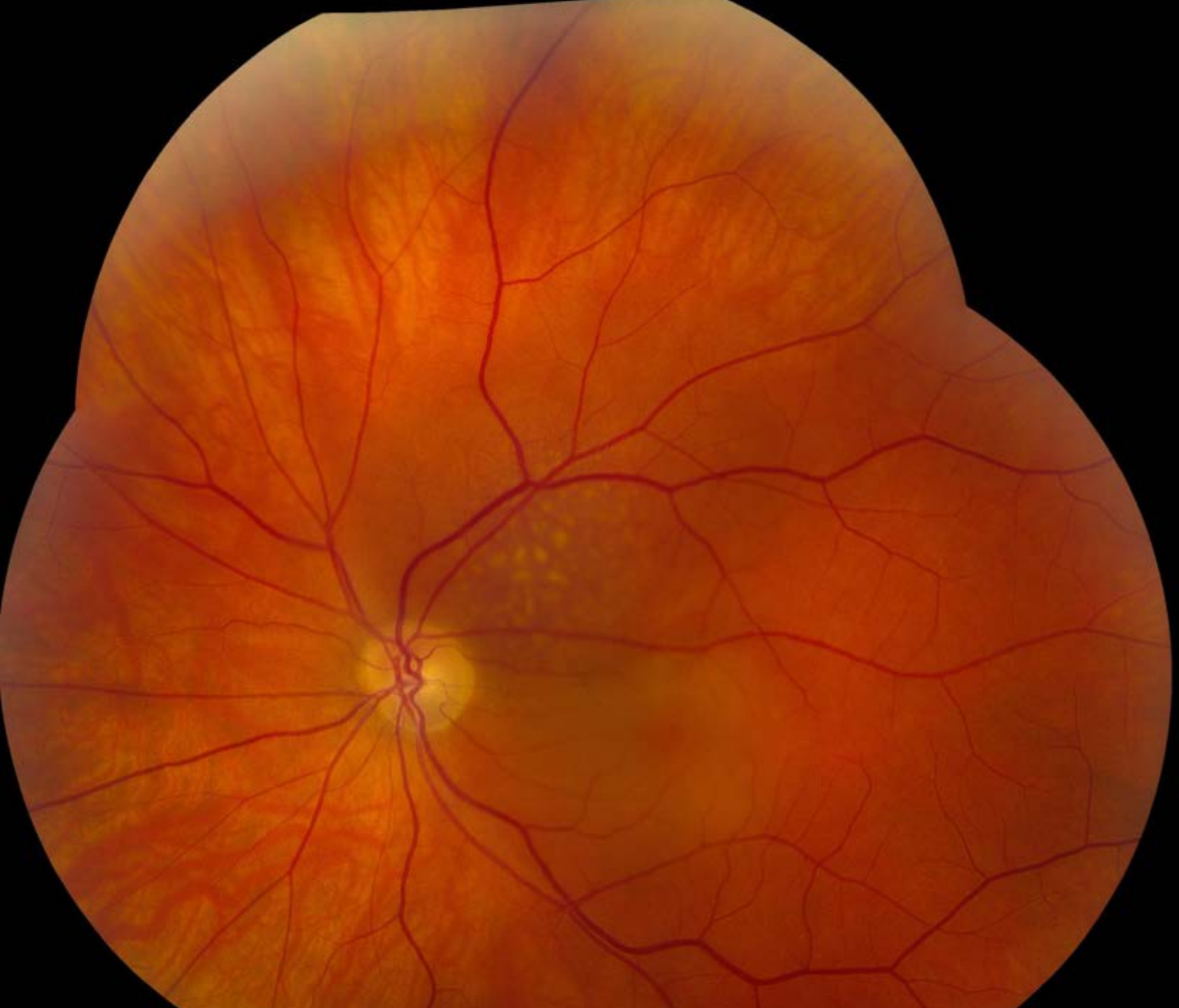
CIRCUMSCRIBED CHOROIDAL HEMANGIOMA

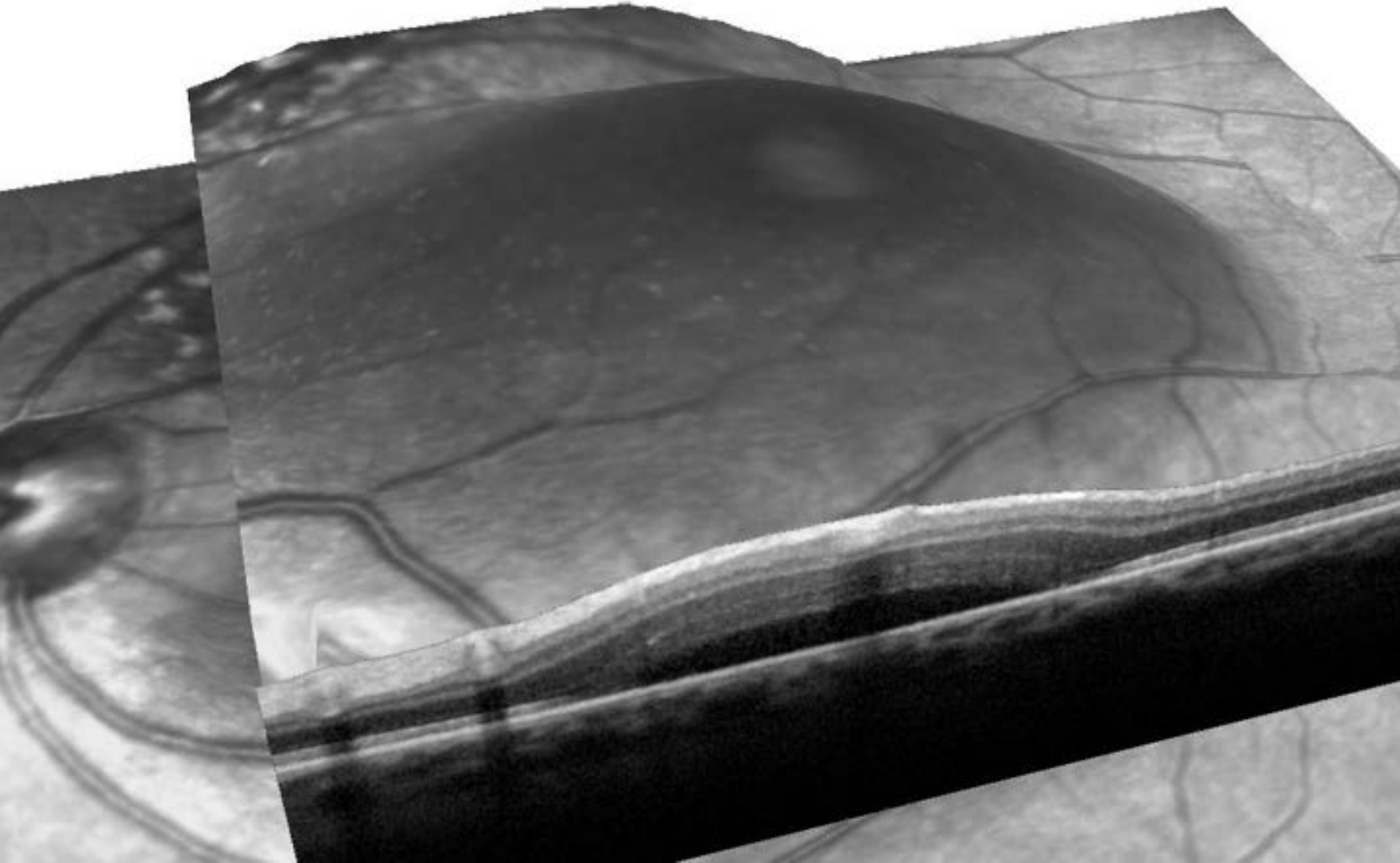
- May remain asymptomatic throughout life
- However, visual symptoms may present between the second and fifth decades
  - Caused by secondary, exudative retinal detachment and macular edema.
- If left untreated, many patients eventually develop severe retinal detachments with secondary neovascular glaucoma.

MURRAY
Ocular Oncology & Retina

DIAGNOSTIC FEATURES

- Ultrasonography shows acoustic solidity with a high internal acoustic reflectivity
  - Also typically shows no vascular activity (WHY?)
- Fluorescein angiography shows a highly vascularized choroidal lesion that typically fills rapidly, simultaneously with the normal choroidal vessels
- OCT can identify and quantify any associated macular edema and exudative retinal detachments

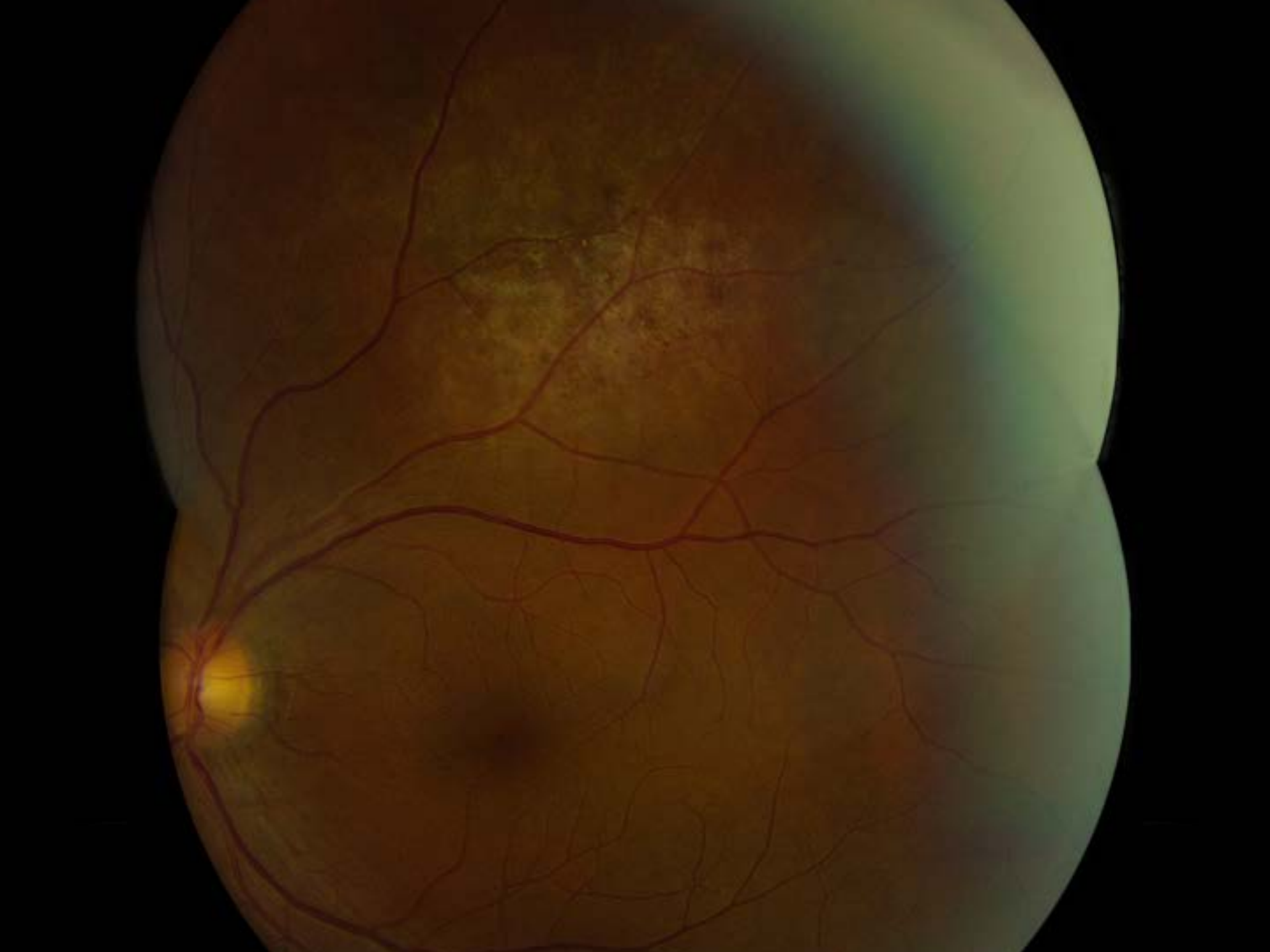


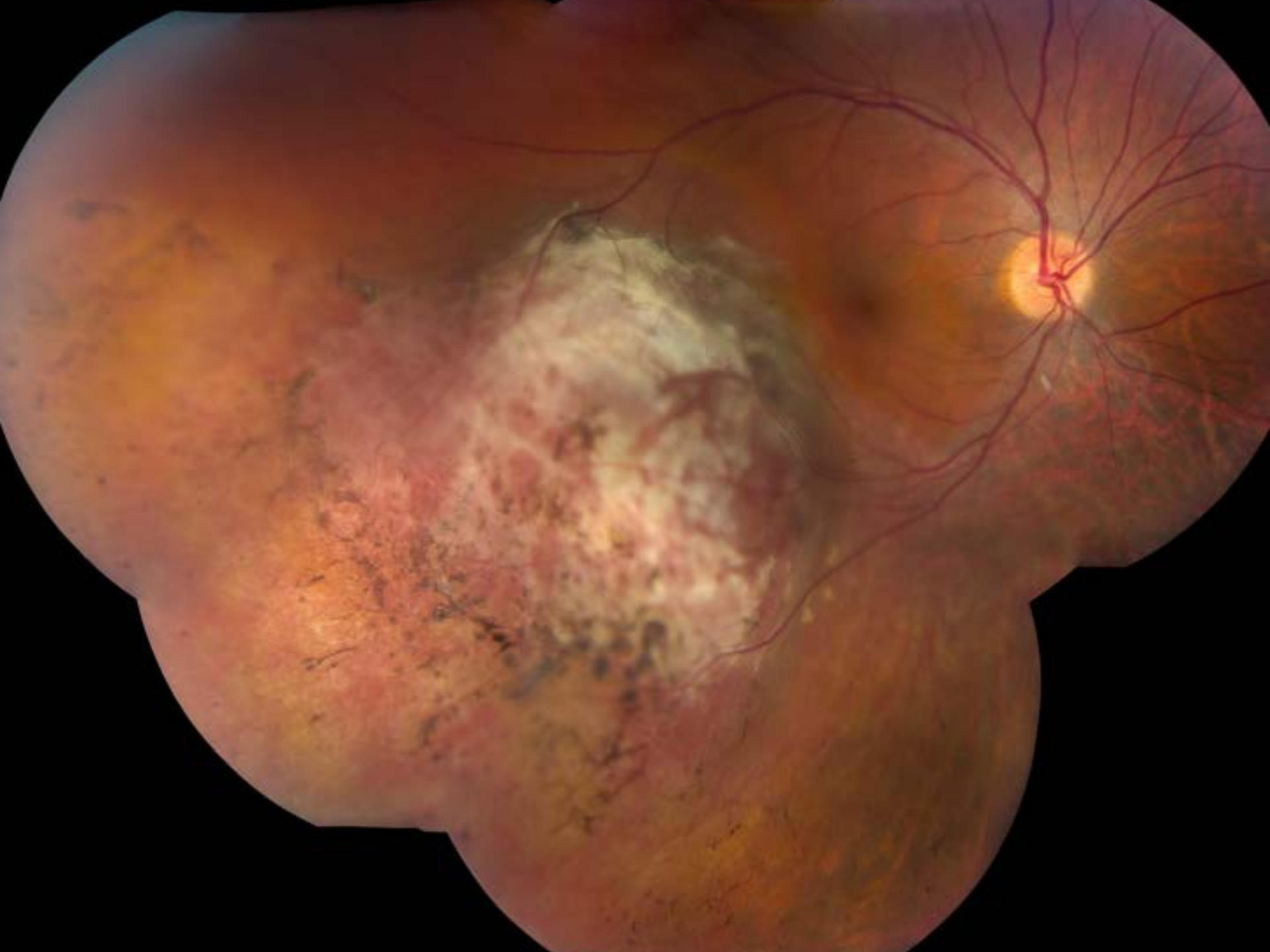


CIRCUMSCRIBED CHOROIDAL HEMANGIOMA TREATMENT

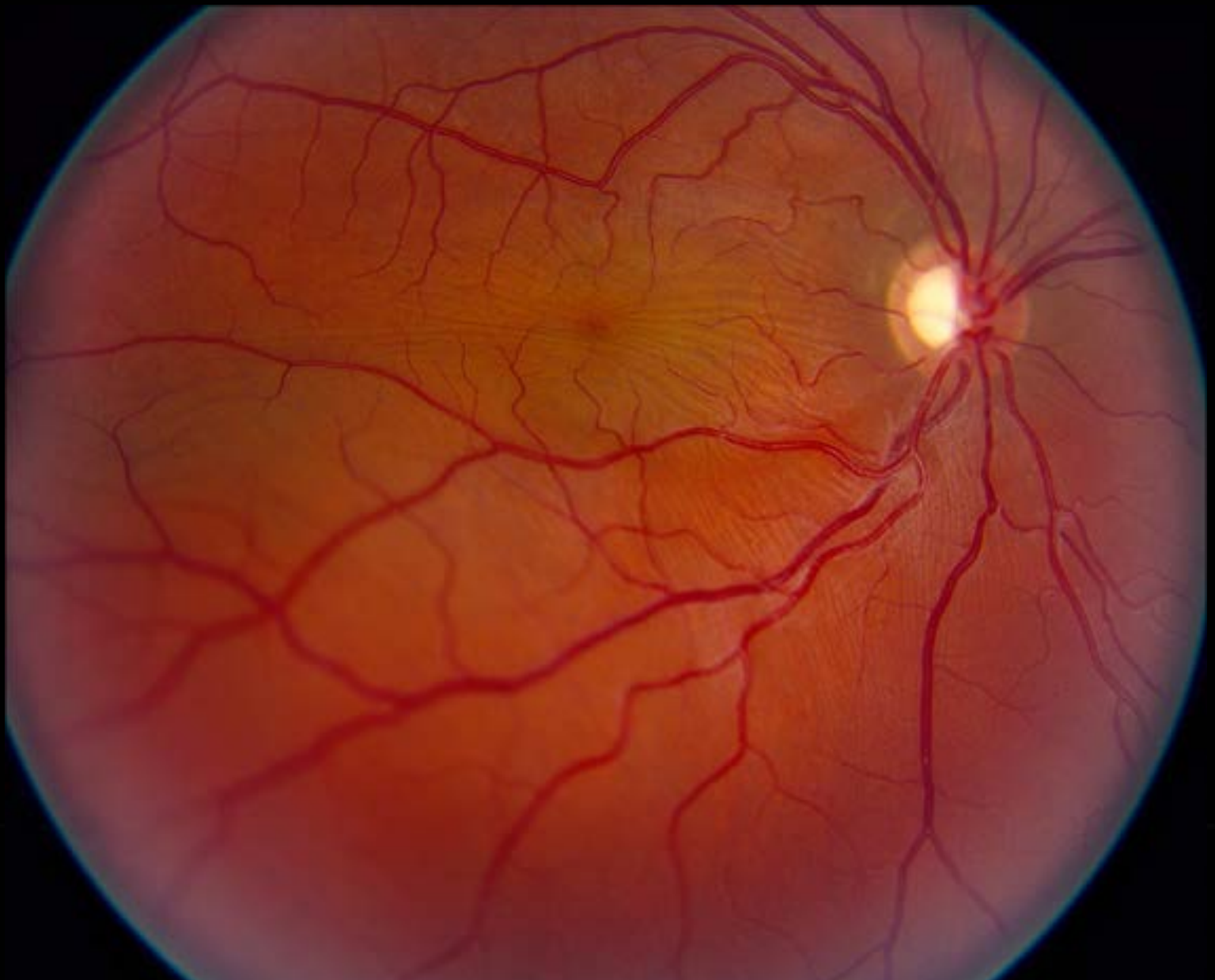
- Indicated for symptomatic patients due to:
  - Exudative retinal detachment
  - Macular edema
  - Severe exudative retinal detachment threatening to cause neovascular glaucoma
- PDT has been an effective treatment
- Other treatment modalities include:
  - Anti-VEGF therapy
  - External beam or proton beam radiotherapy
  - Transpupillary thermotherapy or laser photocoagulation

MURRAY
Ocular Oncology & Retina





DIFFUSE CHOROIDAL HEMANGIOMA

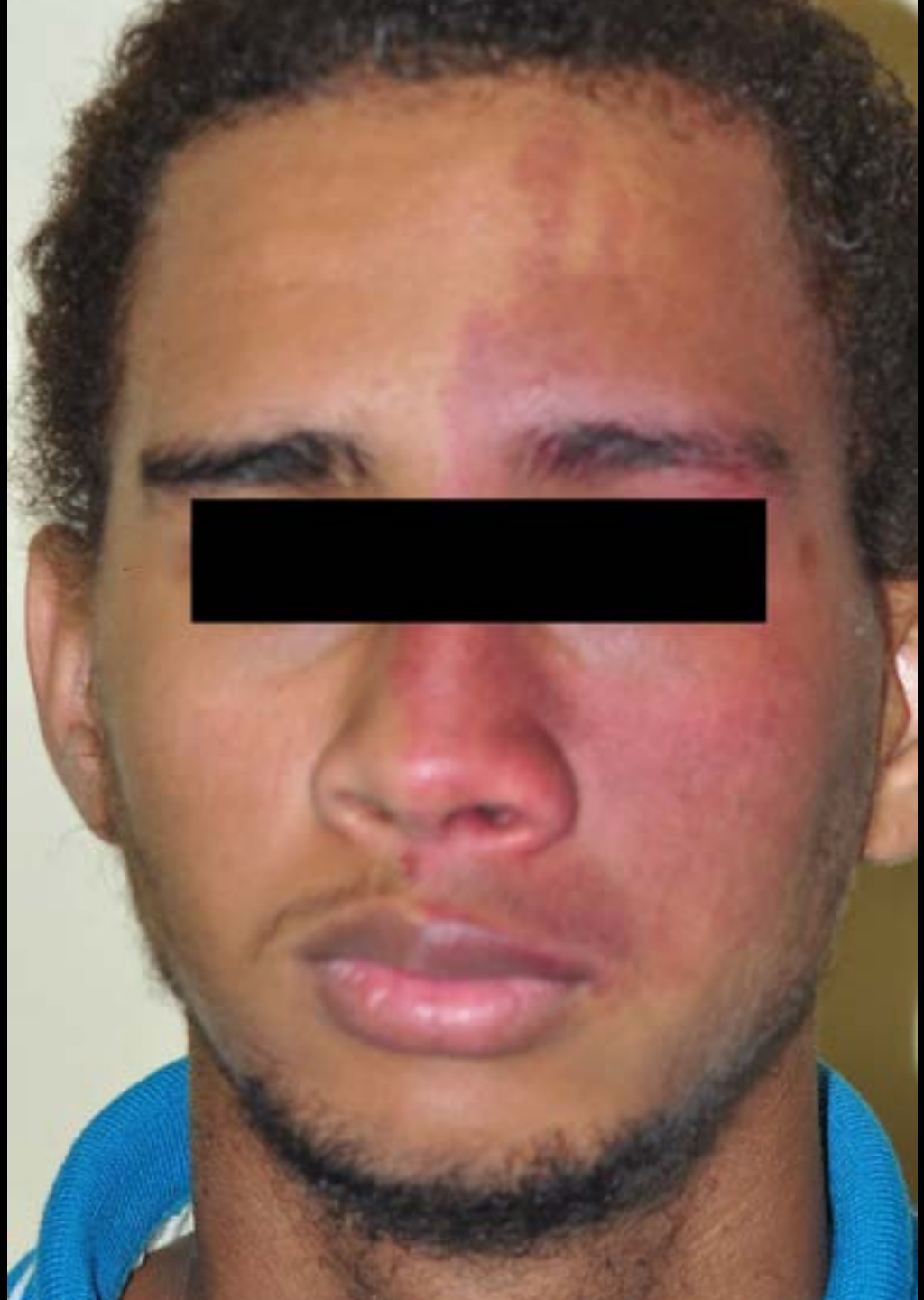


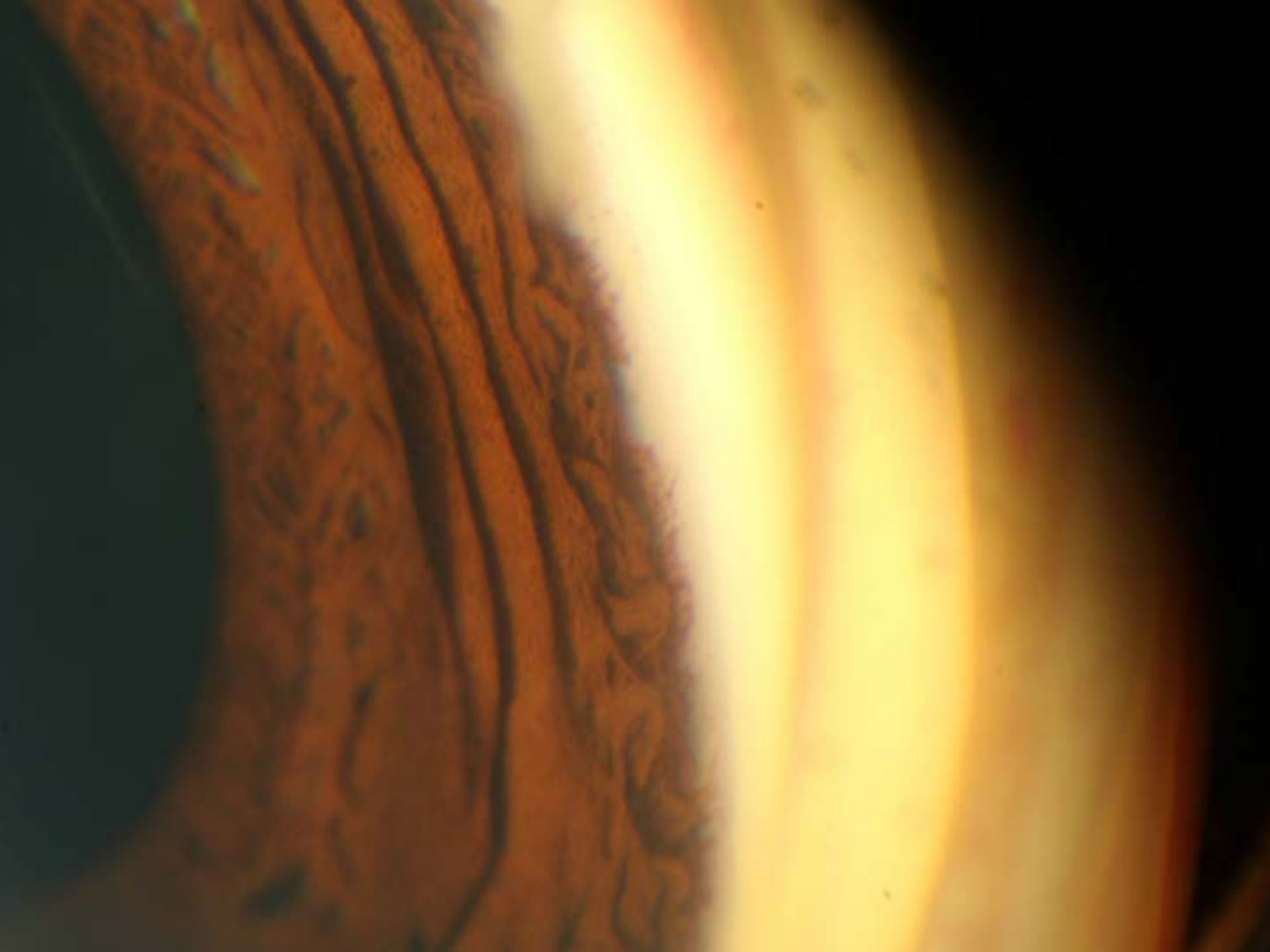
STURGE–WEBER SYNDROME

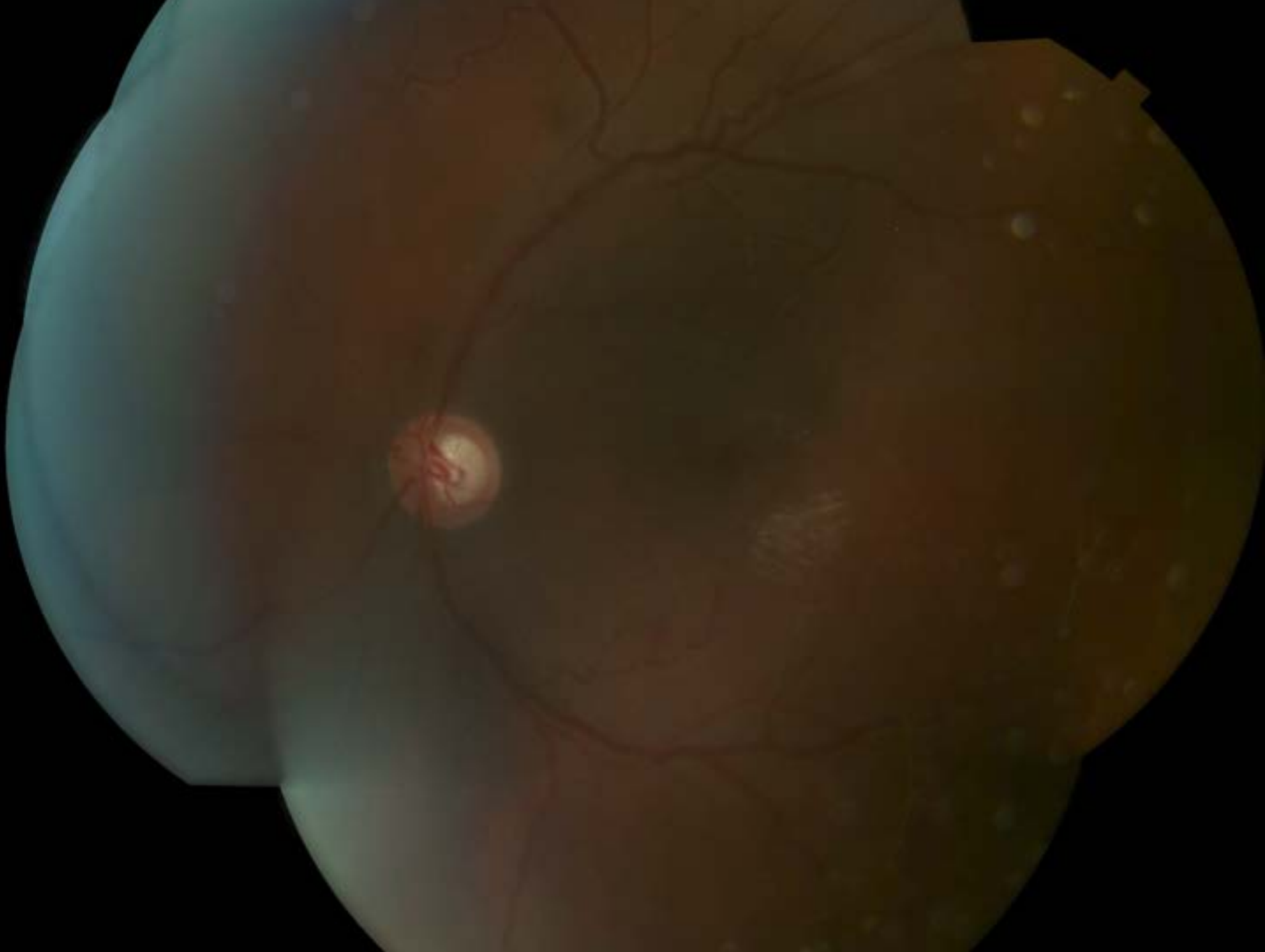
- Sporadic neurocutaneous disorder
- Characterized by:
  - Facial capillary malformation (port-wine stain)
  - Leptomeningeal angioma
  - Vascular ocular abnormalities
- Diagnosed clinically in the presence of the facial cutaneous changes with neurological changes and/or ocular manifestations

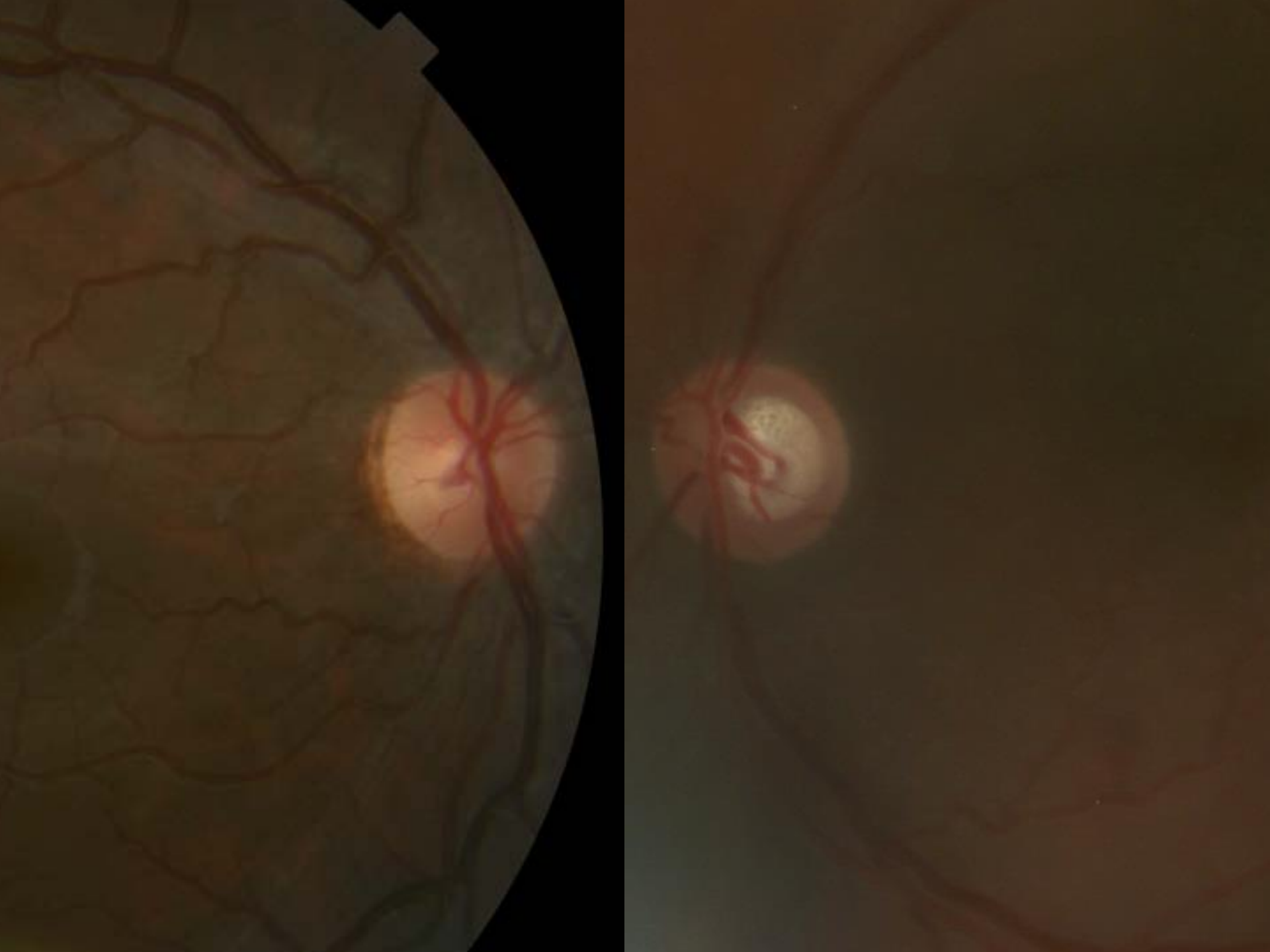
STURGE–WEBER SYNDROME

- Ocular manifestations include:
  - Glaucoma (71%)
  - Conjunctival or episcleral hemangiomas (69%)
  - Diffuse choroidal hemangiomas (55%)
- Only 8% of children born with facial port-wine stains are associated with Sturge–Weber syndrome, however, the association is more common if the facial nevus involves the eyelids.





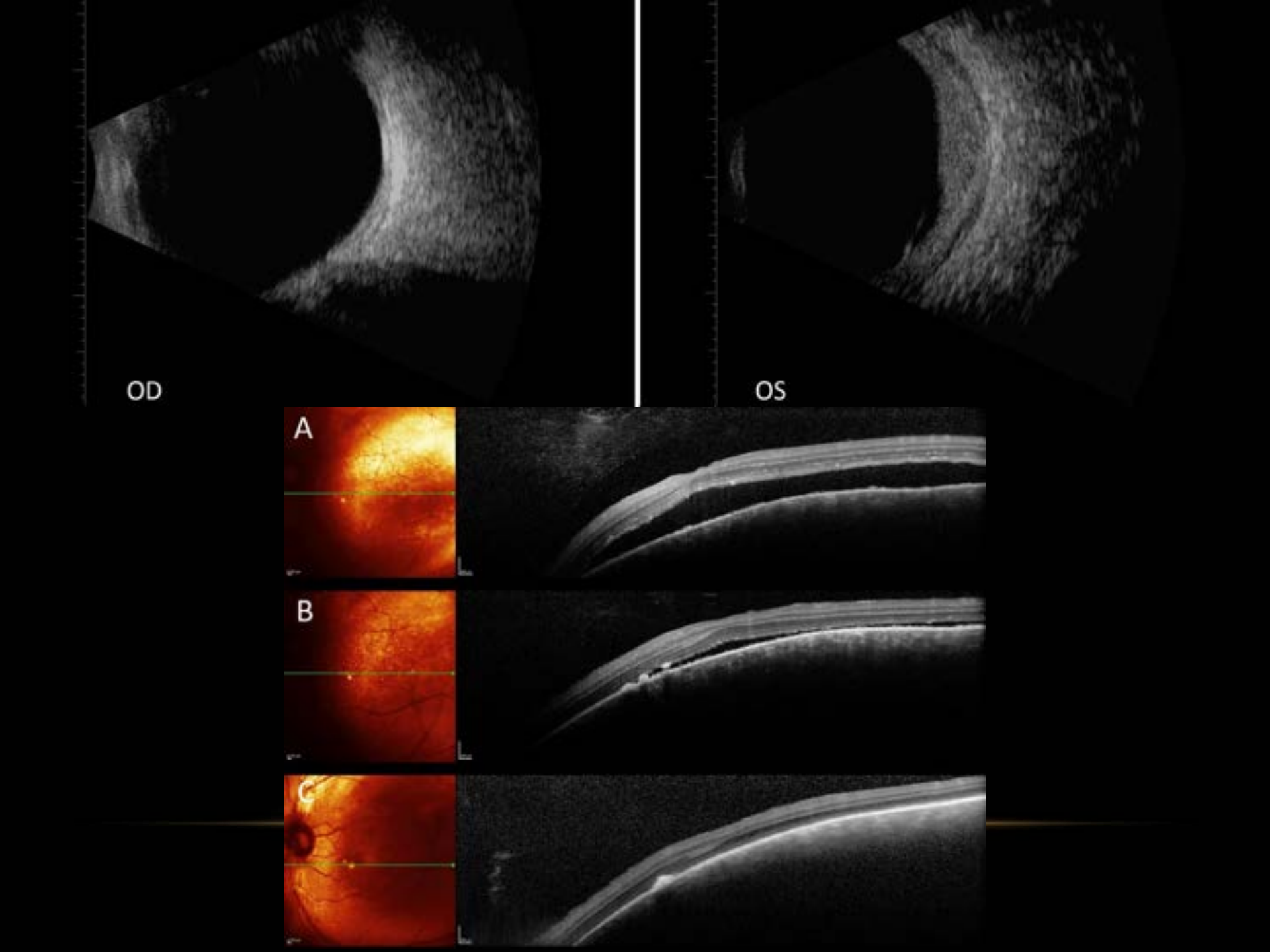




DIFFUSE CHOROIDAL HEMANGIOMA TREATMENT

- The main objective of treating diffuse choroidal hemangiomas is to prevent or treat severe retinal detachment, thereby avoiding secondary glaucoma and loss of the eye
- Because of the large size of the hemangioma, external beam radiotherapy or proton beam radiotherapy is commonly used.
- Anti-VEGF treatment may be utilized for small exudative detachments

MURRAY
Ocular Oncology & Retina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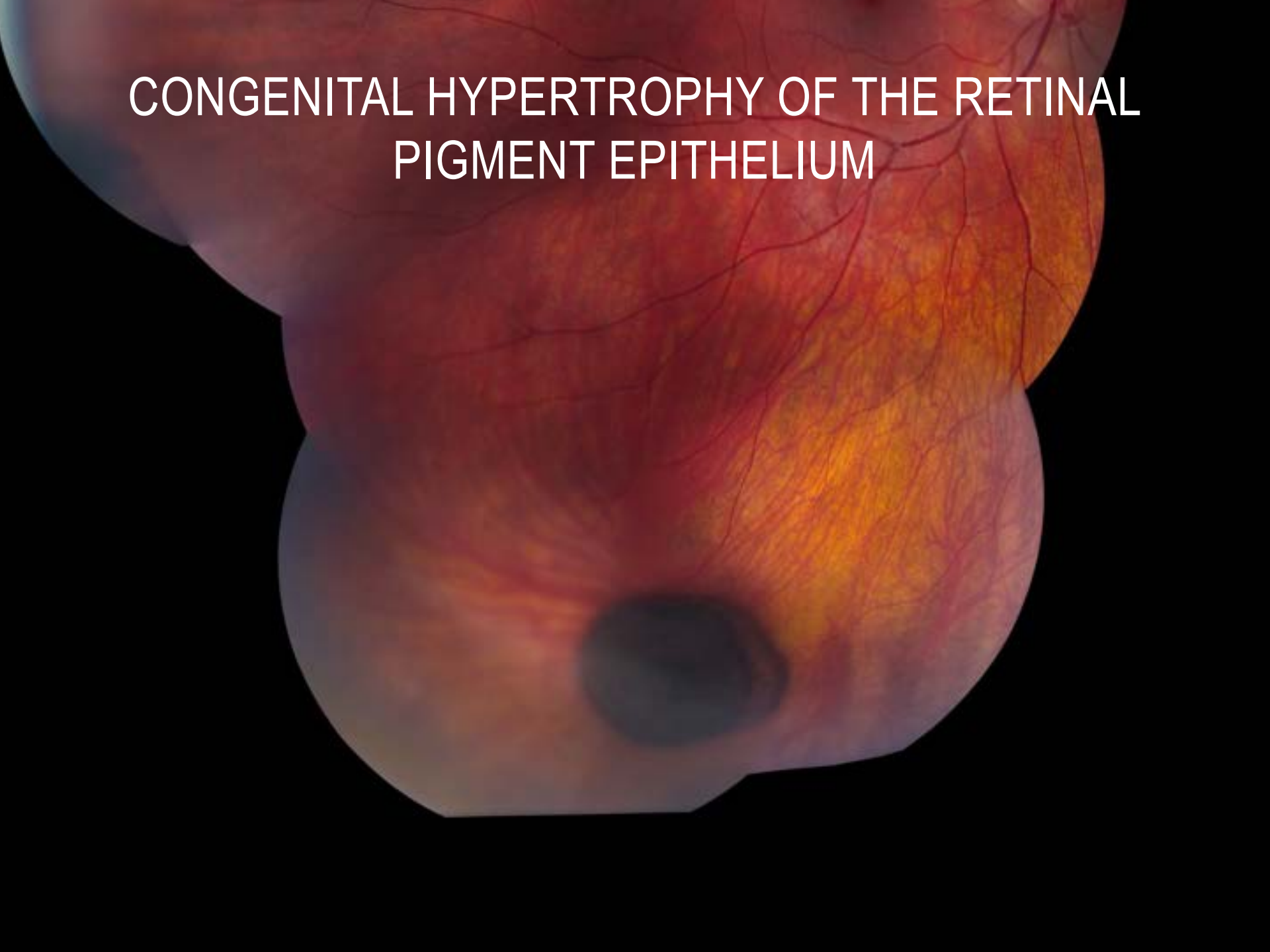
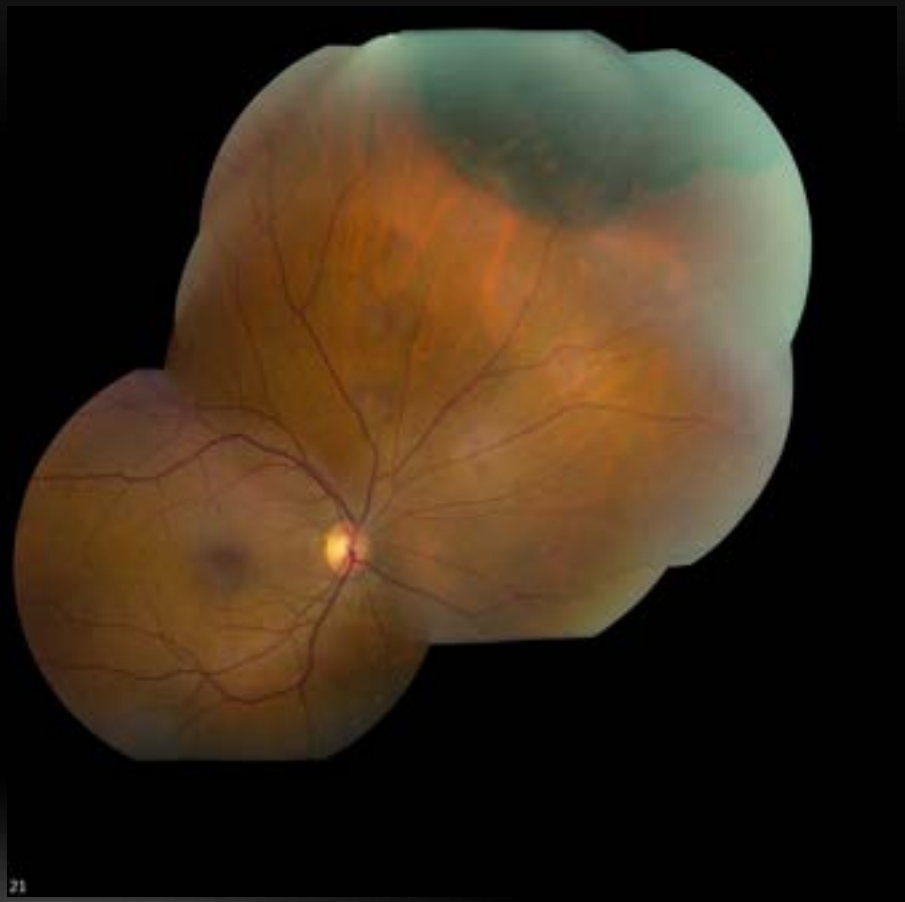
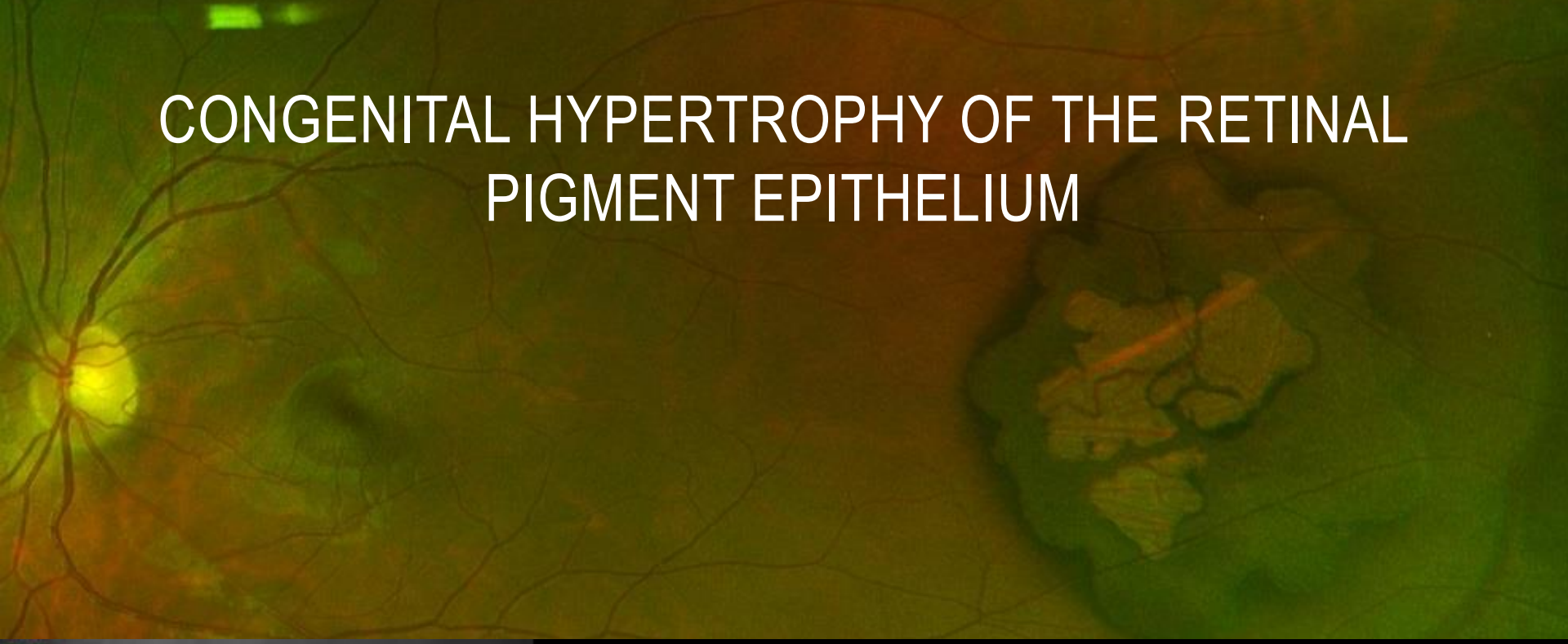

CONGENITAL HYPERTROPHY OF THE RETINAL
PIGMENT EPITHELIUM

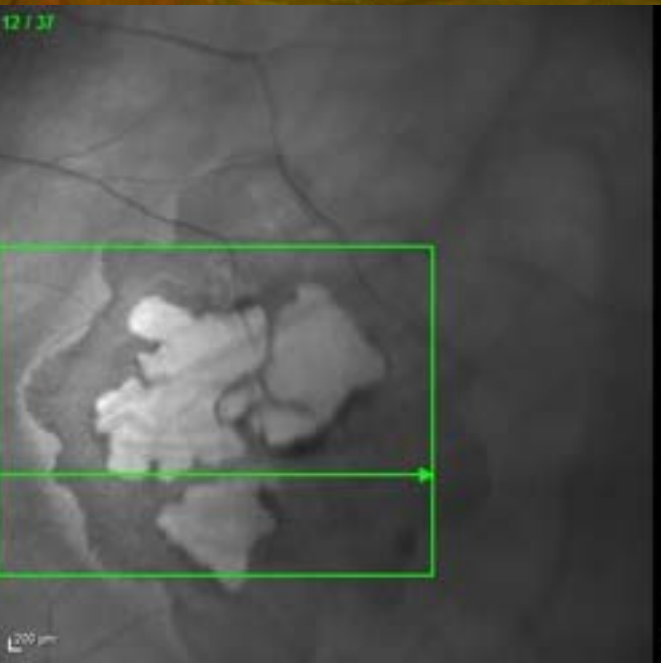
CONGENITAL HYPERTROPHY OF THE RETINAL PIGMENT EPITHELIUM

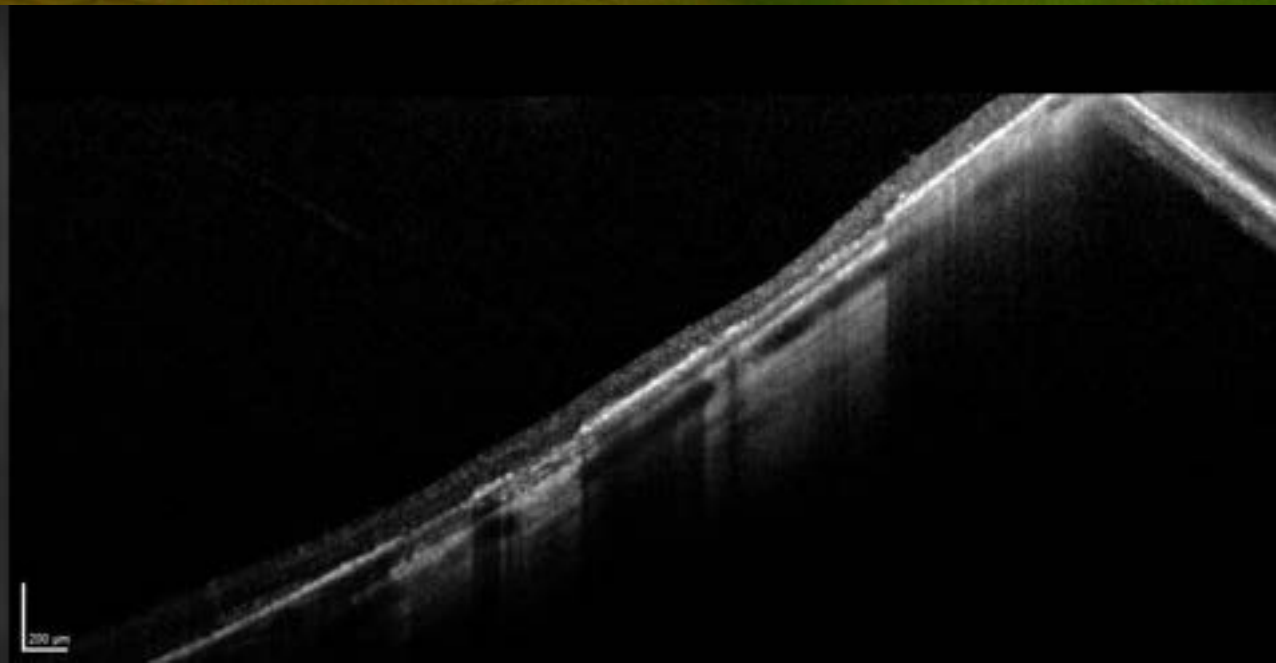
- Flat, variably pigmented lesion at the level of the RPE
- ~1.2% of the population
- May have depigmented lacunae and/or a surrounding halo
- may occur in clusters or “bear tracks”
- Malignant transformation has been reported, but exceptionally rare
- Appear similar to RPE lesions of Gardner syndrome



CONGENITAL HYPERTROPHY OF THE RETINAL PIGMENT EPITHELIUM



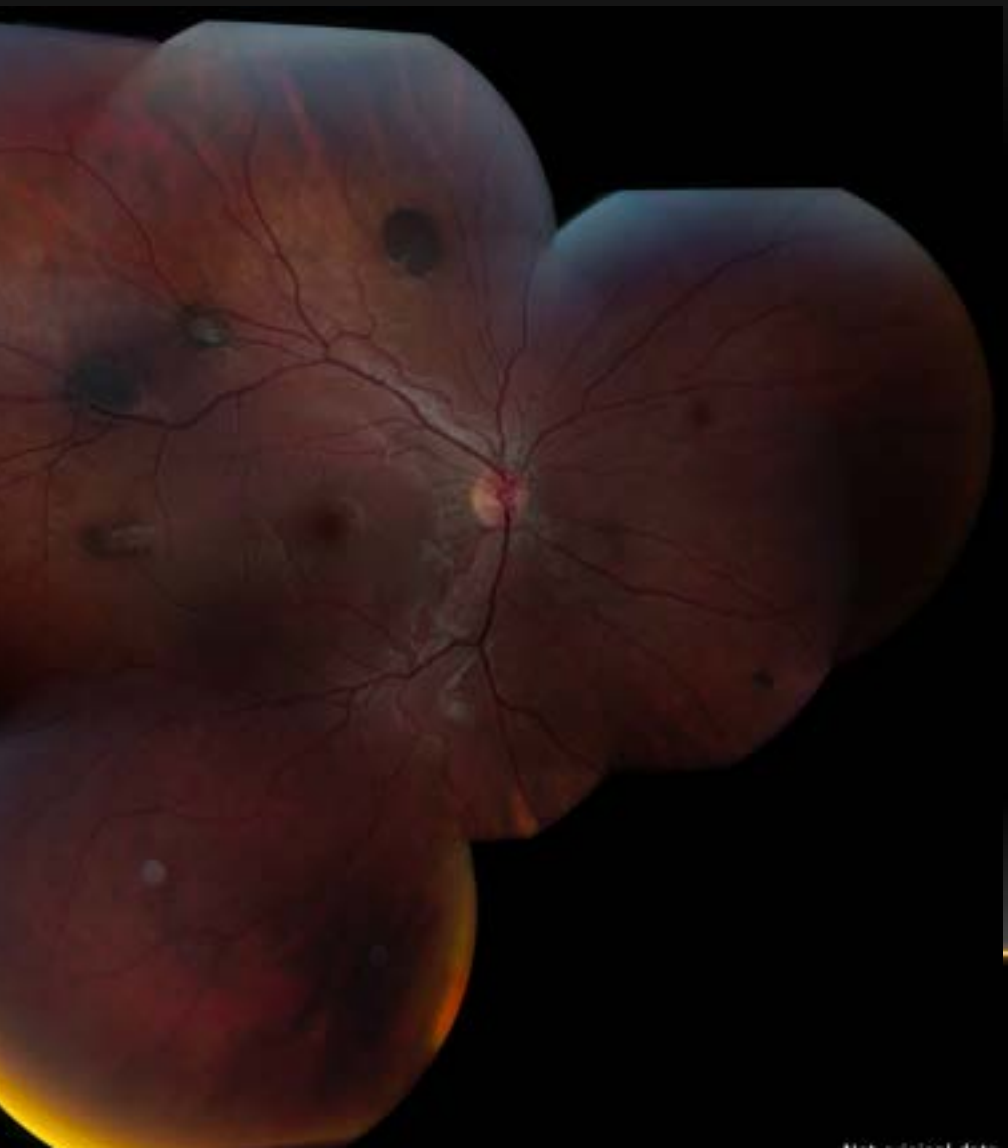




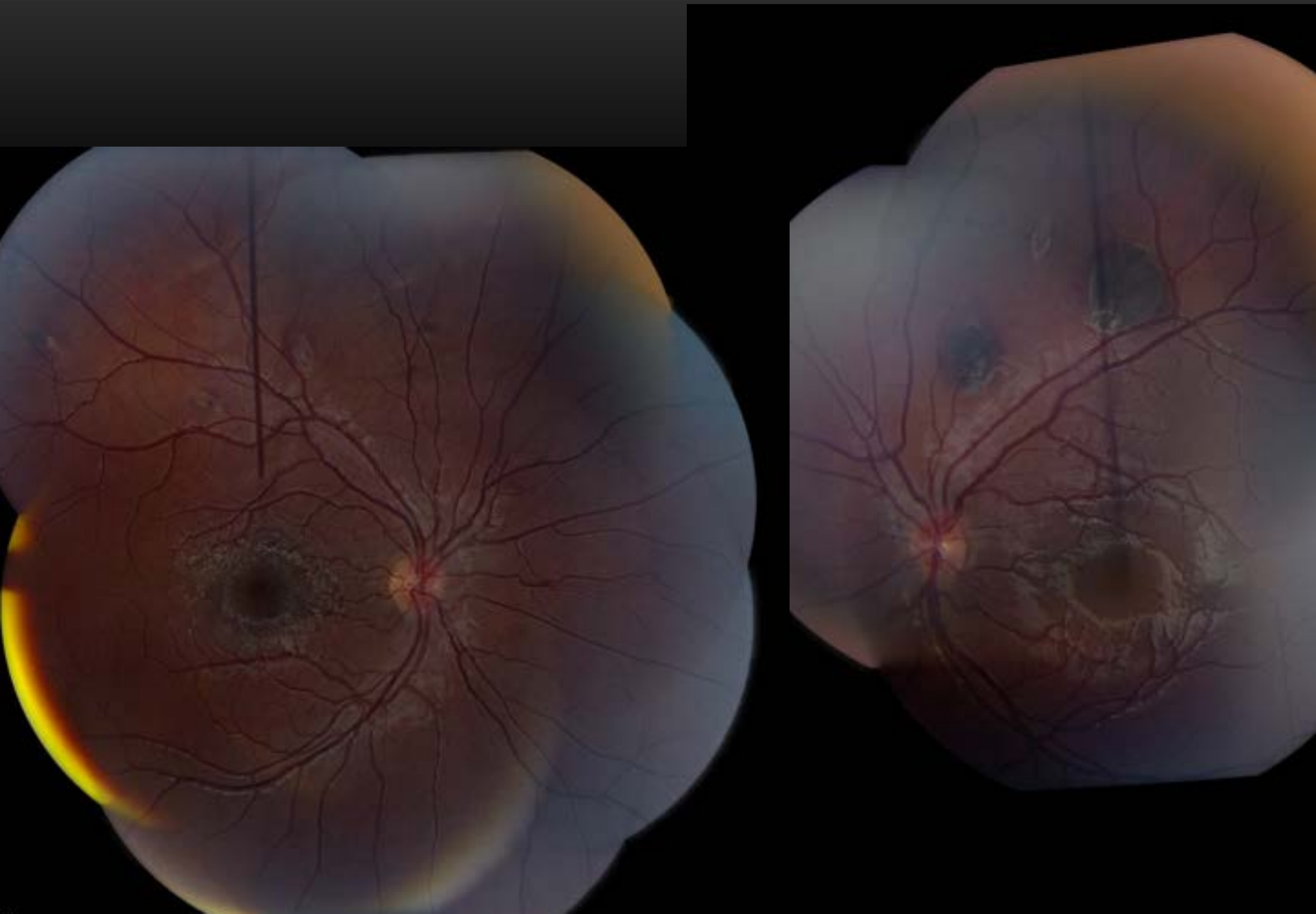
GARDNER SYNDROME

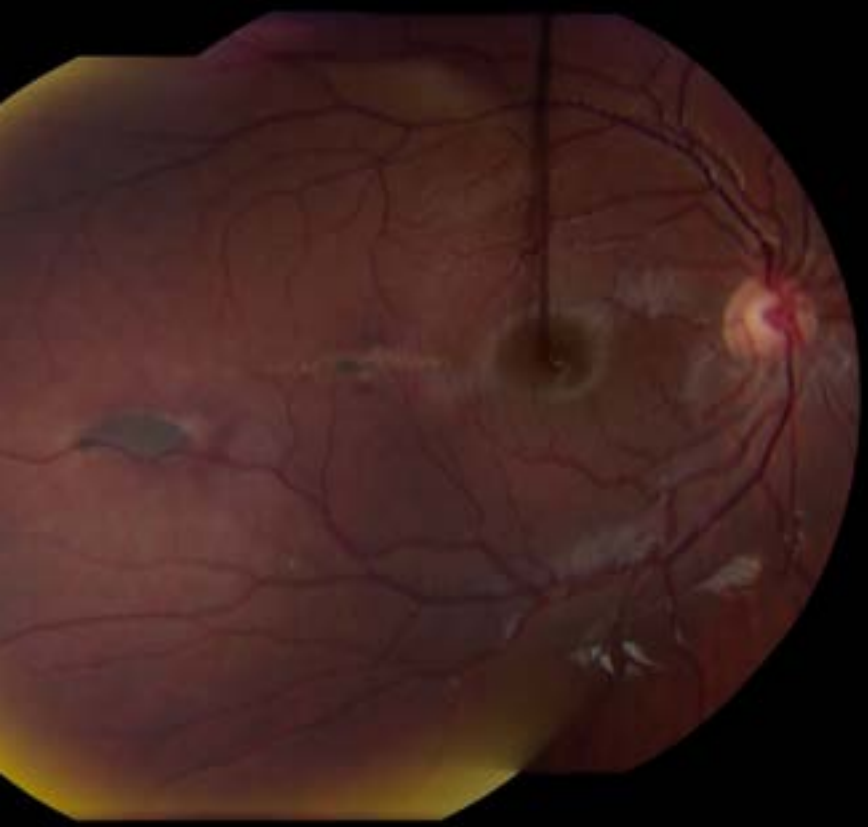
- Variant of Familial Adenomatous polyposis (FAP)
- Autosomal dominant
- Mutation in adenomatous polyposis coli (APC) gene – tumor suppressor gene
- Characterized by multiple polyps in the colon AND outside of the colon
- Extracolonic lesions include skull (and jaw) osteoma, fibromas, thyroid tumors
- High predisposition to develop colon cancer
- Treatment is typically surgical resection of malignancies

RPE LESIONS OF GARDNER SYNDROME



- Round to ovoid, pisciform
- Typically multiple and bilateral
- Usually <1mm
- Usually in midperiphery
- More spread out than typical bear tracks





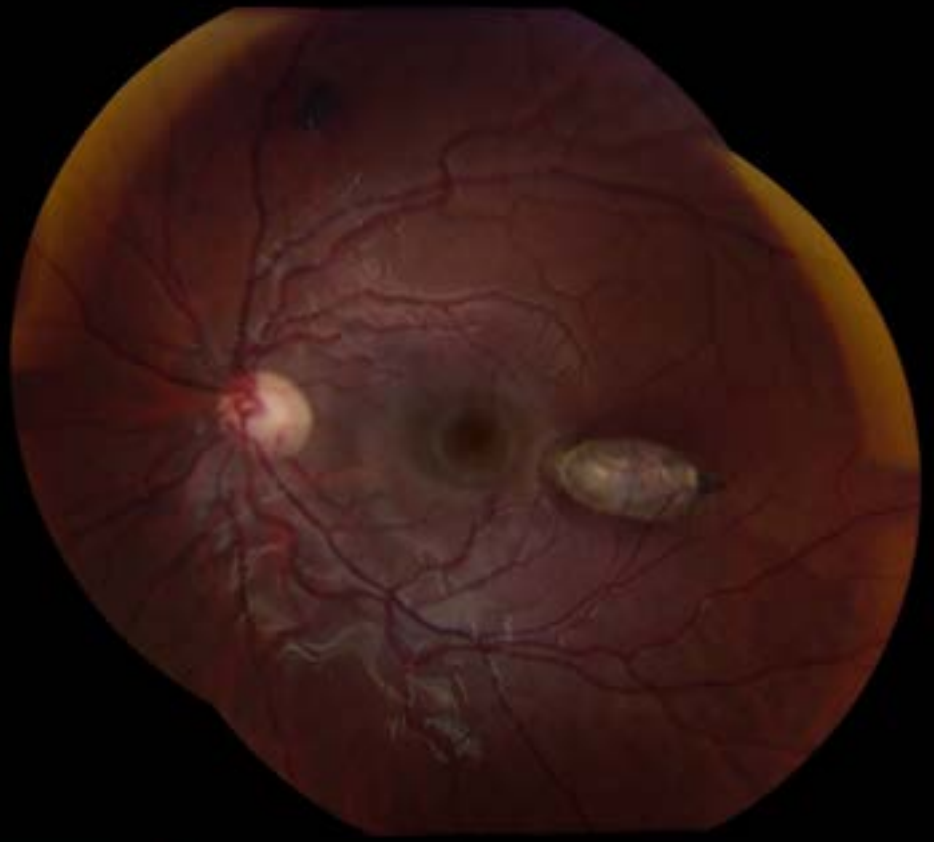
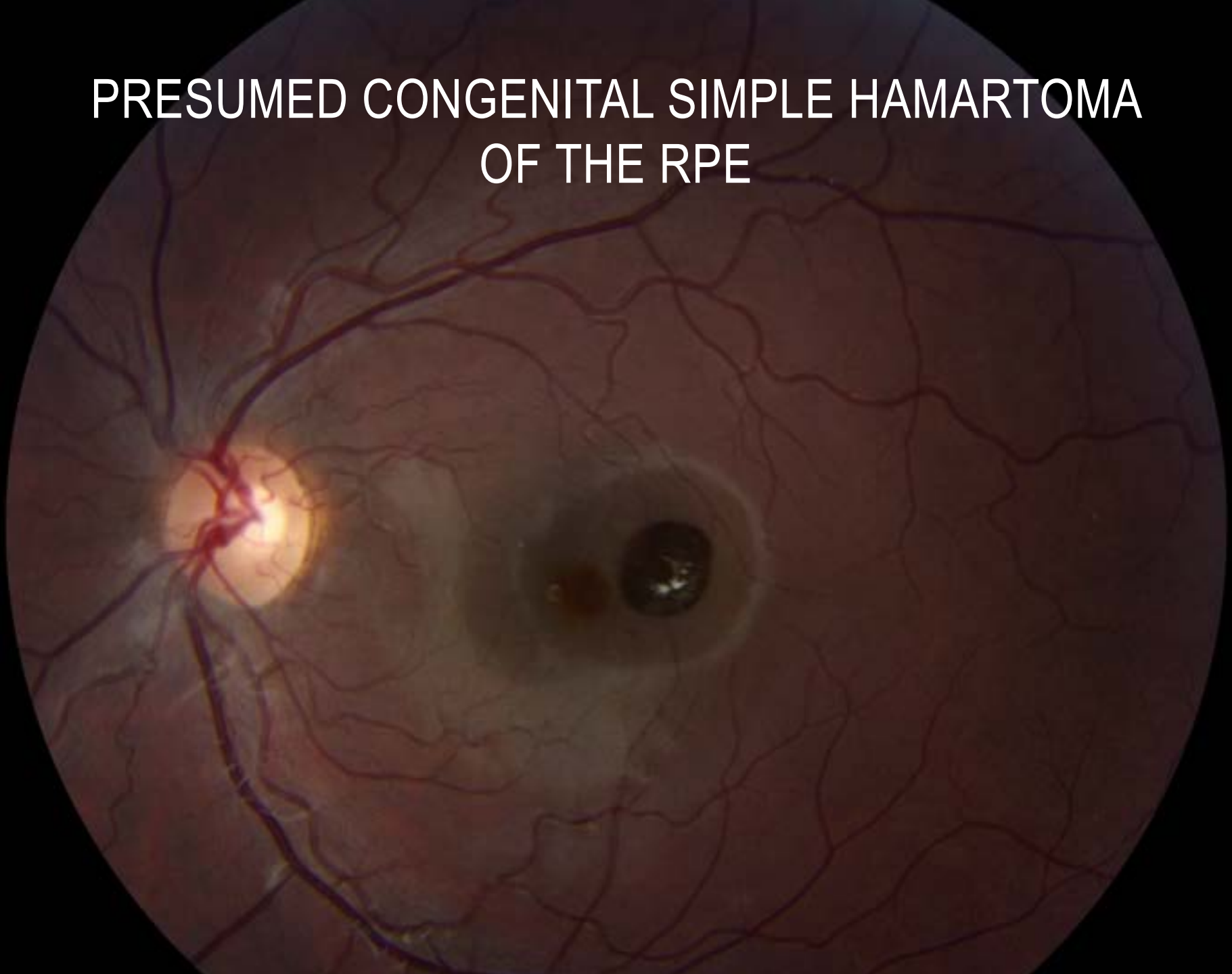
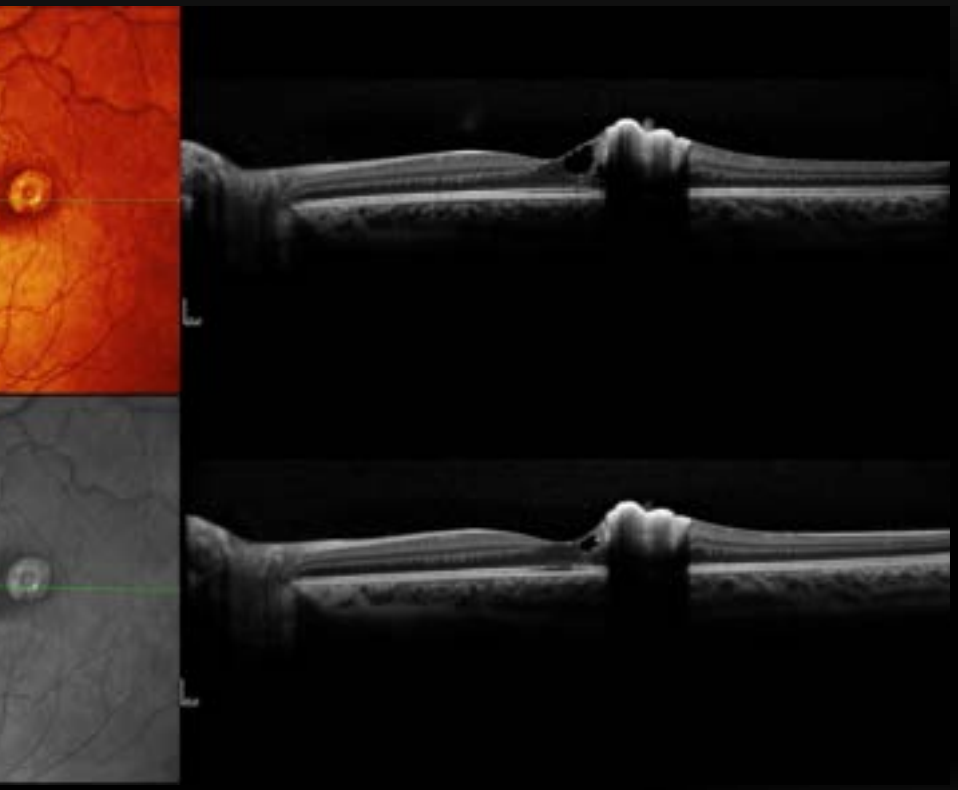


Image Source: Mike Dunn, NOAA Photo Library

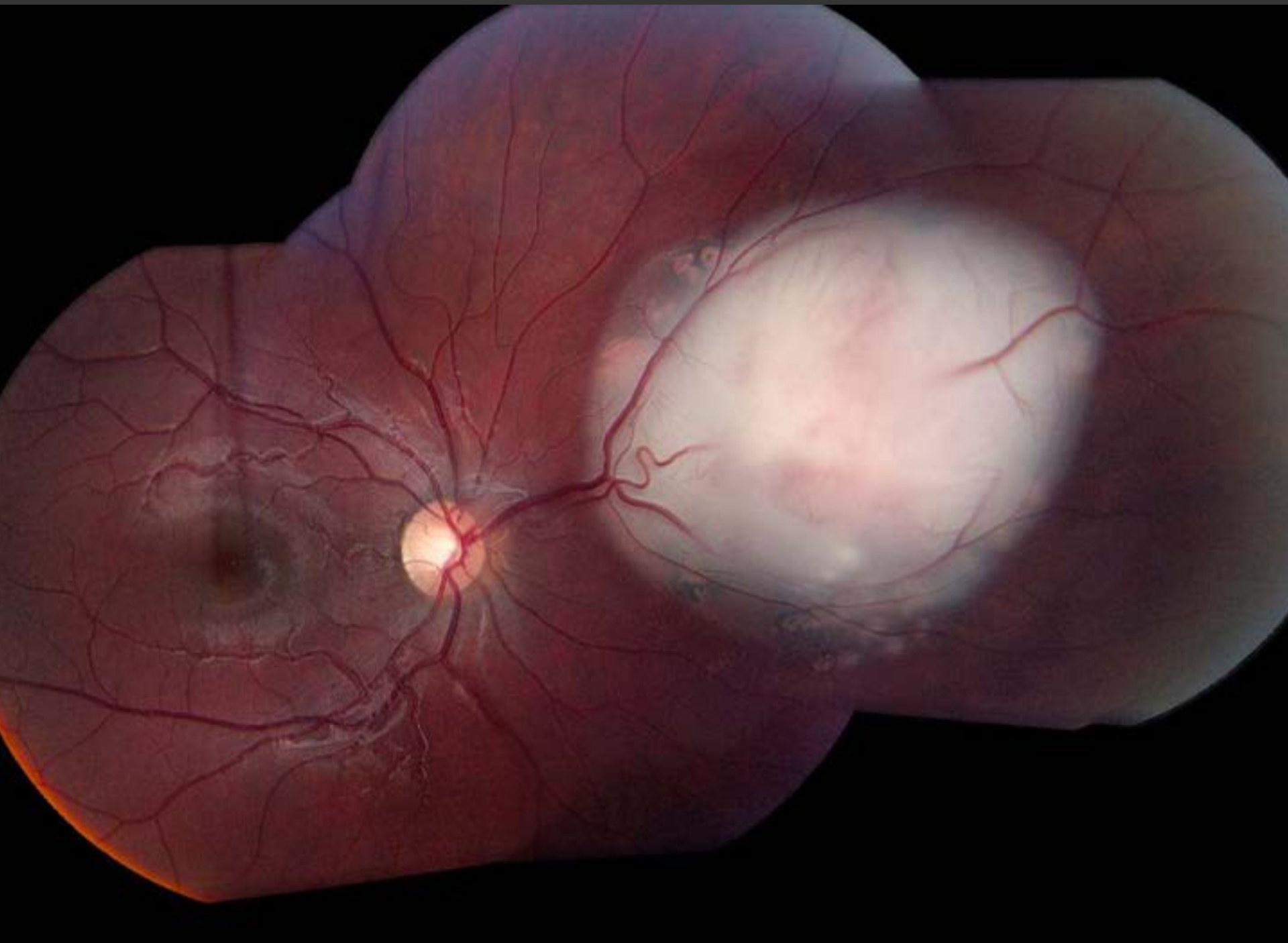
PRESUMED CONGENITAL SIMPLE HAMARTOMA OF THE RPE



SIMPLE HAMARTOMA OF THE RPE



- Focal, nodular, jet black lesions
- Frequently occur at or near the macula
- Usually have no known association with changes in the surrounding neurosensory retina
- Highly reflective and well demarcated on OCT with dense shadowing



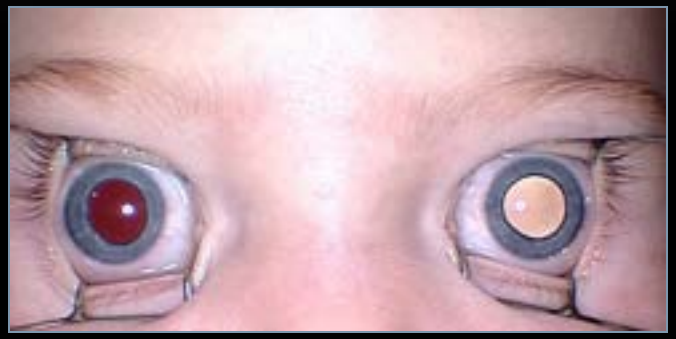
RETINOBLASTOMA

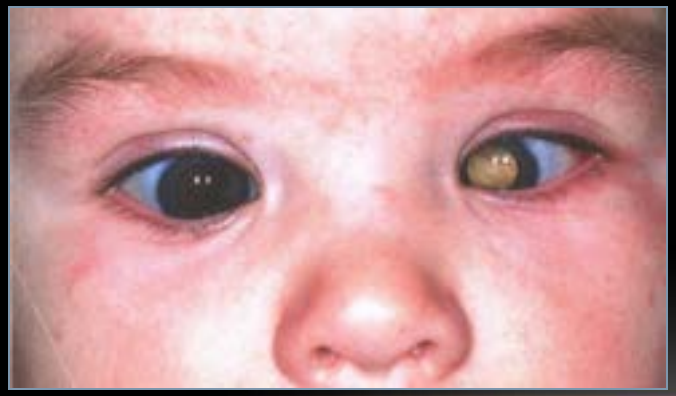
- The most common primary intraocular malignant tumor in children
- Affects 1 in 15,000 live births
- Current treatments include chemotherapy, laser, radiotherapy, and enucleation
- Advanced tumors respond poorly to traditional chemotherapy and laser treatments
  - (25-75% failure rates)

PRESENTING SIGNS & SYMPTOMS

- Leukocoria – 50-60%
- Strabismus – 20%
- Red, painful eye – 7%
- Well baby examination – 3%
- Other – 10%

Leukocoria





REESE-ELLSWORTH STAGING (TRADITIONAL)

- **Group 1: Eye preservation - very favorable**
  - 1A: one tumor, smaller than 4 DD, at or posterior to equator
  - 1B: multiple tumors smaller than 4 DD, all at or posterior to equator
- **Group 2: Eye preservation - favorable**
  - 2A: one tumor, 4 to 10 DD, at or behind the equator
  - 2B: multiple tumors, with at least one 4 to 10 DD, and all at or posterior to equator
- **Group 3: Eye preservation - doubtful**
  - 3A: any tumor anterior to equator
  - 3B: one tumor, larger than 10 DD, posterior to equator
- **Group 4: Eye preservation - unfavorable**
  - 4A: multiple tumors, some larger than 10 DD
  - 4B: any tumor extending toward the front of the eye to the ora serrata
- **Group 5: Eye preservation - very unfavorable**
  - 5A: tumors involving more than half of the retina
  - 5B: vitreous seeding

(2015, March 12). Retrieved from https://www.cancer.org/cancer/retinoblastoma/detection-diagnosis-staging/staging.html

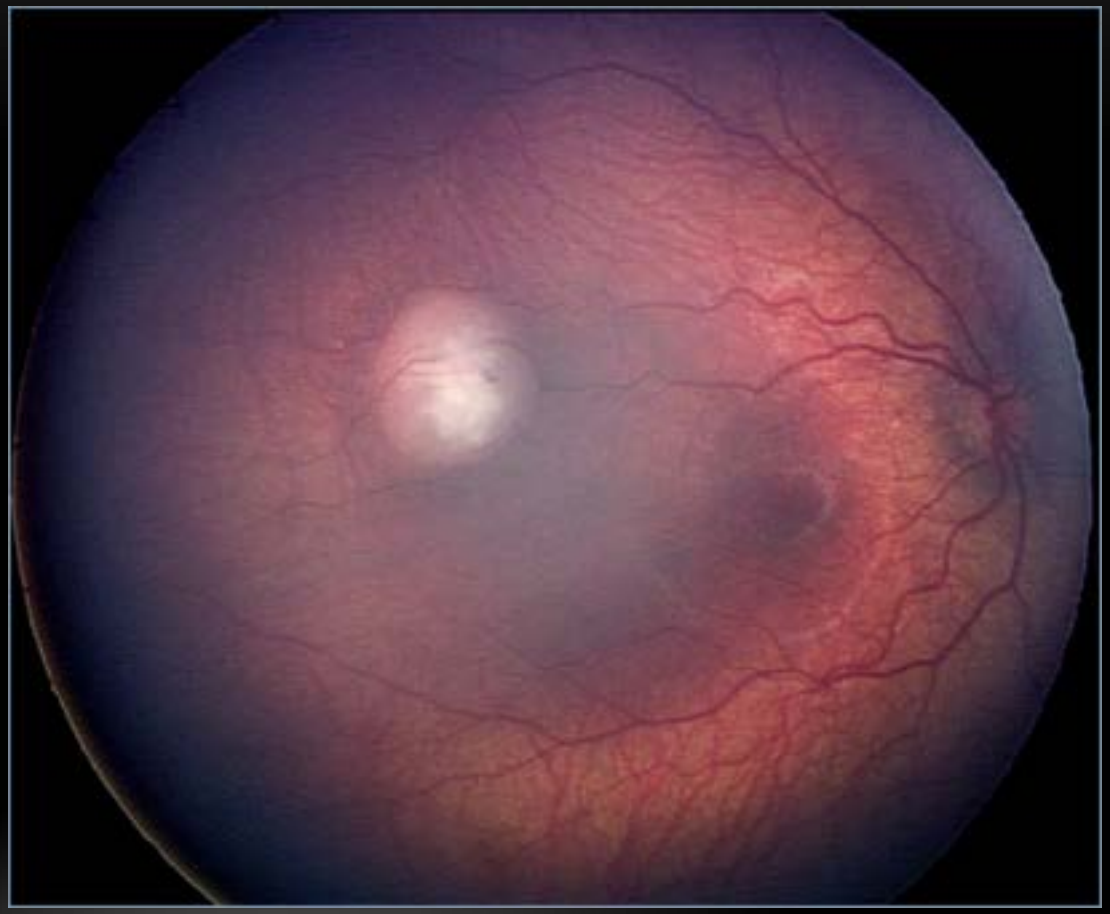
NEWER STAGING

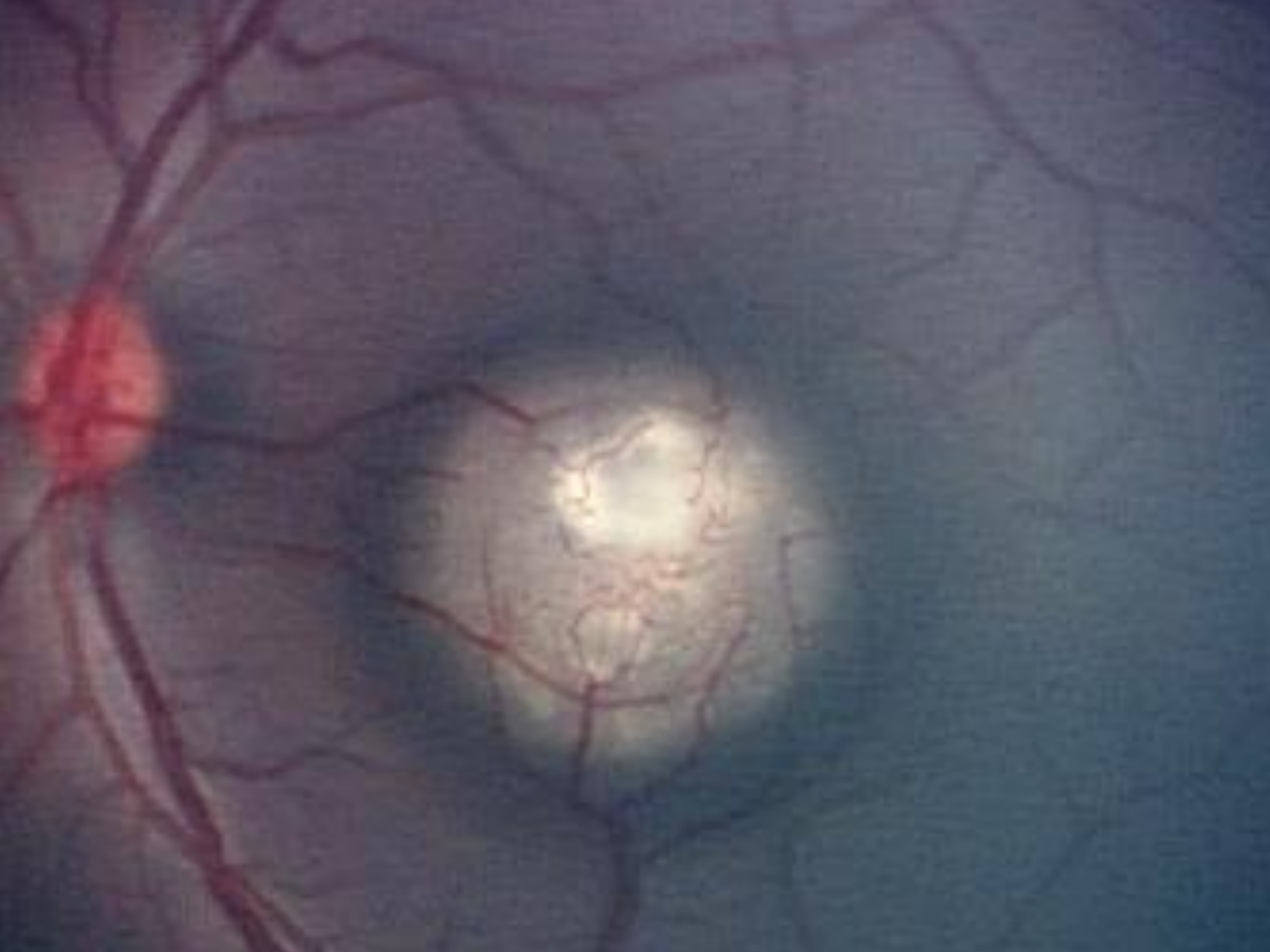
- The International Classification for Intraocular Retinoblastoma
  - Group A
    - Small tumors (3 millimeters [mm] across or less) that are only in the retina and are not near optic disc or foveola.
  - Group B
    - All other tumors (either larger than 3 mm or small but close to the optic disc or foveola) that are still only in the retina.
  - Group C
    - Well-defined tumors with minimal subretinal seeding or vitreous seeding.
  - Group D
    - Large or poorly defined tumors with widespread vitreous or subretinal seeding and/or retinal detachment.
  - Group E
    - The tumor is very large, extends near the front of the eye, is bleeding or causing glaucoma.

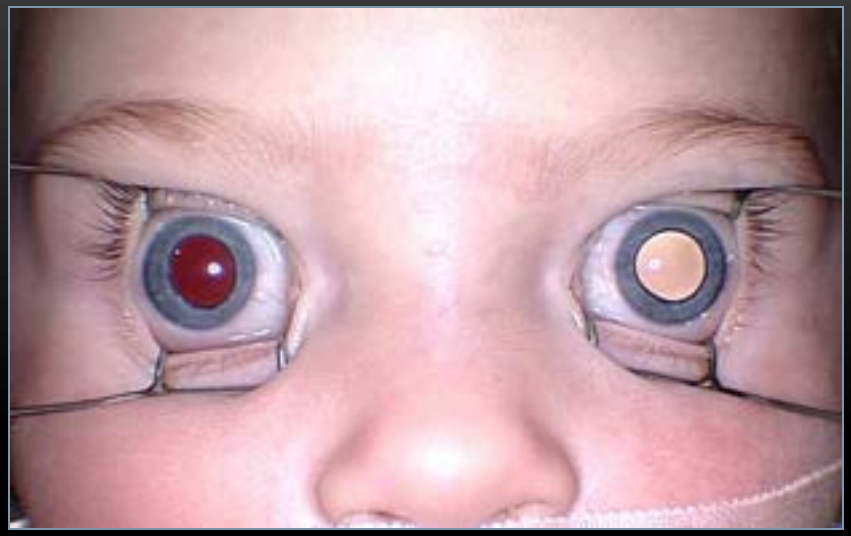
(2015, March 12). Retrieved from https://www.cancer.org/cancer/retinoblastoma/detection-diagnosis-staging/staging.html

EARLY INTRARETINAL RETINOBLASTOMA

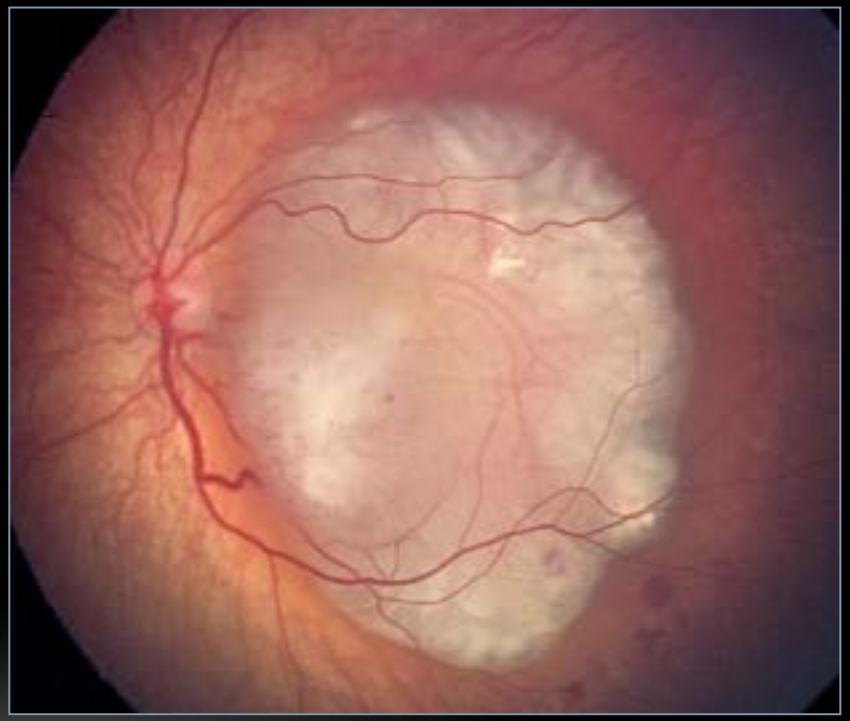
- Translucent white-gray mass within the retina
- Early dilated feeding vessels
- Micro-calcification

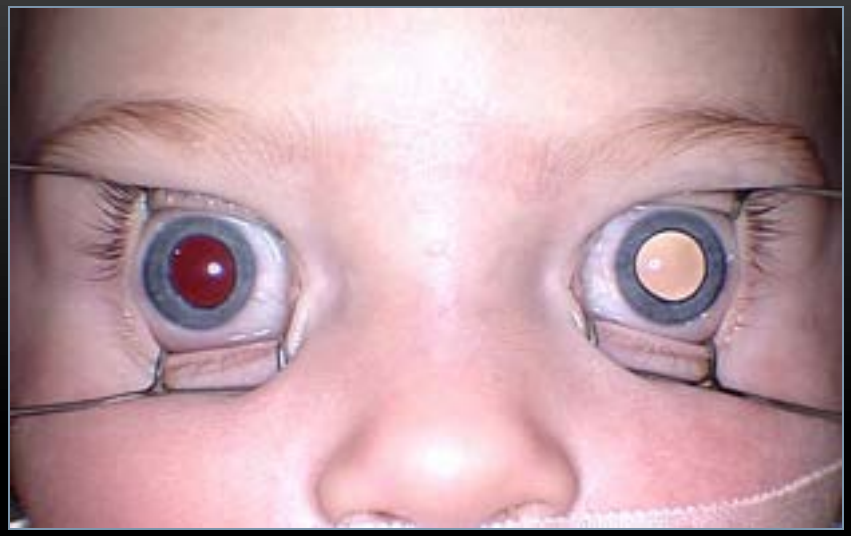




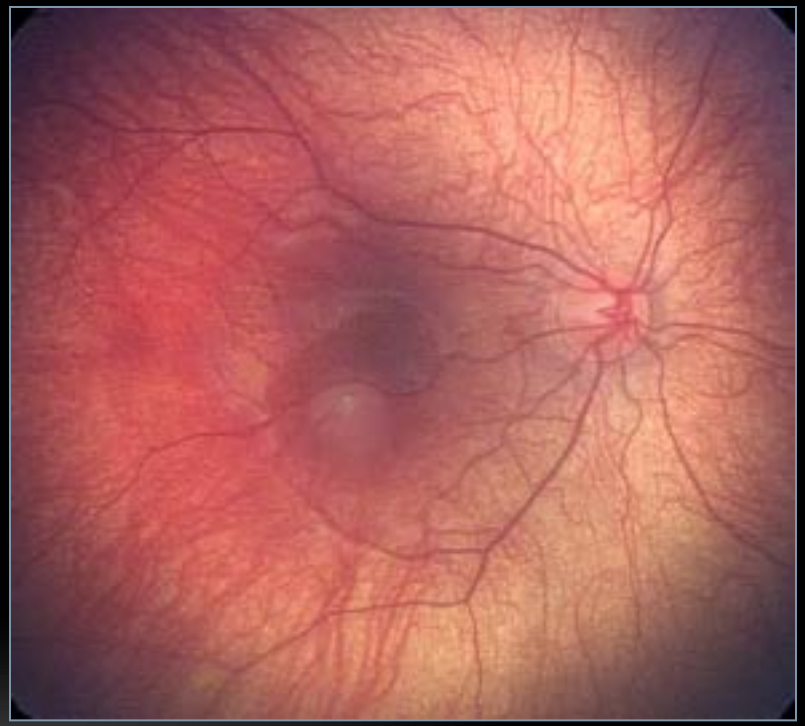


Leukocoria with Large Macular RB OS

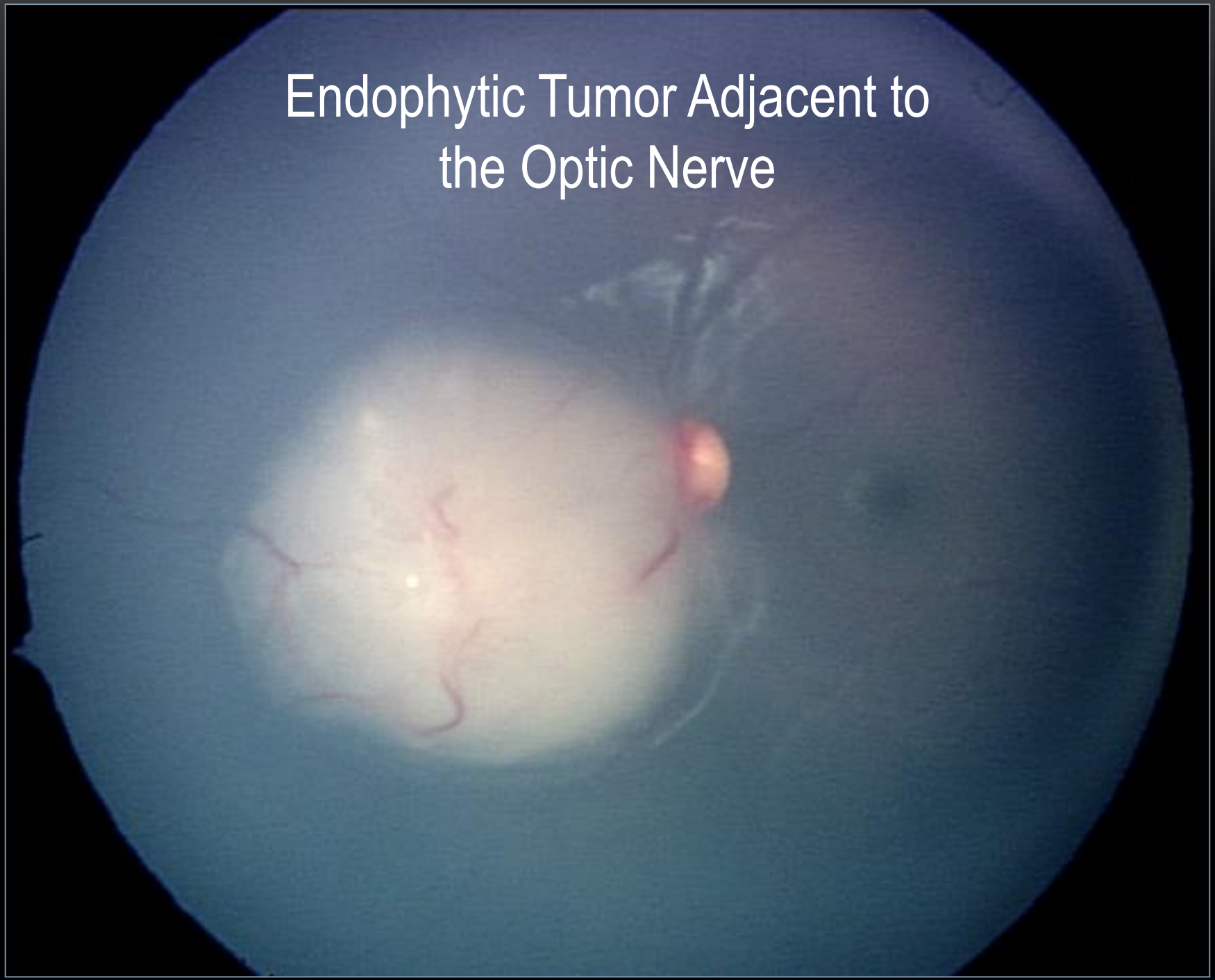




Early Macular RB OD

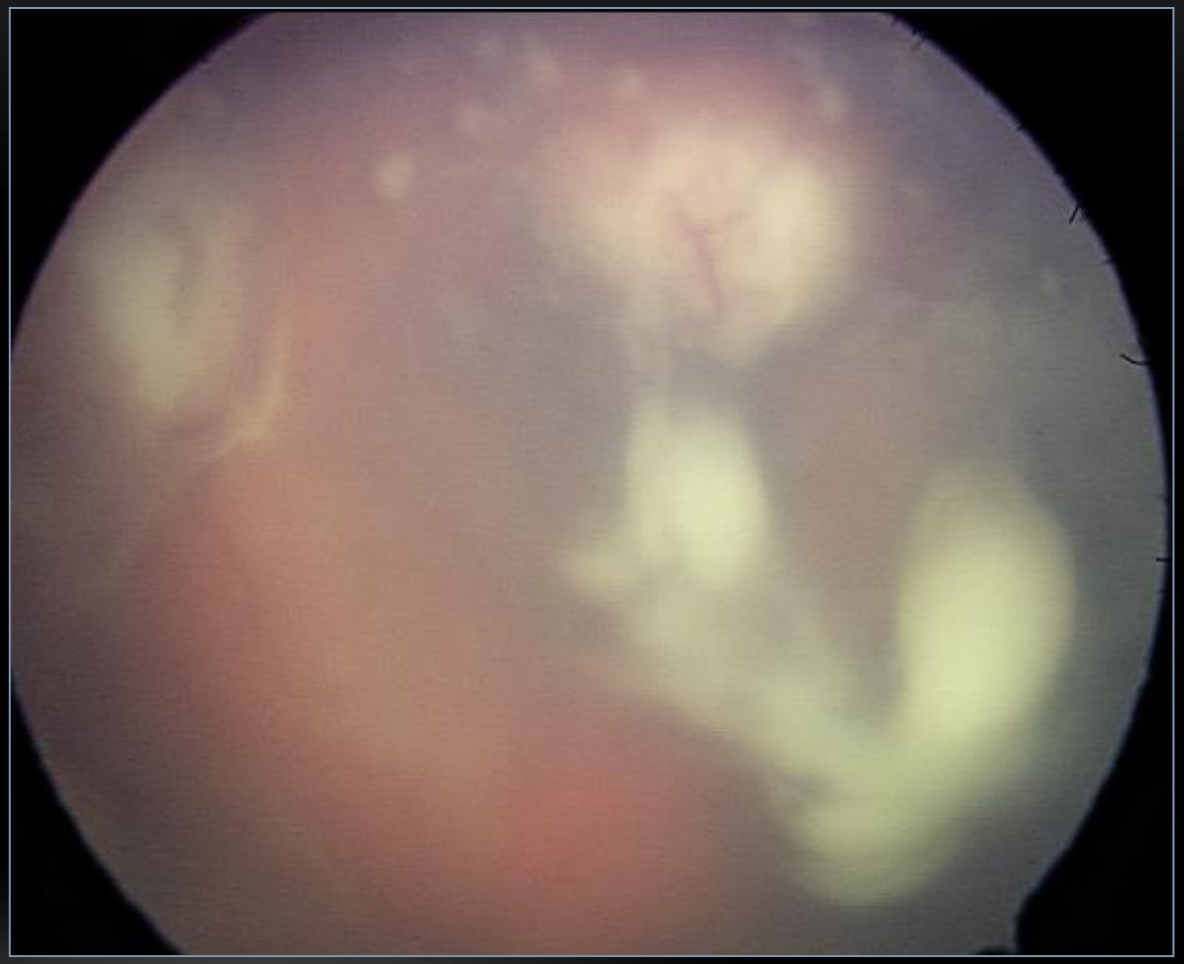


Endophytic Tumor Adjacent to the Optic Nerve

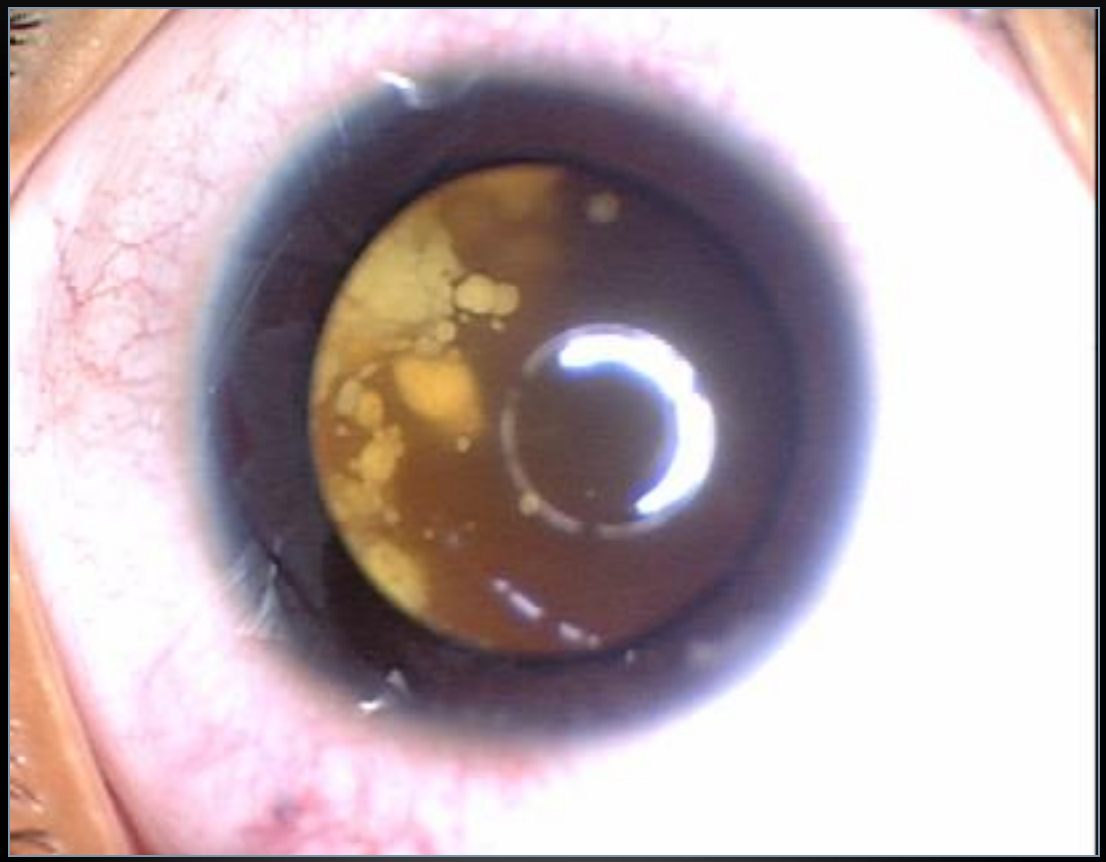


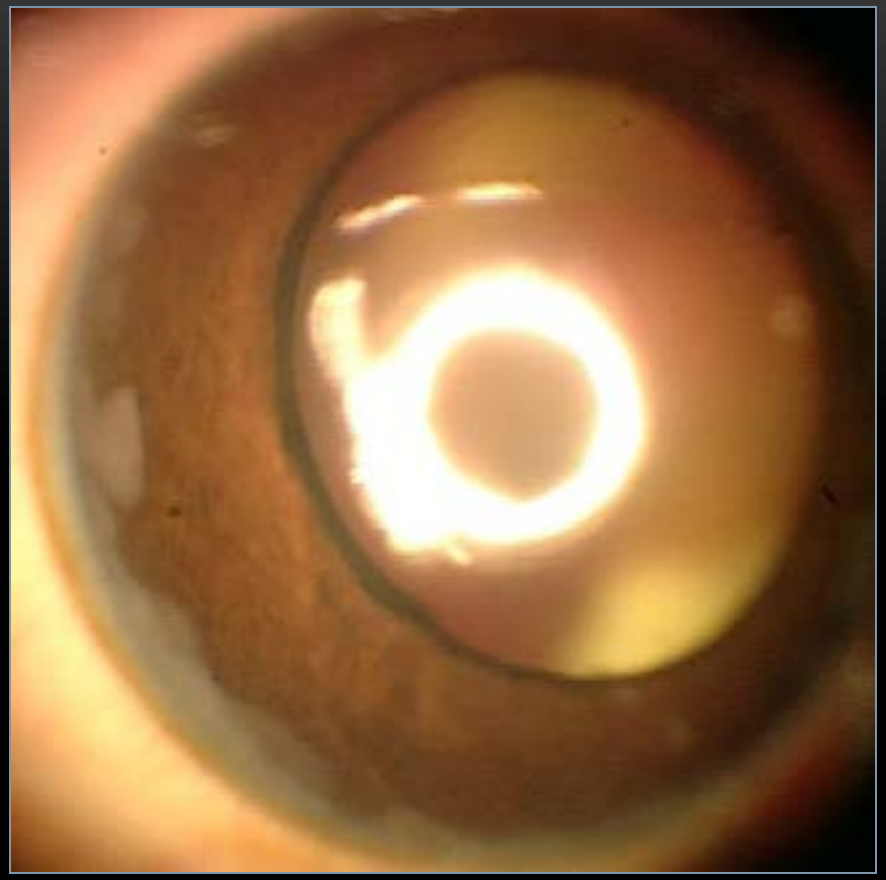
ADVANCED RETINOBLASTOMA

- Large tumor mass
- Advanced seeding can create iris nodules or pseudohypopyon appearance
- Rubeosis irides with spontaneous hyphema and neovascular glaucoma
- Tumor necrosis with intraocular and periocular inflammation

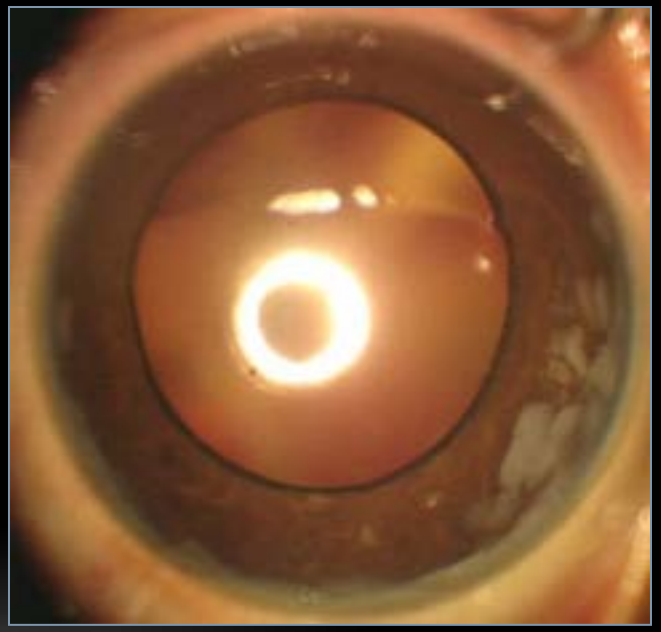


Extensive Vitreous Seeding

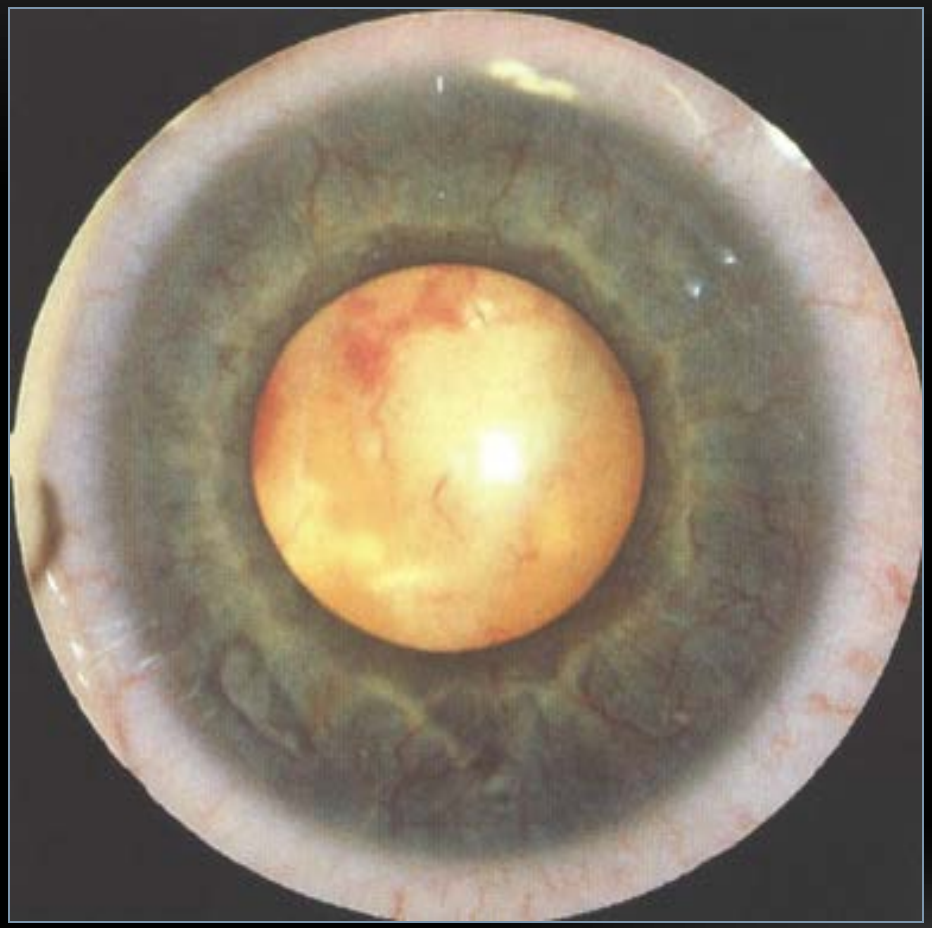




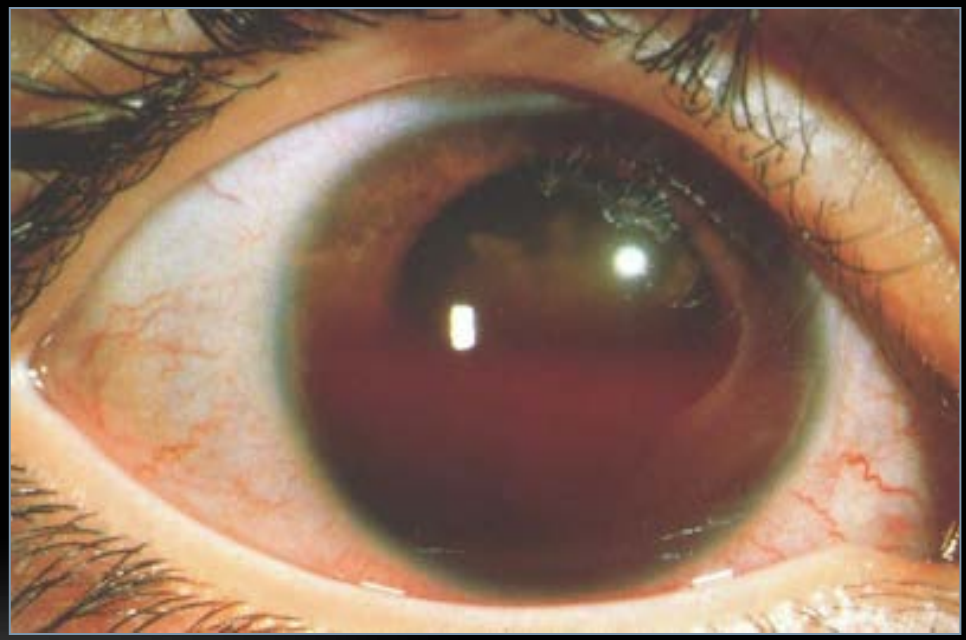
Anterior Segment Seeding



Iris Neovascularization from RB



Spontaneous Hyphema



ADVANCES IN RETINOBLASTOMA MANAGEMENT

- Clinical Focus
- Survival
- Functional globe retention
- Improved visual function outcomes
- Decreased treatment morbidity

SYSTEMIC CHEMOTHERAPY/LASER TUMOR ABLATION

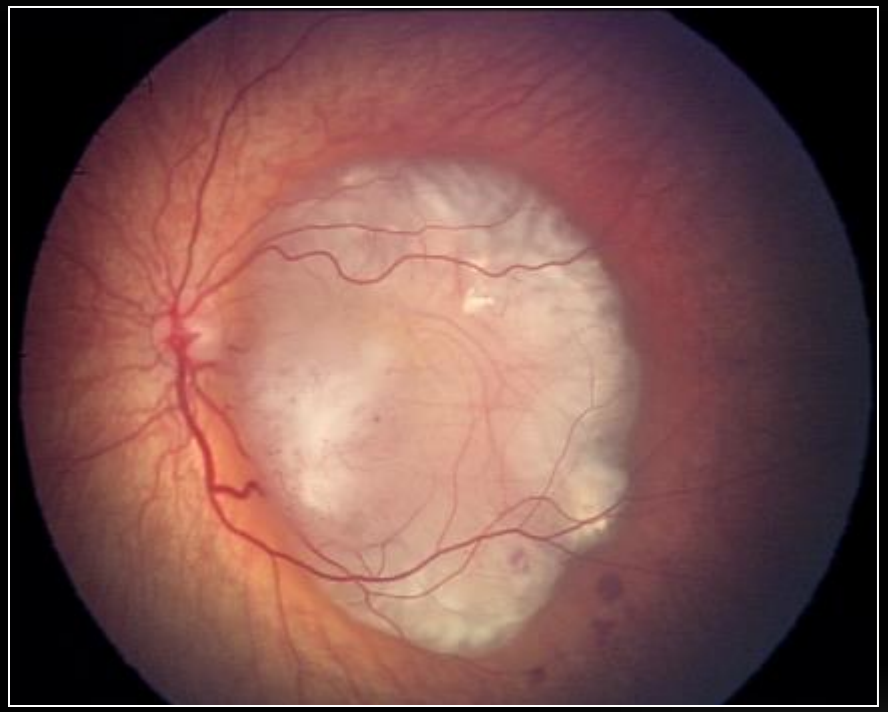
- Reduce tumor volume to allow more focal tumor treatment – never a stand-alone treatment
- Chemotherapy usually involves carboplatin, etoposide, and vincristine (with/without cyclosporine)
  - 6-9 cycles of chemotherapy given every 3/4 weeks
  - Dramatic reduction averaging >50% decrease in volume after 3 sessions

SYSTEMIC CHEMOTHERAPY PLUS DIODE LASER

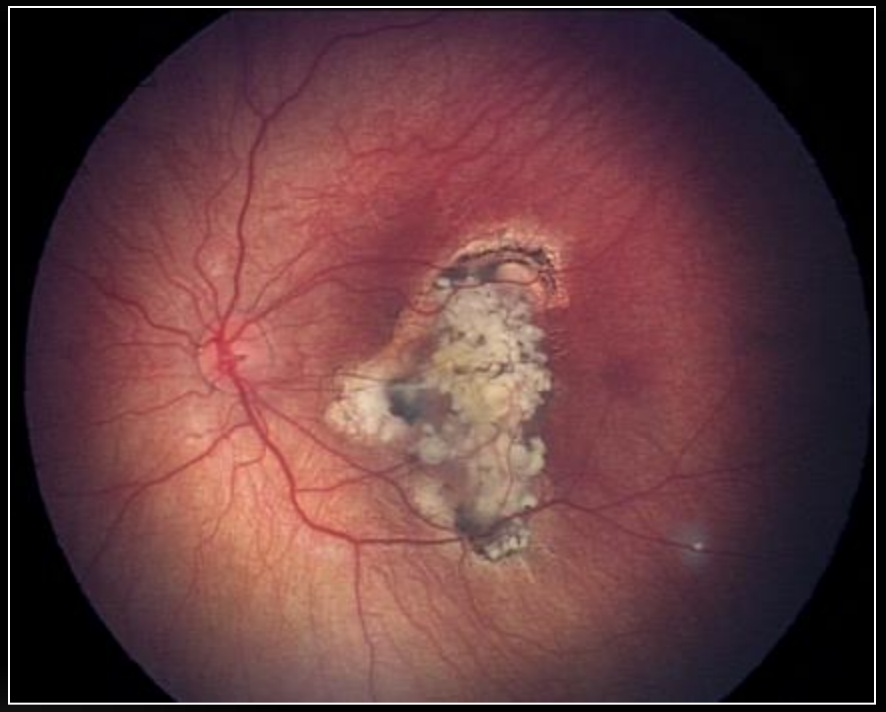
- Synergistic interaction
- Enhanced chemoreduction therapy
- Laser is applied prior to each systemic treatment, during EUA

Large Macular Retinoblastoma

Before treatment



4 mos after chemoreduction/laser



SYSTEMIC CHEMOTHERAPY COMPLICATIONS

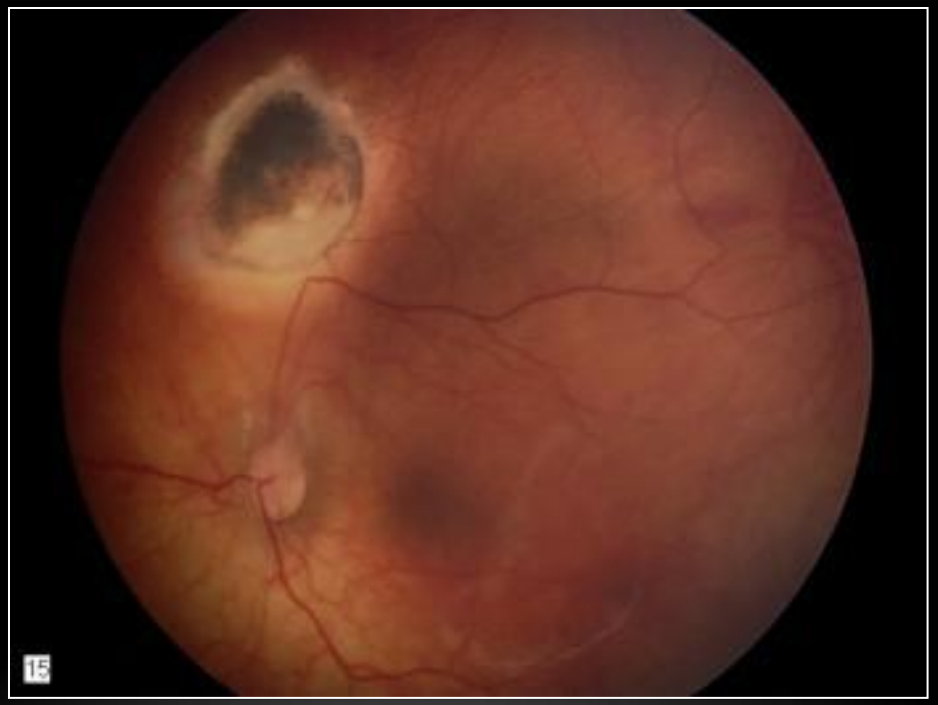
- Increasing reports of adverse systemic findings
- Ototoxicity
  - Carboplatin – Tx w/in first 6 months of life have 33% chance of hearing impairment within 5 years (Ocular Oncology Meeting 2009)
- Secondary acute myelocytic leukemia (AML) (incredibly rare)
- Neutropenia/thrombocytopenia/anemia

NON-SYSTEMIC CHEMOTHERAPY IN RB

- Novel ways to delivery chemotherapy locally to the eye while minimizing systemic exposure
- Implanted in depot gels, solid polymers, miniature catheters

PERIOCULAR CARBOPLATIN

- 1/10 of systemic dose, but delivers 10x the concentration to the eye

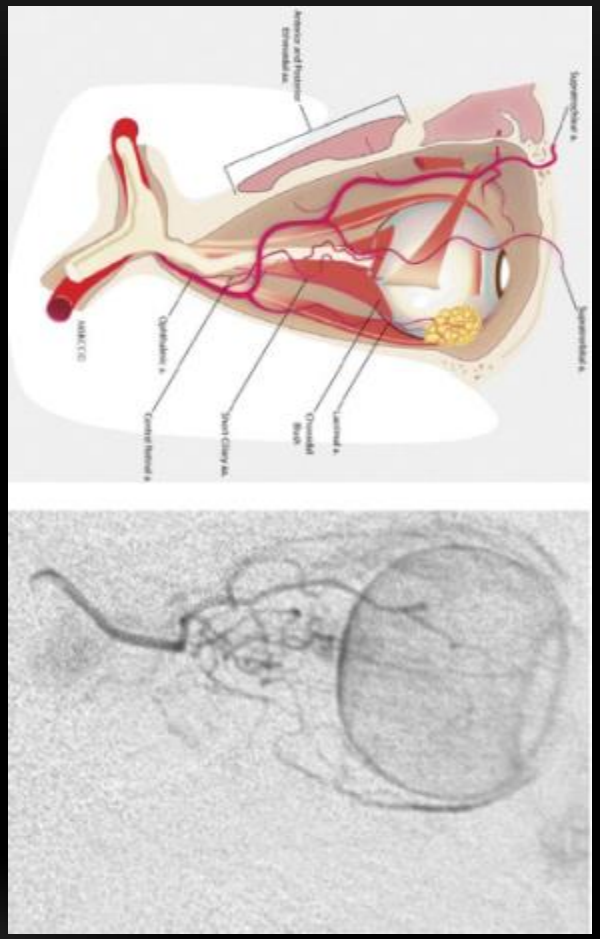


INTRA-ARTERIAL INFUSION OF CHEMOTHERAPY

- Initiated in Japan and now being used in USA (Miami, New York, Philadelphia)
- Initially used mostly on eyes with poor prognosis (‘salvage’ therapy)
- Now used as primary treatment
- Drugs used: melphalan, topotecan, carboplatin

SUPRASELECTIVE OPHTHALMIC ARTERY CHEMOTHERAPY IN RB

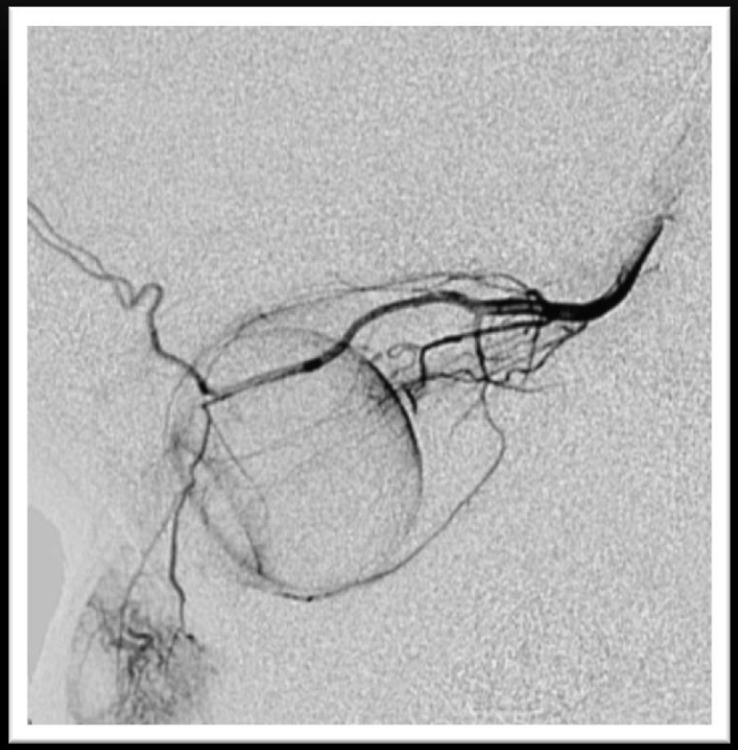
- Children are placed under general anesthesia and anticoagulated for cannulation of the ophthalmic artery with microcatheters via femoral artery approach
  - Initially reported by Kaneko group, then modified by Abramson group
- Angiography (ophthalmic, internal and external carotid arteries) is performed, followed by intra-arterial ophthalmic Melphalan infusion to the affected eye



Abramson DH et al. Superselective Ophthalmic After Chemotherapy. Ophthalmology. April 2010.

INTRA-ARTERIAL OPHTHALMIC CHEMOTHERAPY PROCEDURE

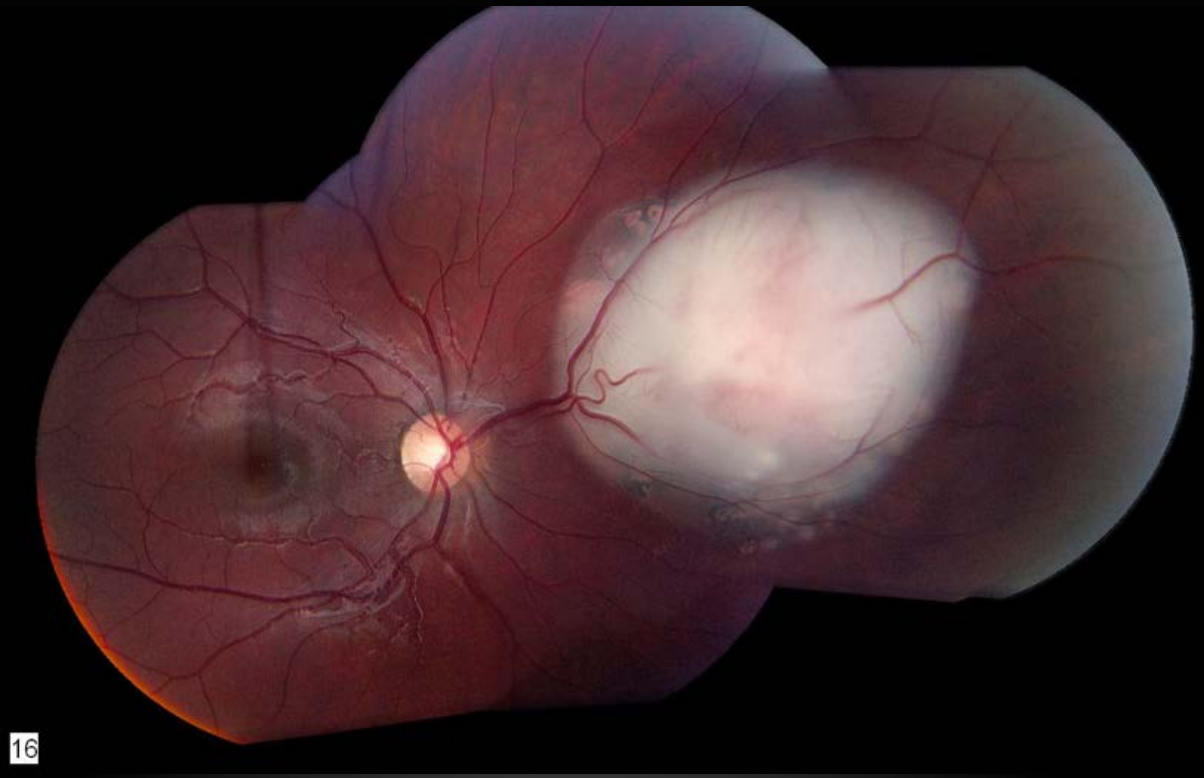
- Infusion is performed in a pulse-injection fashion over a 30-minute period
- Ophthalmic examinations, tumor laser ablation, retinal photography, and ultrasonographic imaging are performed at 3 weeks, 6 weeks then every 3 months
- Treatment strategy evolving



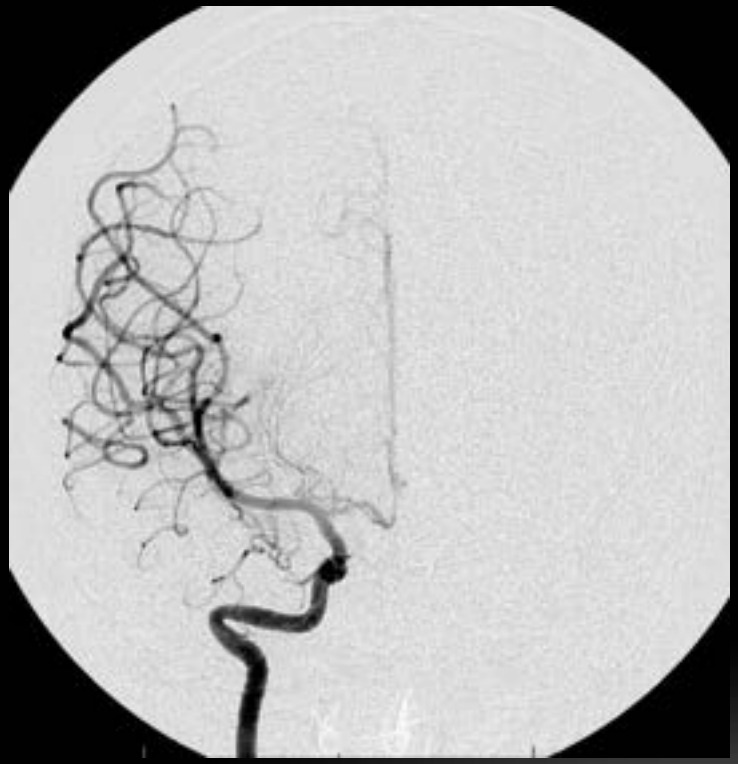
CASE PRESENTATION

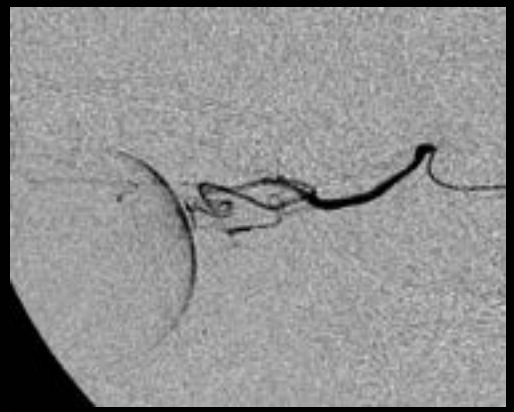
- A 7 year old Greek girl presents with unilateral, advanced retinoblastoma
- Family history: Negative

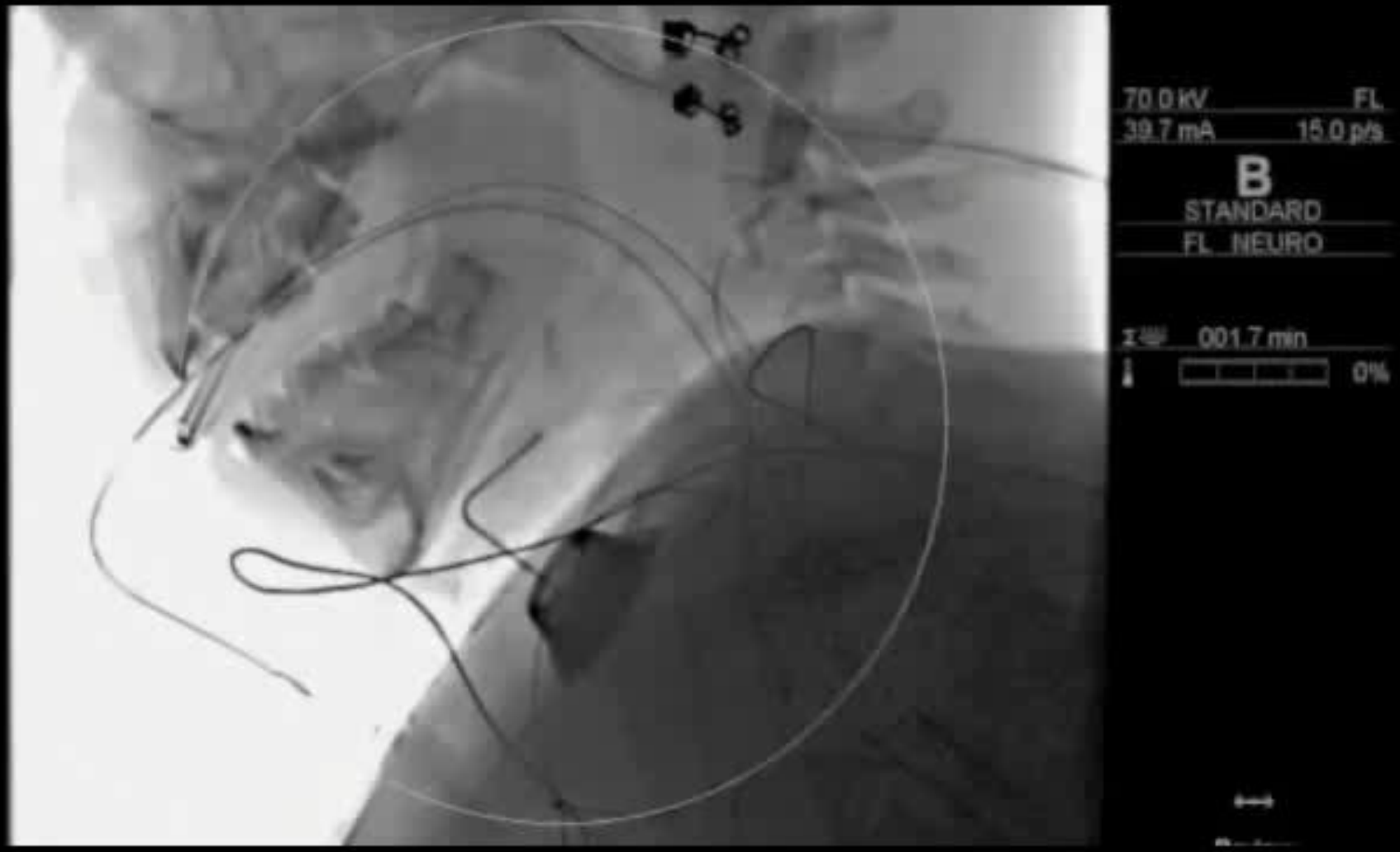
RETINOBLASTOMA
INITIAL PRESENTATION



AP AND LATERAL INJECTION OF THE RIGHT OPHTHALMIC ARTERY






70.0 kV
FL
39.7 mA
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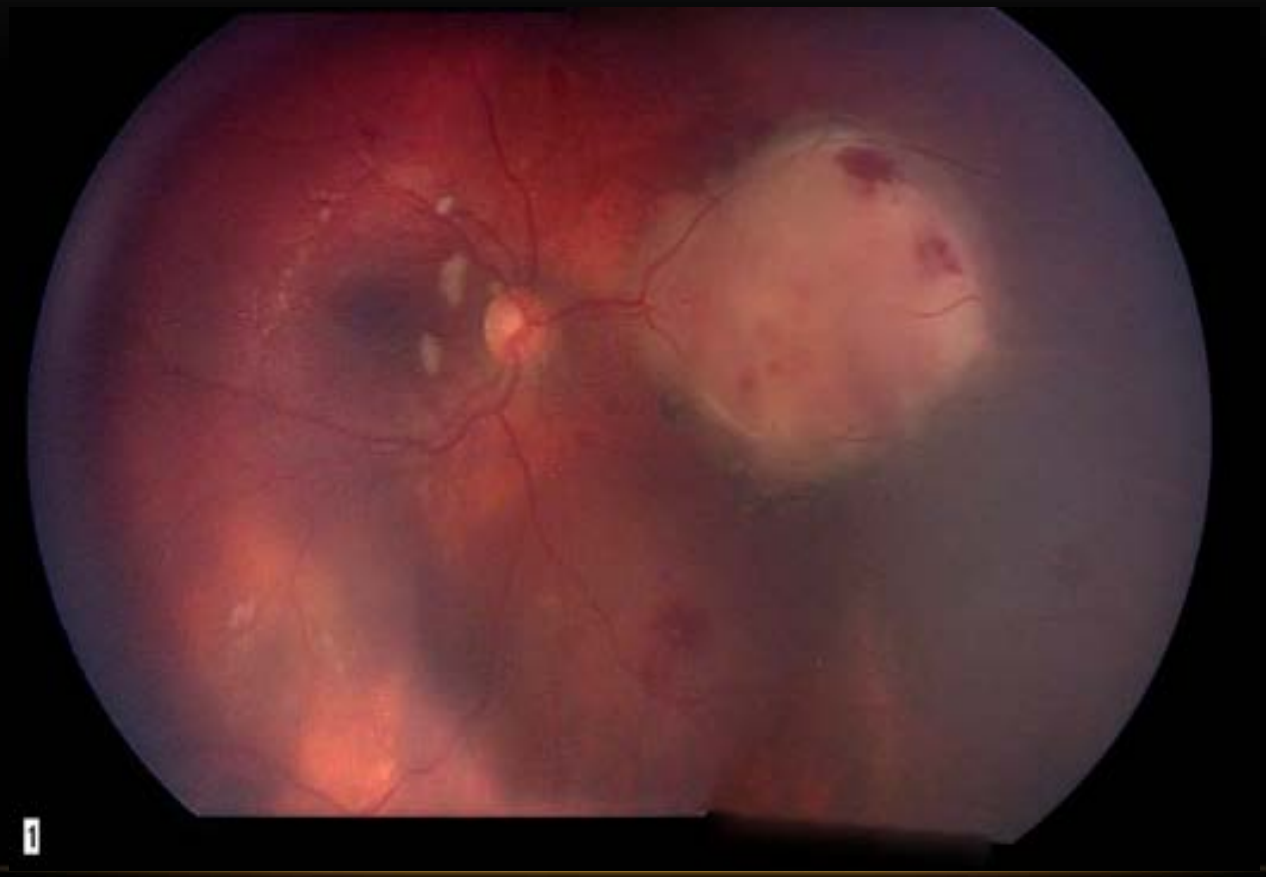
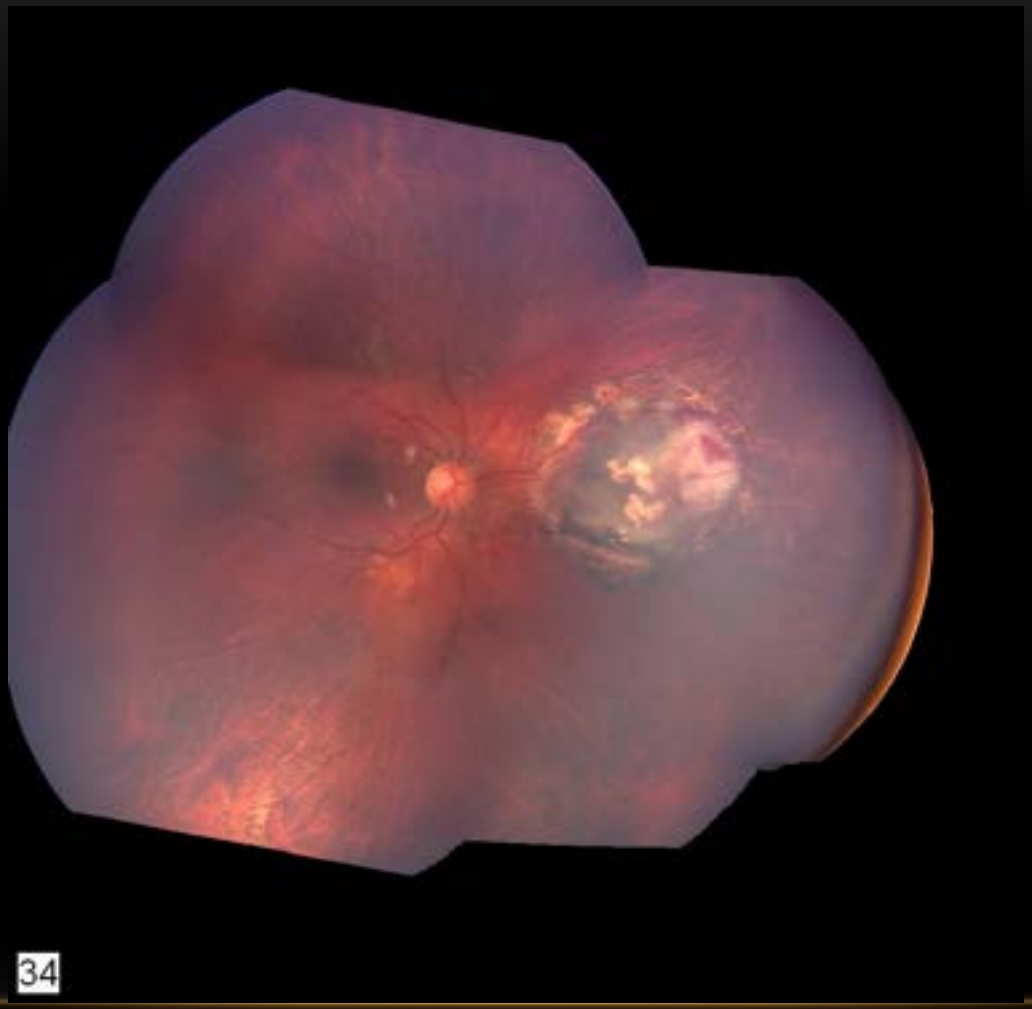
0%

POST IA MELPHALAN: PURTCHER'S LIKE RETINOPATHY



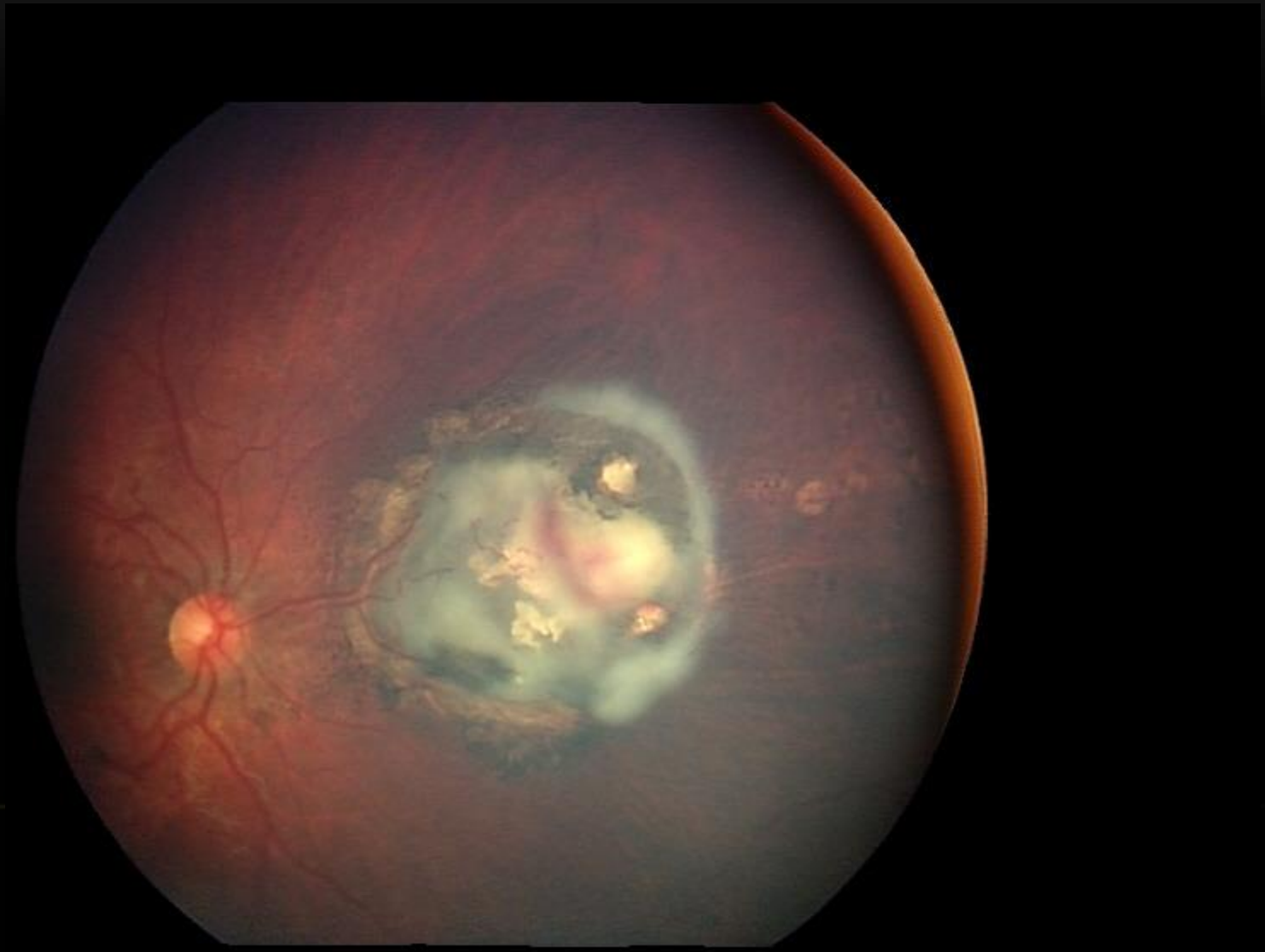
1 MONTH LATER

RESIDUAL TUMOR ACTIVITY

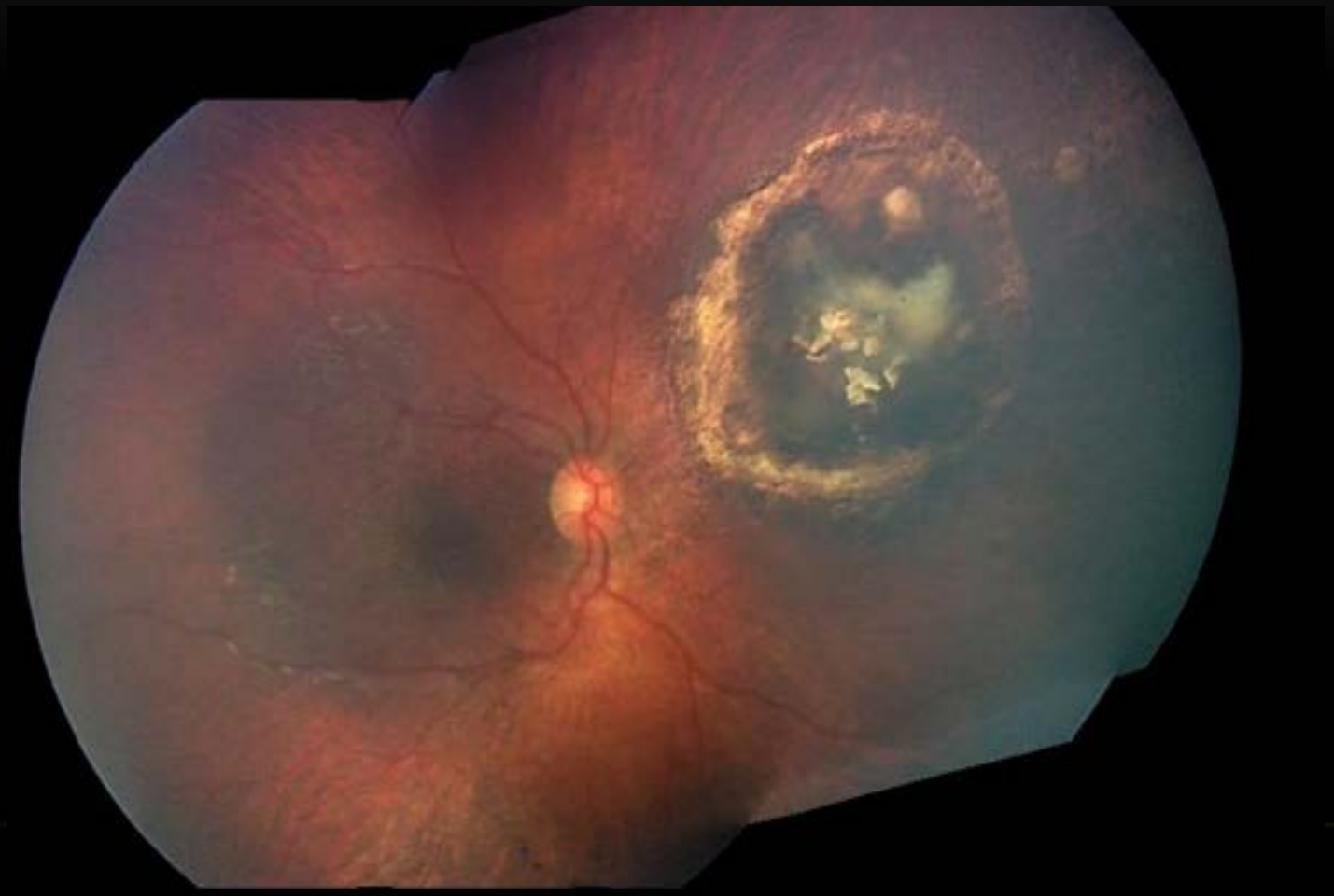


2 MONTHS LATER

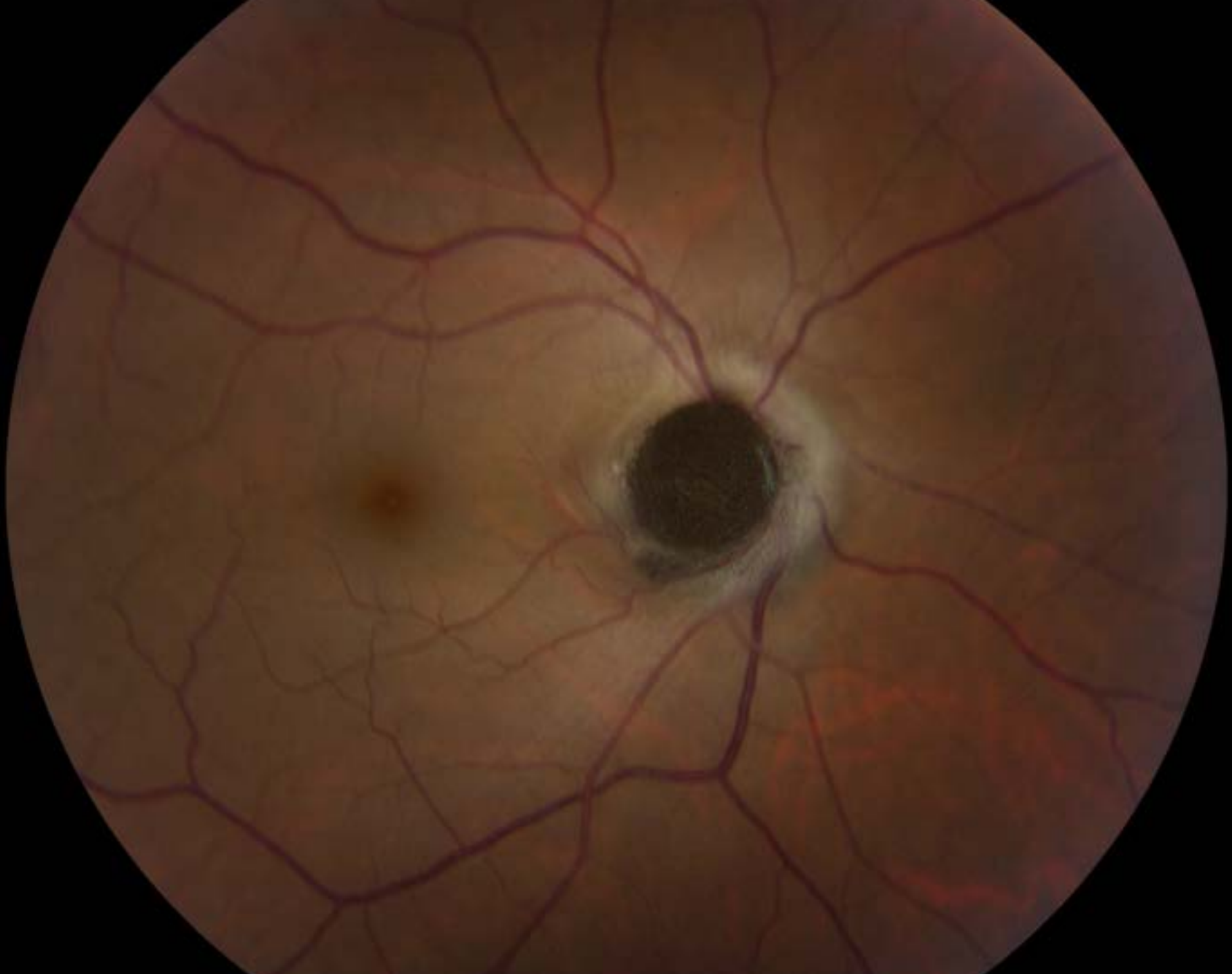
SUPPLEMENTAL LASER ABLATION



RETINOBLASTOMA:
NO CLINICAL ACTIVITY

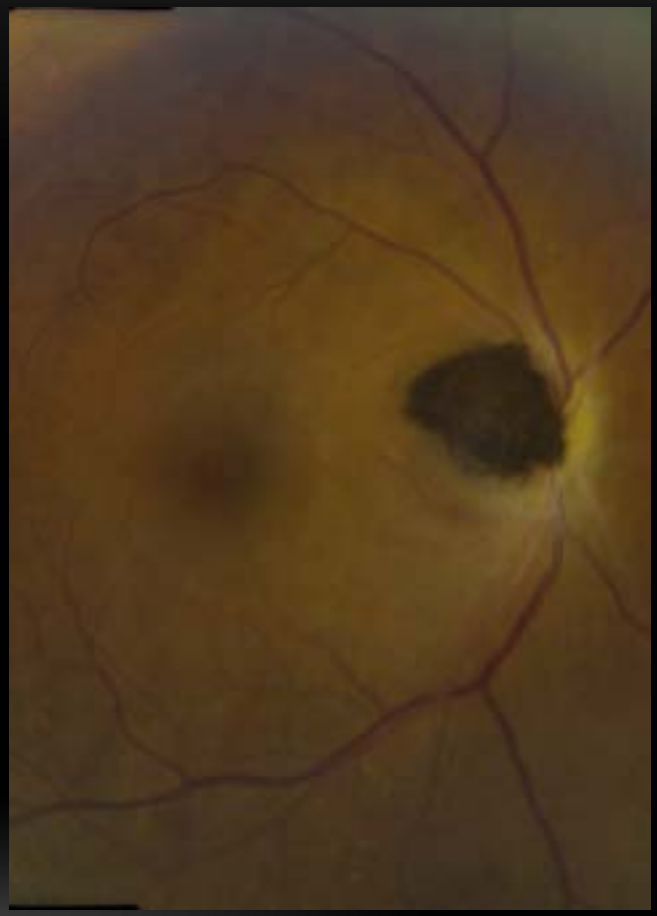


3 MONTHS LATER

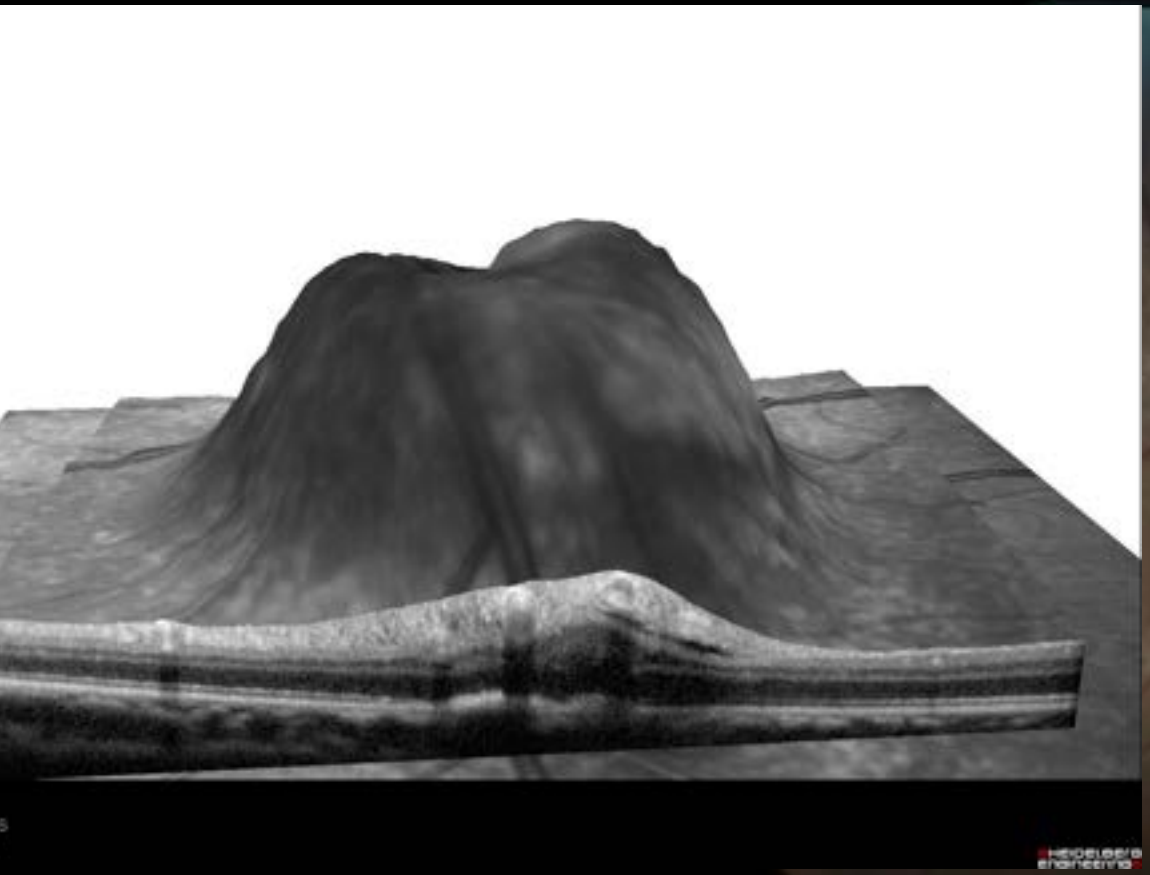


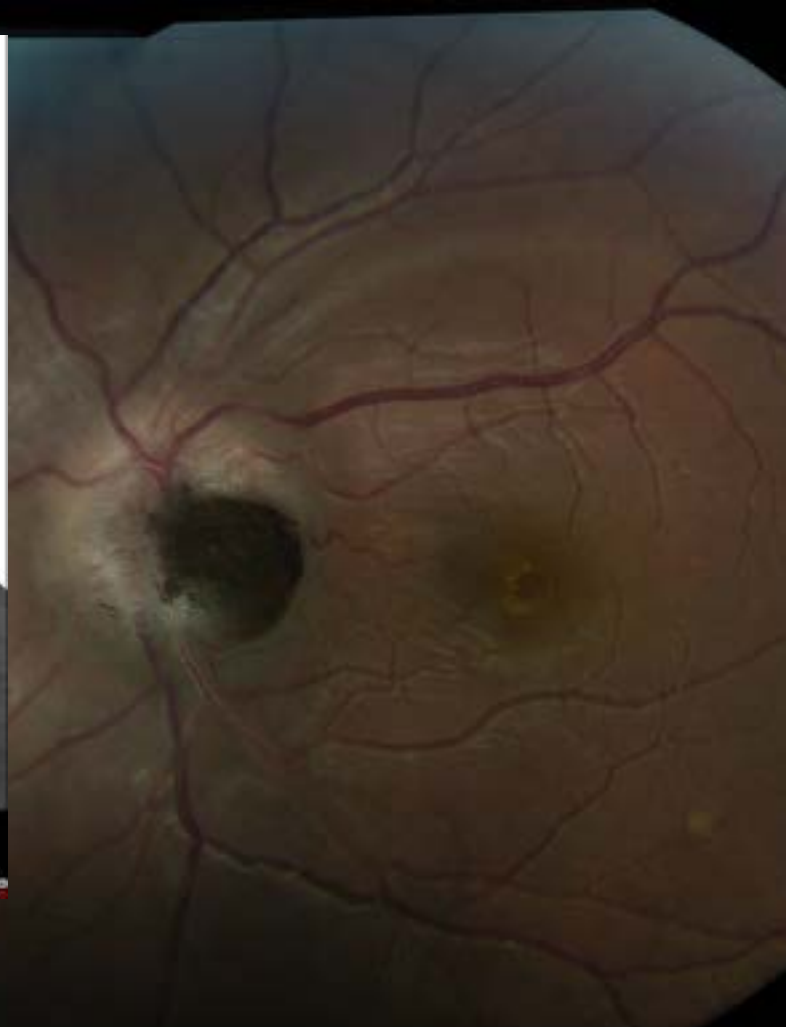
OPTIC DISC MELANOCYTOMA

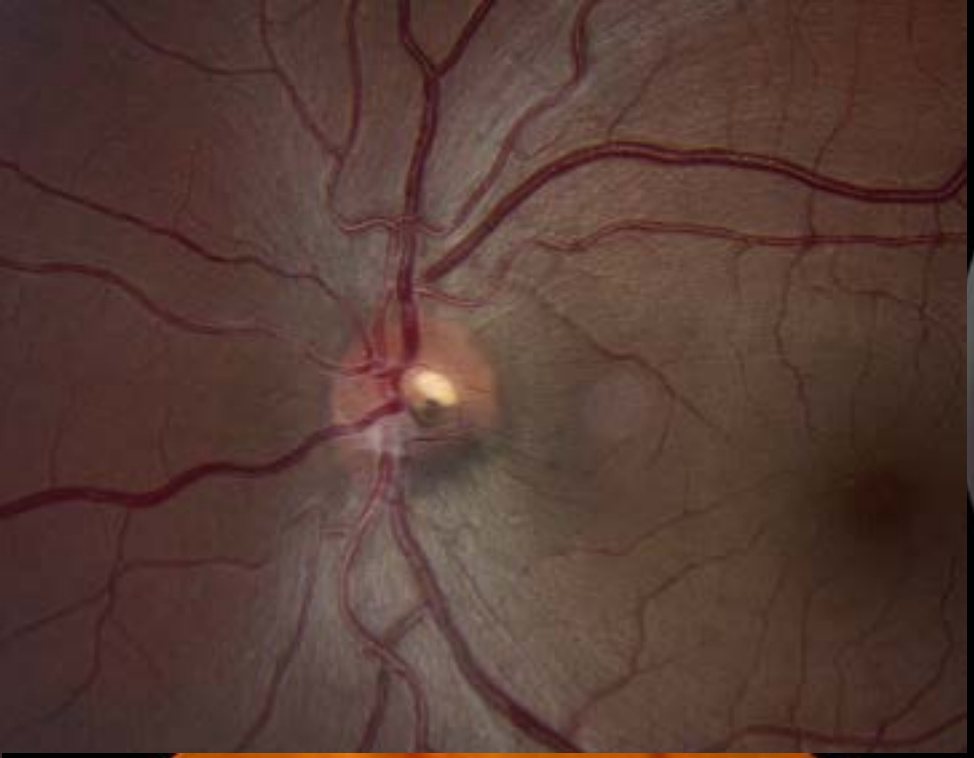
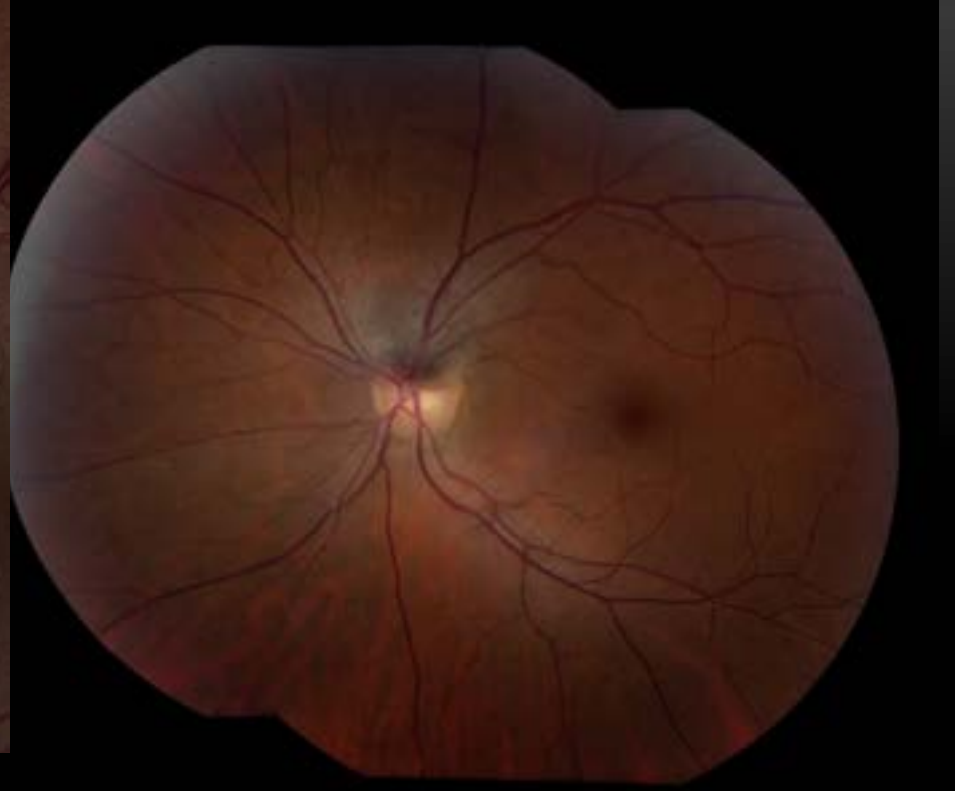
- Dark brown to black lesions, often with feathery margins
- High internal acoustic reflectivity on ultrasound
- On SD-OCT dense pigmentation of the lesion prevents laser penetration and results in marked shadowing
- Slow progressive enlargement has been documented in 10 to 15% of the cases
- Transformation into melanoma is rare ~2%
- Treatment for malignant transformation is enucleation

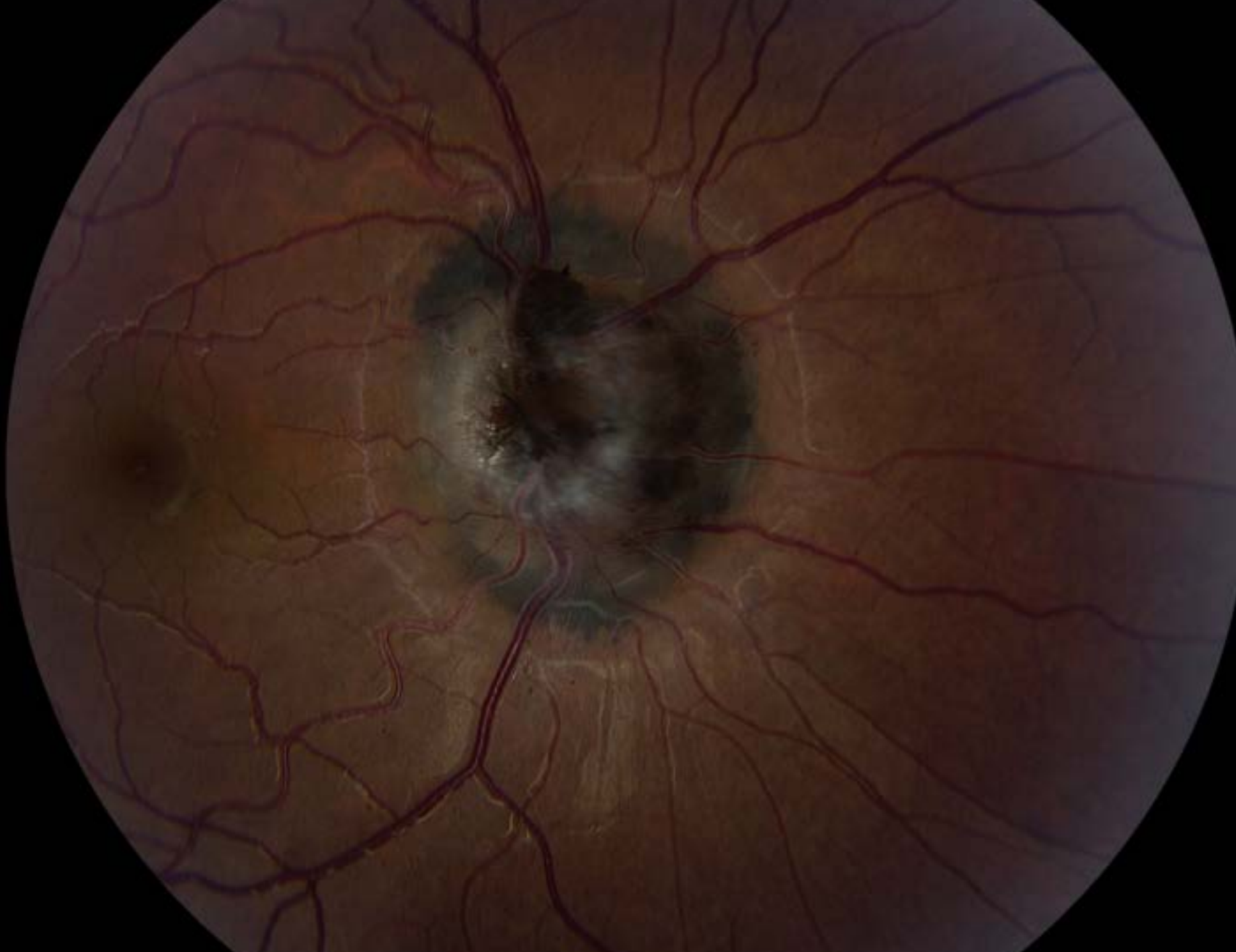


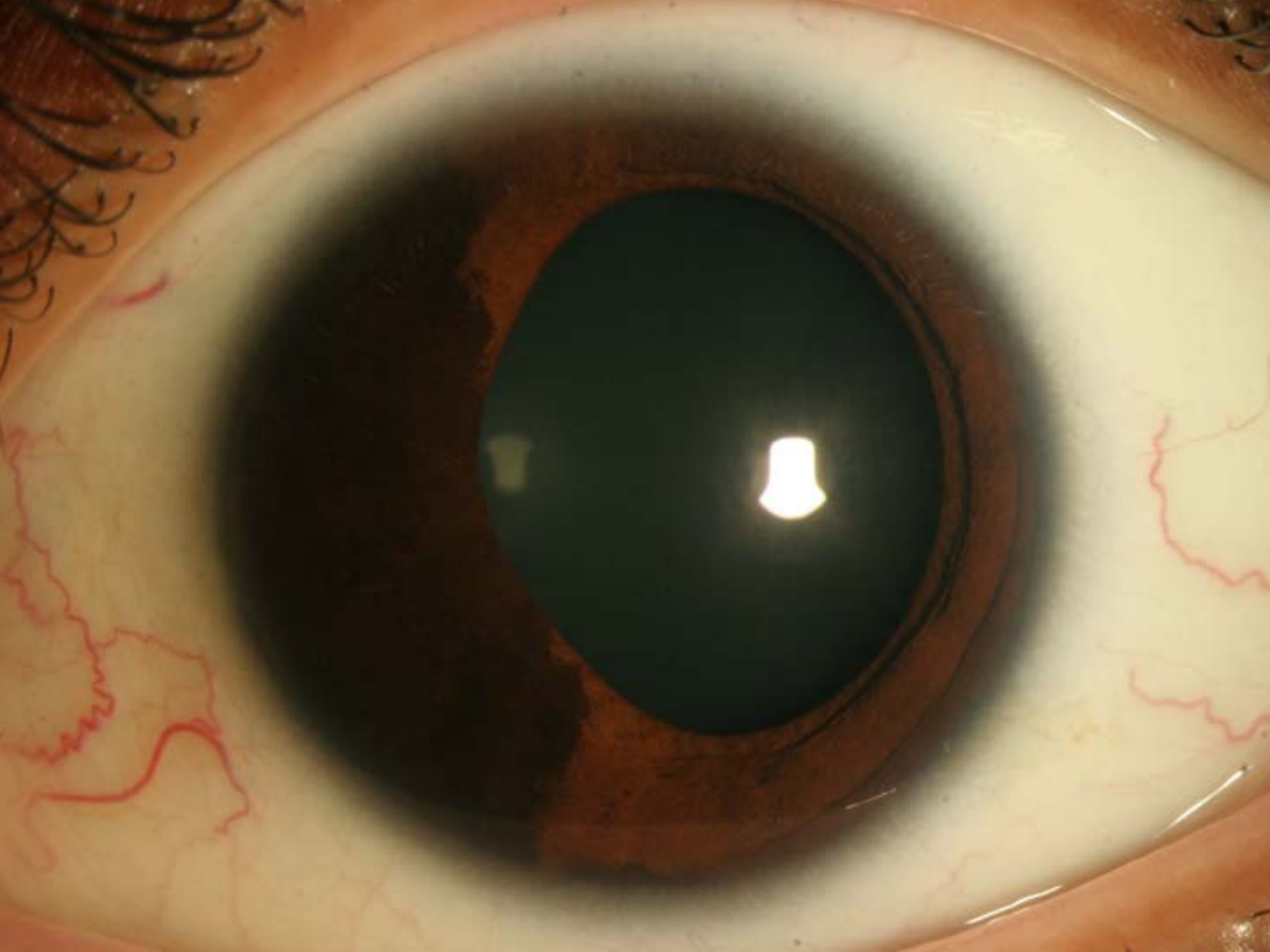
OPTIC DISC MELANOCYTOMA SD-OCT

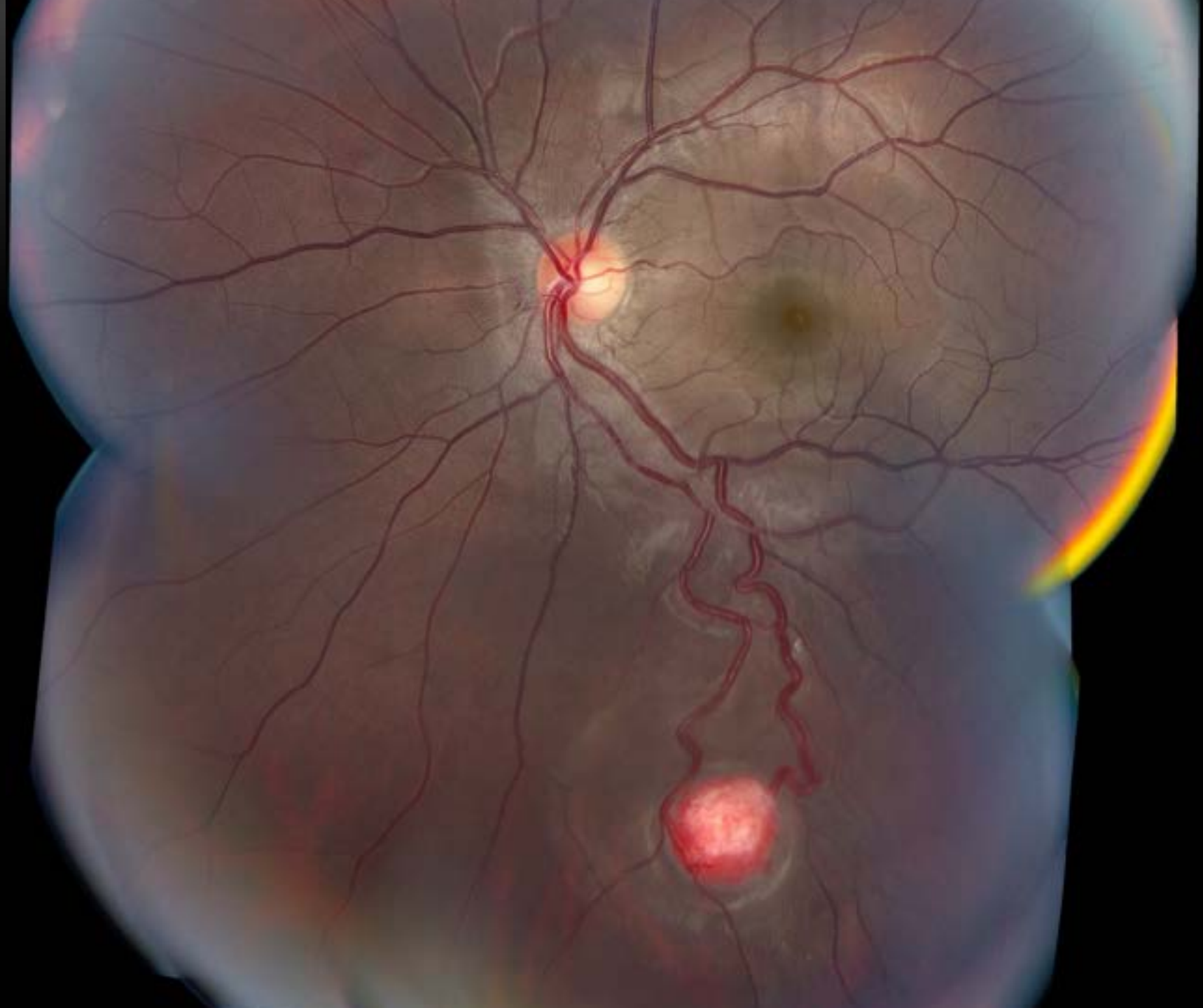










CAPILLARY HEMANGIOMA

- Orange–red vascular tumors within the retina with feeder vessels
- Can occur sporadically or in association with von Hippel–Lindau (VHL) disease
- VHL diagnosed at around 20 years of age
- Sporadic tumors present later in life, at around 30–40 years of age

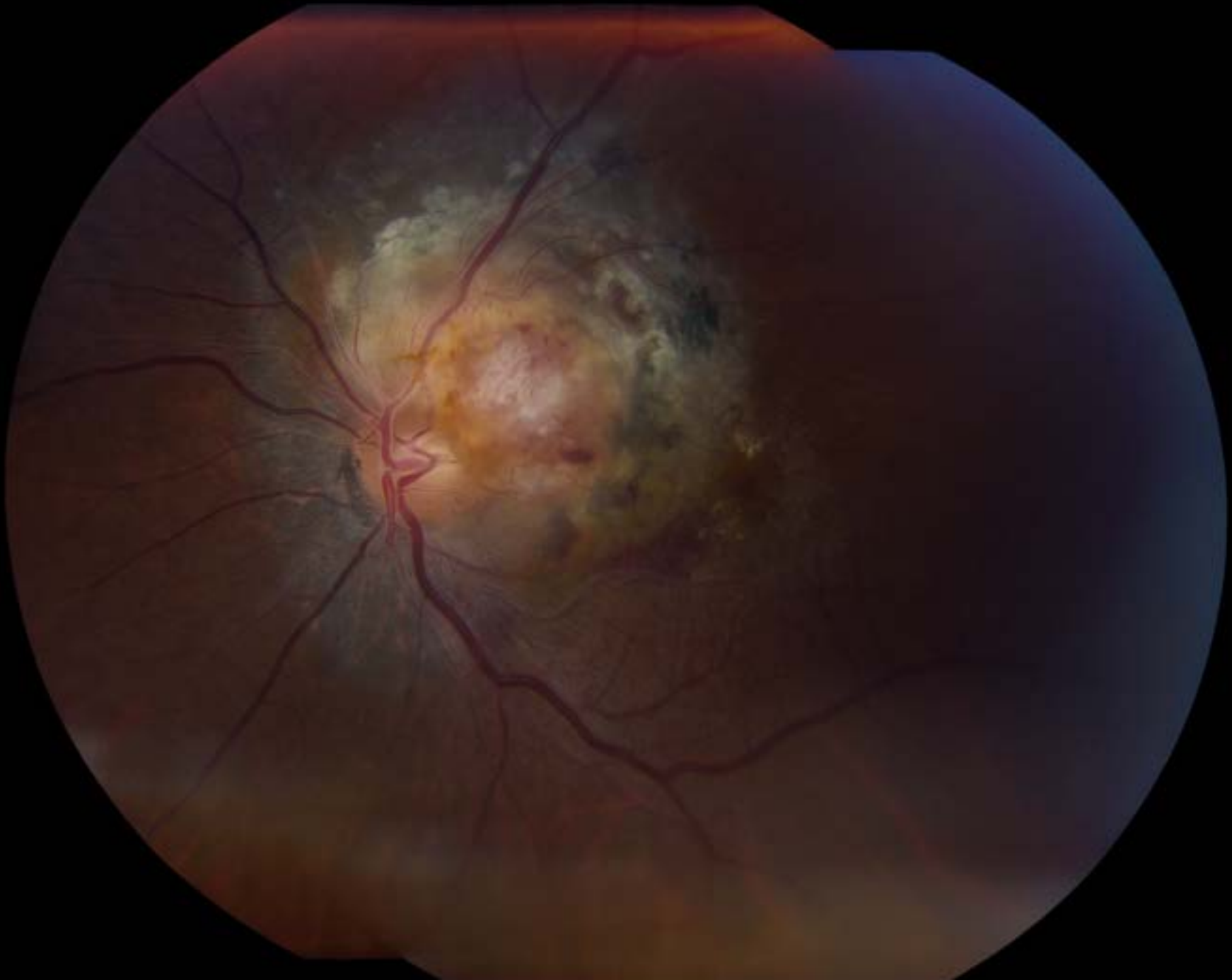
CAPILLARY HEMANGIOMA

- Large lesions produce intra- and subretinal exudates in the surrounding part of the fundus and at the macula
- Advanced lesions give rise to vitreous membranes, which cause tractional retinal detachments
- Severe exudative retinal detachment can also occur
- In the advanced stages, secondary glaucoma and uveitis commonly occur

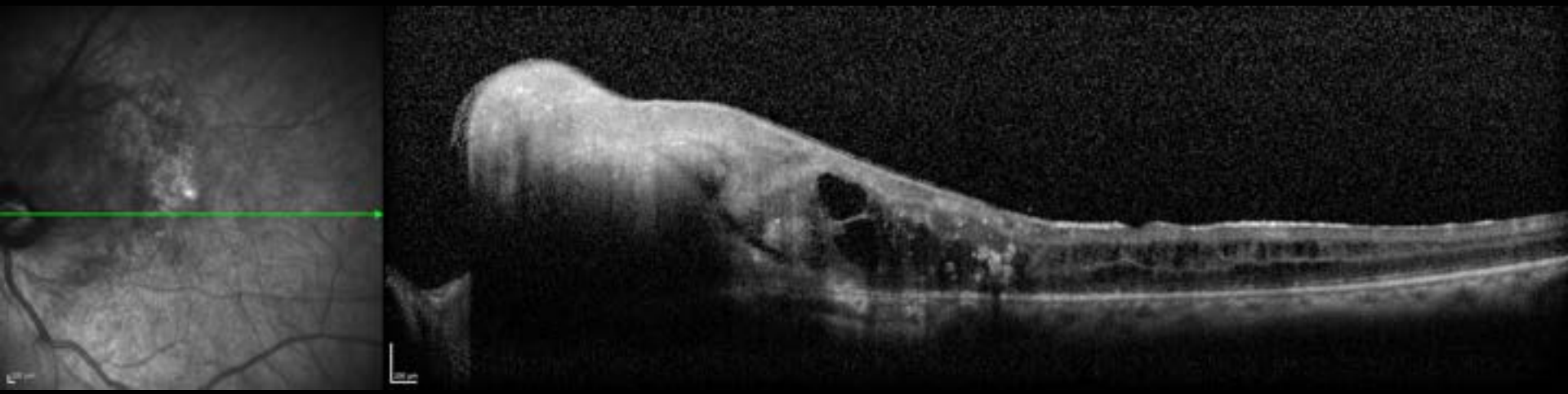
CAPILLARY HEMANGIOMA

- ~85% are located in the peripheral retina
- ~15% arise at or around the optic nerve head
- Juxtapapillary tumors appear in 3 different forms:
  - Endophytic -- grow on the surface of the nerve or retina, protrude into the vitreous cavity
  - Exophytic -- nodular, orange-colored lesions that grow into the outer layers of the retina
  - Sessile -- relatively flat, gray or orange in color, and develop in the middle layers of the retina

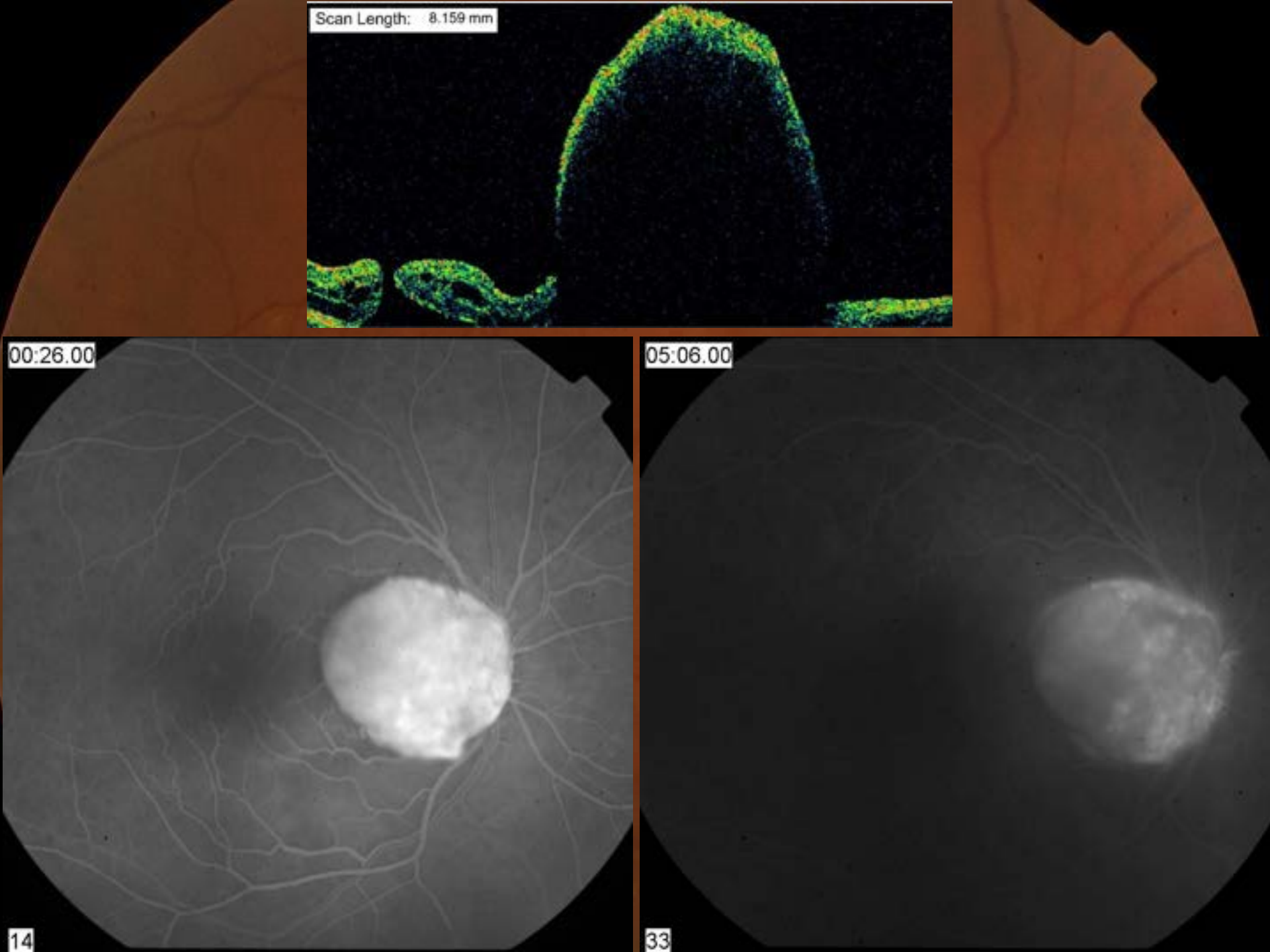
MURRAY
Ocular Oncology & Retina



OCT



MURRAY
Ocular Oncology & Retina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33

CAPILLARY HEMANGIOMA TREATMENT

- Determined by the size, number, and location of the hemangioblastomas, as well as any secondary effects

- Dormant lesions are usually treated if peripherally located and monitored if located juxtapapillary

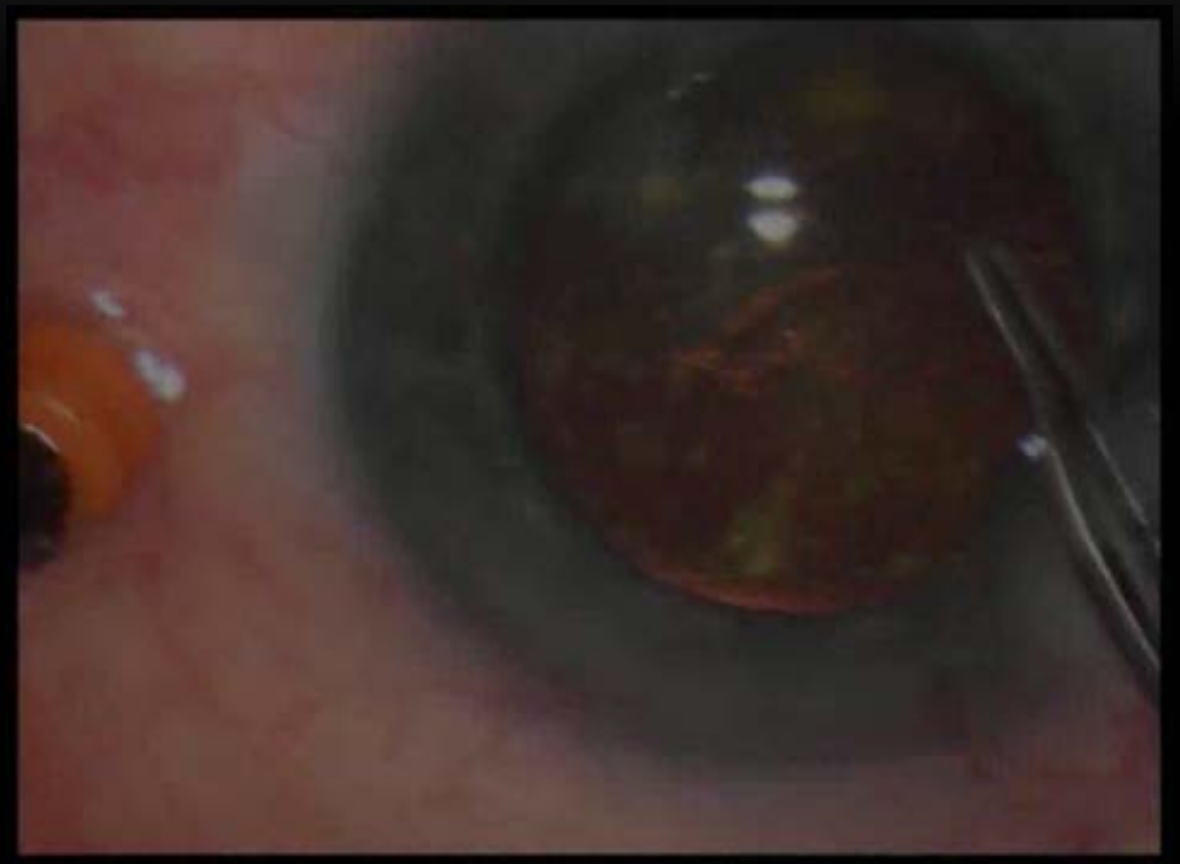
MURRAY
Ocular Oncology & Retina

CAPILLARY HEMANGIOMA TREATMENT

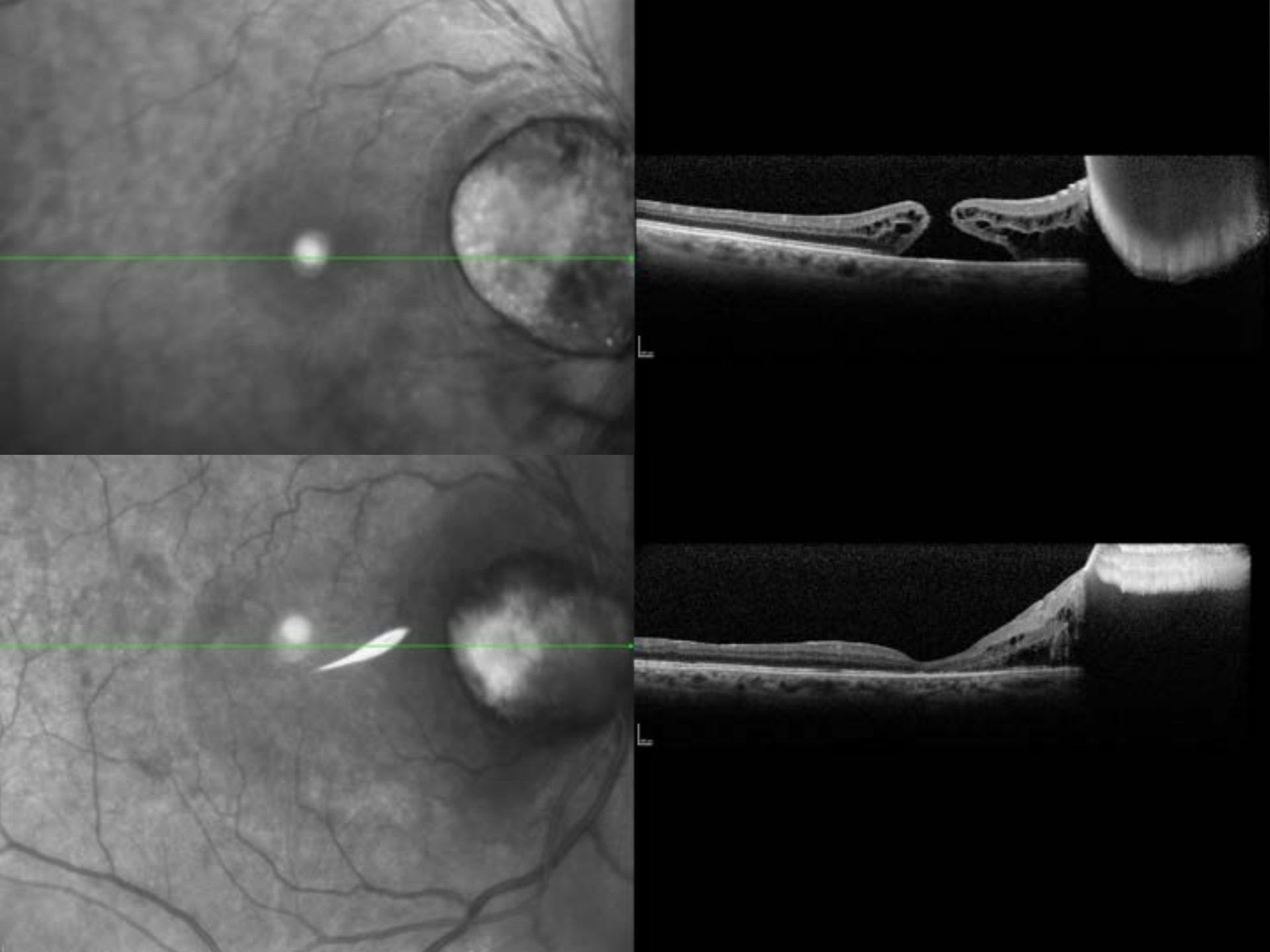
- Treatment options:
  - Observation
  - Vascular endothelial growth factor receptor inhibitor
  - Photodynamic therapy
  - Radiotherapy (for larger tumors)
    - EBRT
    - Plaque brachytherapy,
    - Proton beam radiotherapy
  - Cryotherapy (less than 5mm thick)
  - Laser photocoagulation (1.5mm – 4mm diameter)
  - Vitreoretinal surgery

MURRAY
Ocular Oncology & Retina

PHACO/IOL/PPV/MP(ILM/ICG)/EL/GAS



MURRAY
Ocular Oncology & Retina



IN ADDITION TO TREATMENT…

- Patients must still be screened for VHL
  - Multiple retinal hemangioblastomas are diagnostic for VHL
  - 50% of solitary retinal hemangioblastomas are associated with VHL
- Screenings include:
  - Physical examination
  - Imaging of the abdomen and brain
  - Genetic testing
- Relatives should also be screened

MURRAY
Ocular Oncology & Retina

VHL

- Autosomal dominant
- Benign and malignant tumors and cysts may develop in several organs
- Caused by mutations of the VHL gene on chromosome 3p25-26
- Tumor cells show increased expression of vascular endothelial growth factor (VEGF)

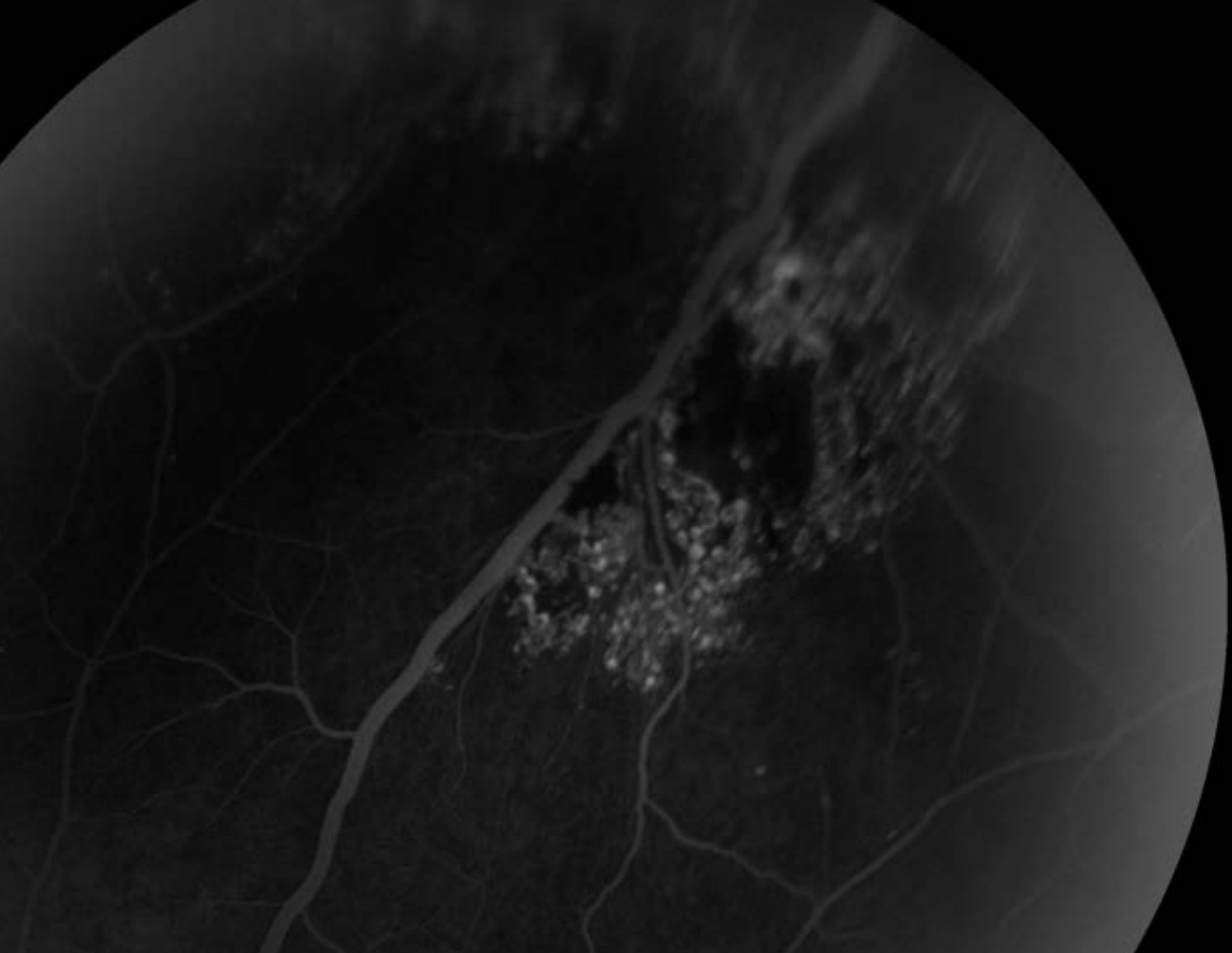
VHL

- In a large series of 327 patients published by Neumann et al, the most common lesions were:
  - hemangioblastoma of the central nervous system (52% of affected patients)
  - retinal hemangioblastoma (48%)
  - renal cysts (33%)
  - pheochromocytoma - tumor of the medulla of the adrenal glands (33%)
  - pancreatic cysts (22%)
  - renal cell carcinoma (22%)

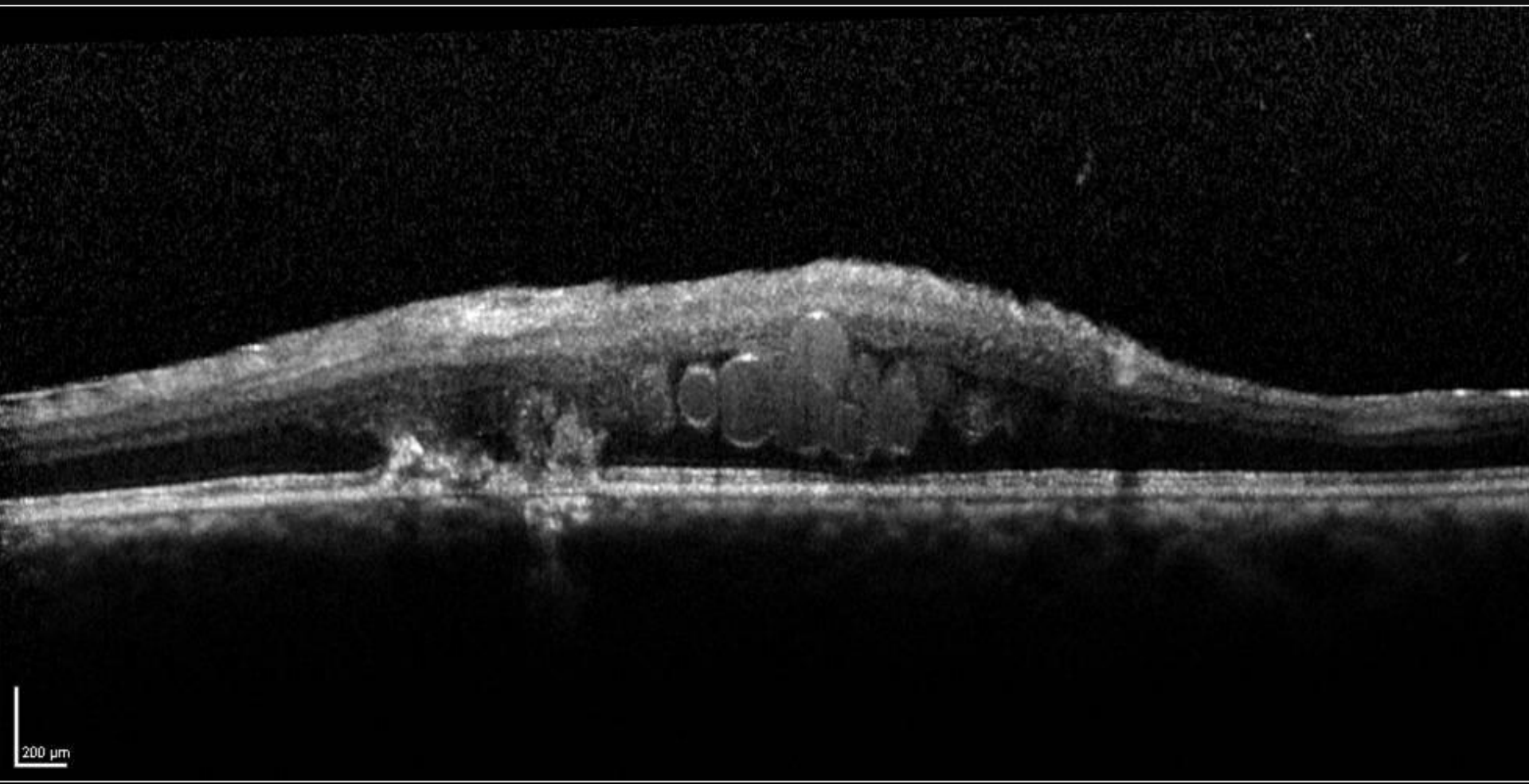
OTHER VASCULAR HAMARTOMAS OF THE RETINA

CAVERNOUS HEMANGIOMA

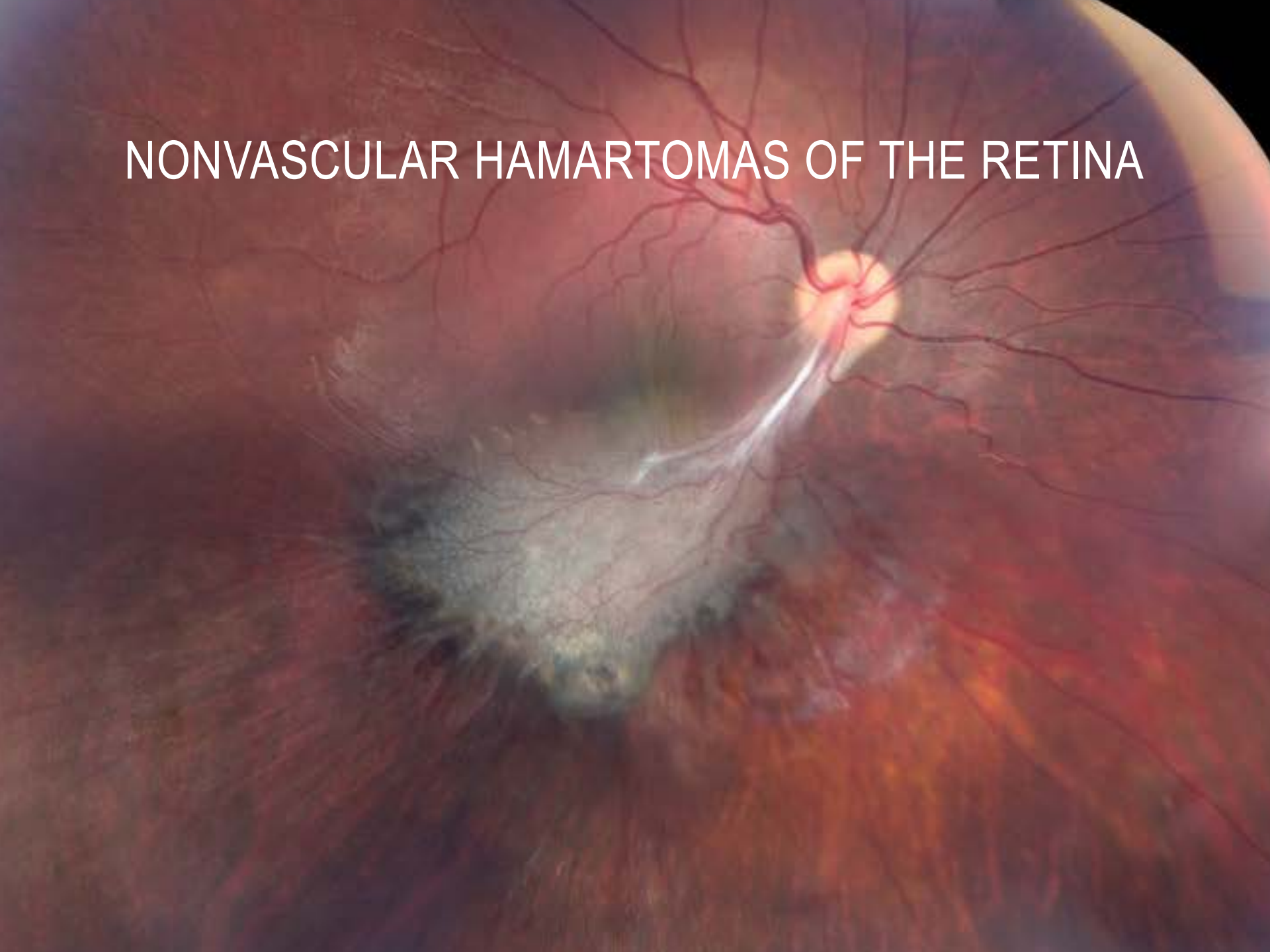
- Clusters of dark-red, saccular aneurysms within the inner retina
- May occur sporadically or can be inherited (autosomal dominant)
- May be associated with cerebral, spinal, and cutaneous angiomas, and aneurysms
- Usually be found away from the posterior pole (but rarely juxtapapillary and macular)
- Normal endothelial cell lining, therefore not associated with exudation
- Fluorescein angiography typically shows slow filling of the aneurysms with little or no leakage and late ‘capping’ of the dye in the superior half of the aneurysms as a result of settling of red blood cells



OCT OF CAVERNOUS HEMANGIOMA

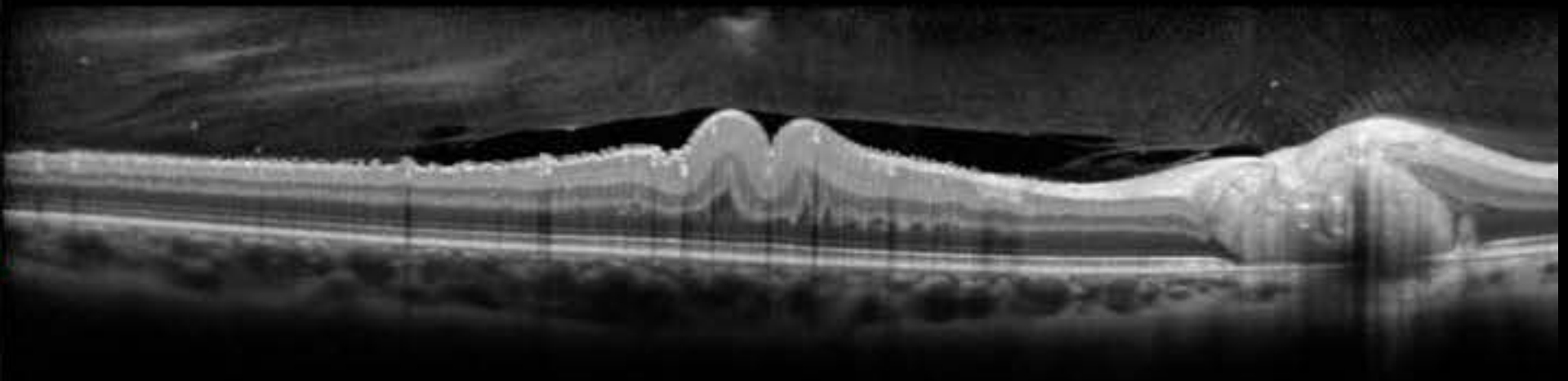


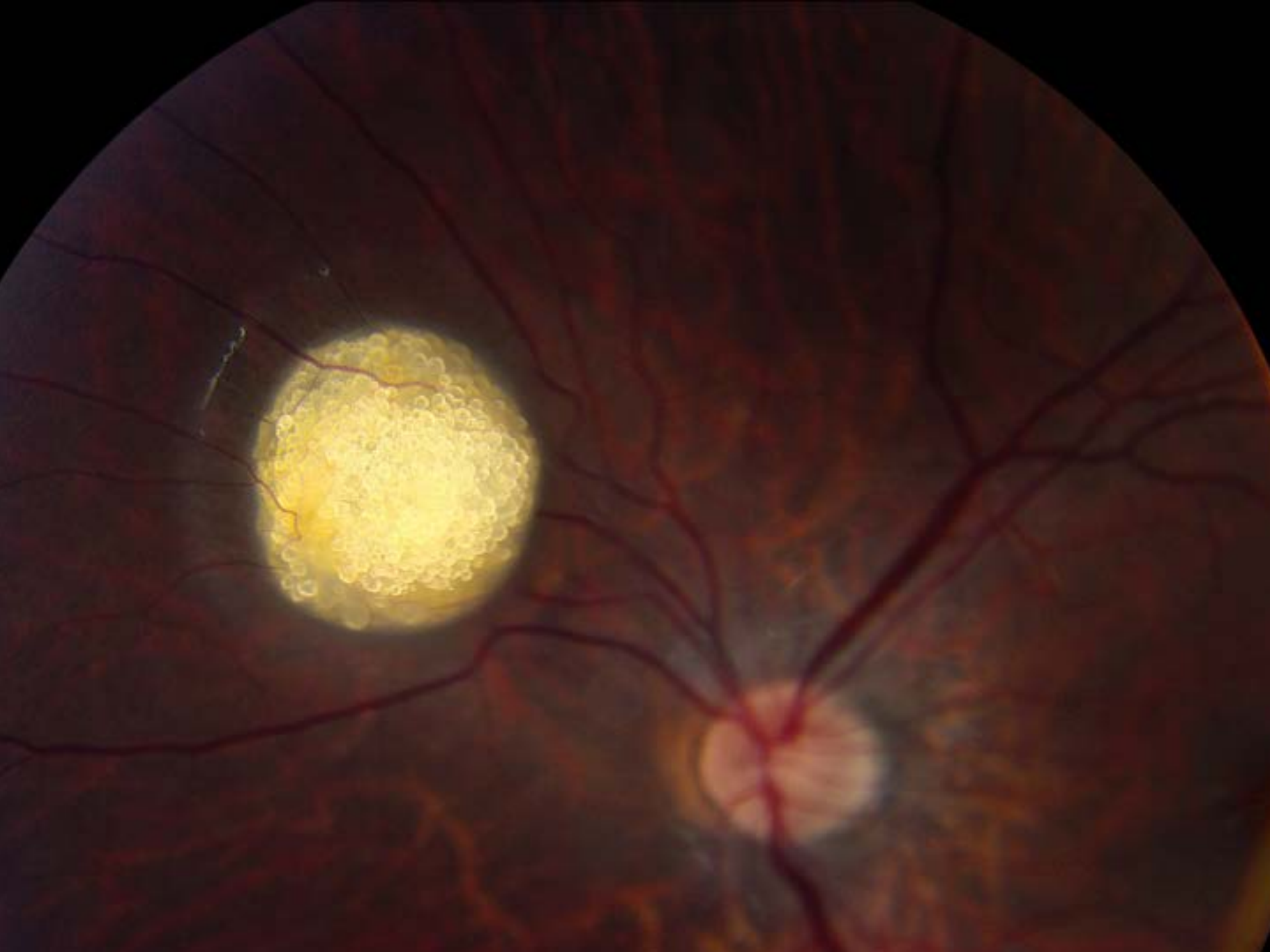
NONVASCULAR HAMARTOMAS OF THE RETINA



COMBINED HAMARTOMA OF THE RETINA AND RPE

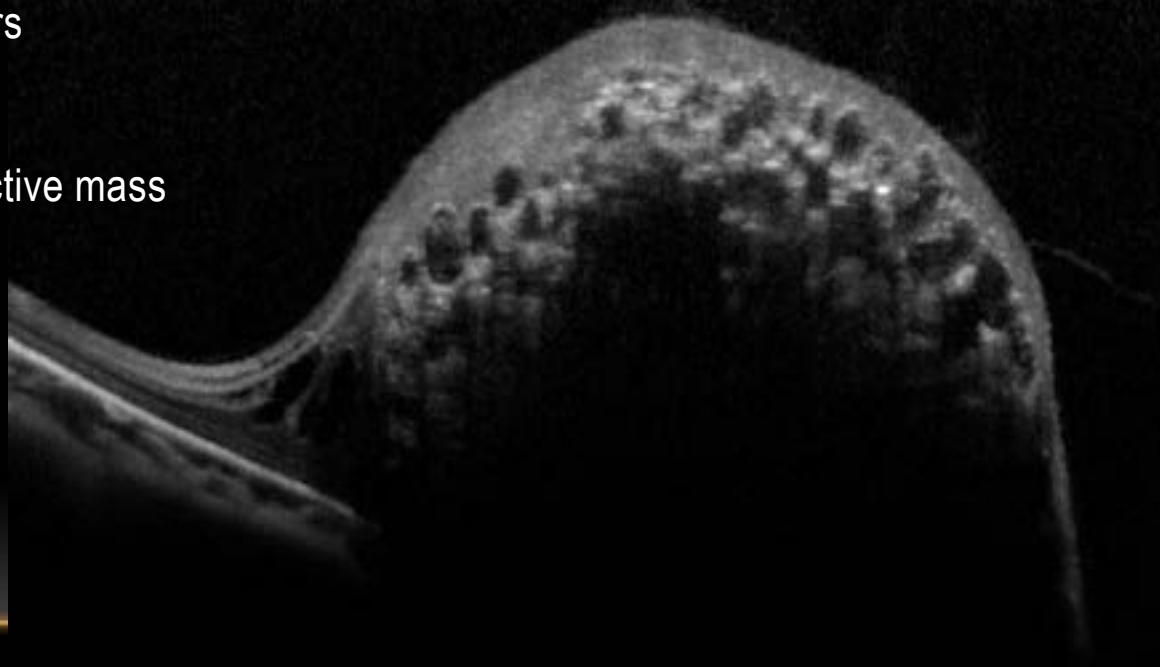
- Composed of glial, vascular, and pigmented cells
- Appears grayish, with twisting intraretinal vasculature and scalloped
- SD-OCT shows retinal folding and highly reflective, disorganized retina
- Tend to cause significant traction to the surrounding retina and may distort vision as a result
- PDT and anti-VEGF therapy have shown to be effective in treating vascular leakage associated with these lesions





ASTROCYTIC HAMARTOMA

- Arises from the supportive glial cells of the sensory retina (astrocytes)
- May present as strabismus or leukocoria if the lesion occurs in or adjacent to the macula
- Clinical presentation varies widely, ranging from flat, translucent, noncalcified intraretinal patches to nodular, opaque, white inner-retinal lesions to a large, yellow-whitish, calcified, multinodular mulberrylike tumors
- OCT typically shows
  - Dome-shaped hyper-reflective mass
  - “Moth-eaten” appearance
  - Posterior shadowing



ASTROCYTIC HAMARTOMA

- Main ocular manifestation of tuberous sclerosis
- In tuberous sclerosis, may present with achromic patches