

# The Pathology and Pathogenesis of Acute Glaucoma in Dogs

Richard R Dubielzig

# Overview of Glaucoma

Intraocular Pressure too High to Support a Healthy Optic Nerve

## Terminology used in the classification of human glaucomas

### I. Open-angle Glaucoma

A. Primary (POAG)

B. Secondary – selected varieties

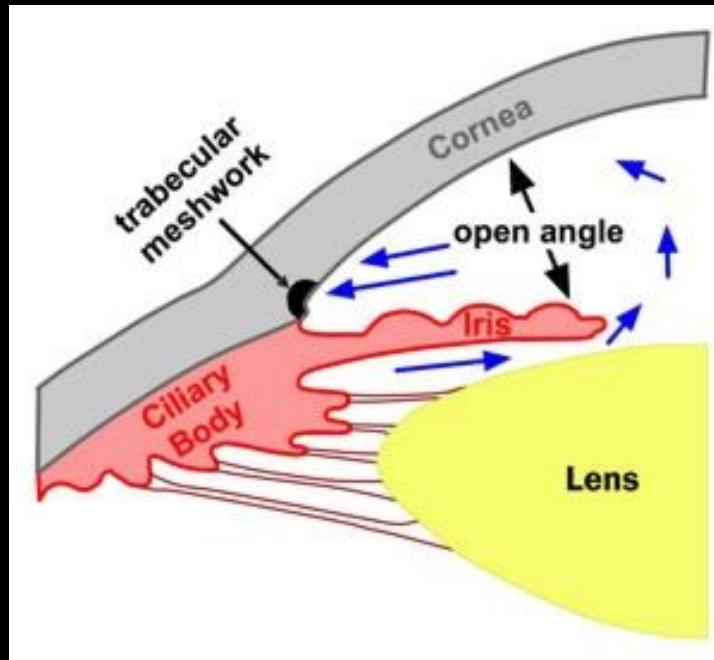
### II. Angle-closure Glaucoma

A. Primary/acute

B. Variants

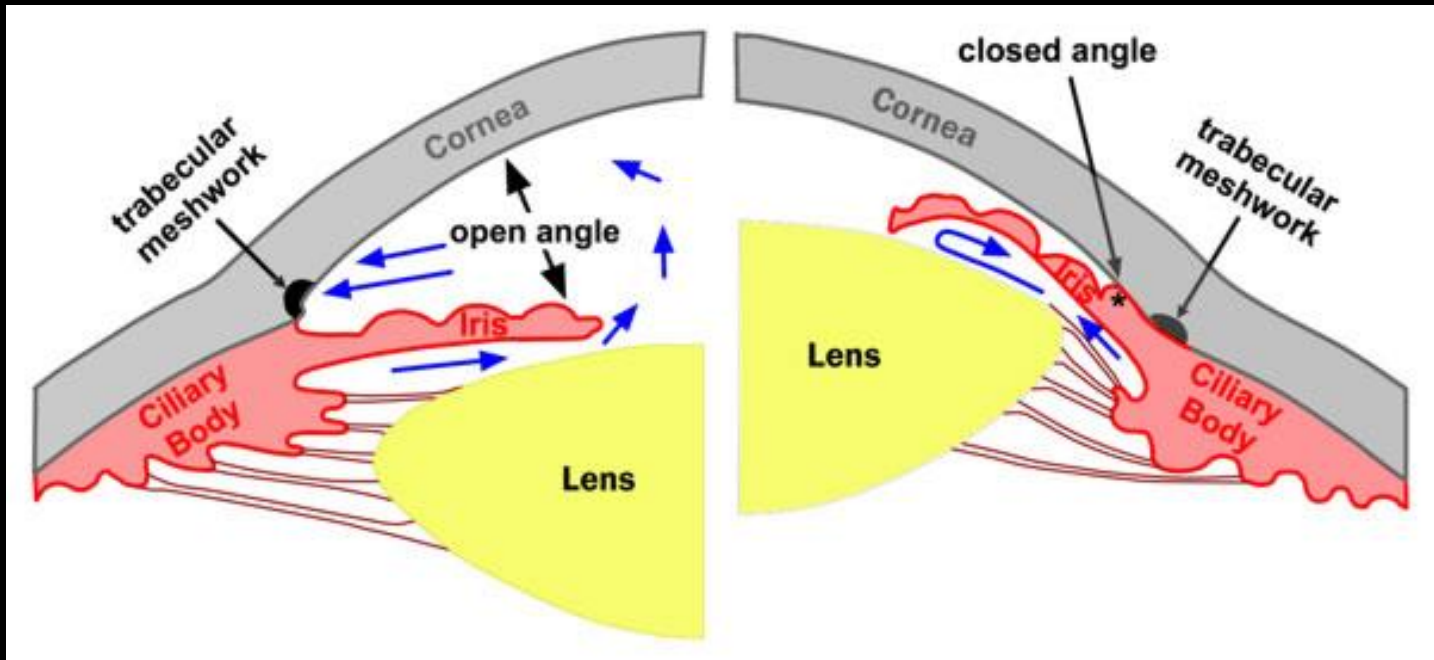
# Aqueous Humor Dynamics

*from human classification*



- A Patient's Guide to Glaucoma [www.medrounds.org](http://www.medrounds.org)

# Aqueous Humor Dynamics *from human classification*



- A Patient's Guide to Glaucoma [www.medrounds.org](http://www.medrounds.org)

# The Common Canine Glaucoma Diseases

- Primary glaucoma
- Primary open angle glaucoma , familial in the Beagle
- Familial lens luxation and glaucoma
- Pigmentary uveitis of Golden Retrievers
- Congenital glaucoma
- Glaucoma as a component of many disease processes
  - Neoplasia
  - Trauma
  - Uveitis

# The Common Feline Glaucoma Diseases

- Aqueous mis-direction syndrome
- Feline open angle glaucoma
- Angle recession
- Congenital glaucoma
- Glaucoma as a component of many disease processes
  - Neoplasia...FDIM
  - Uveitis...Idiopathic L/P uveitis

# The pathogenesis of glaucoma damage in the retina and optic nerve is controversial

Gradual ganglion cell loss from apoptosis and thinning of the nerve fiber layer of the retina is seen in animal models and also fits the pathology in most human glaucoma

This change is thought to be the result of either axon or capillary obstruction in the scleral canal portion of the optic nerve (the level of the lamina cribrosa)

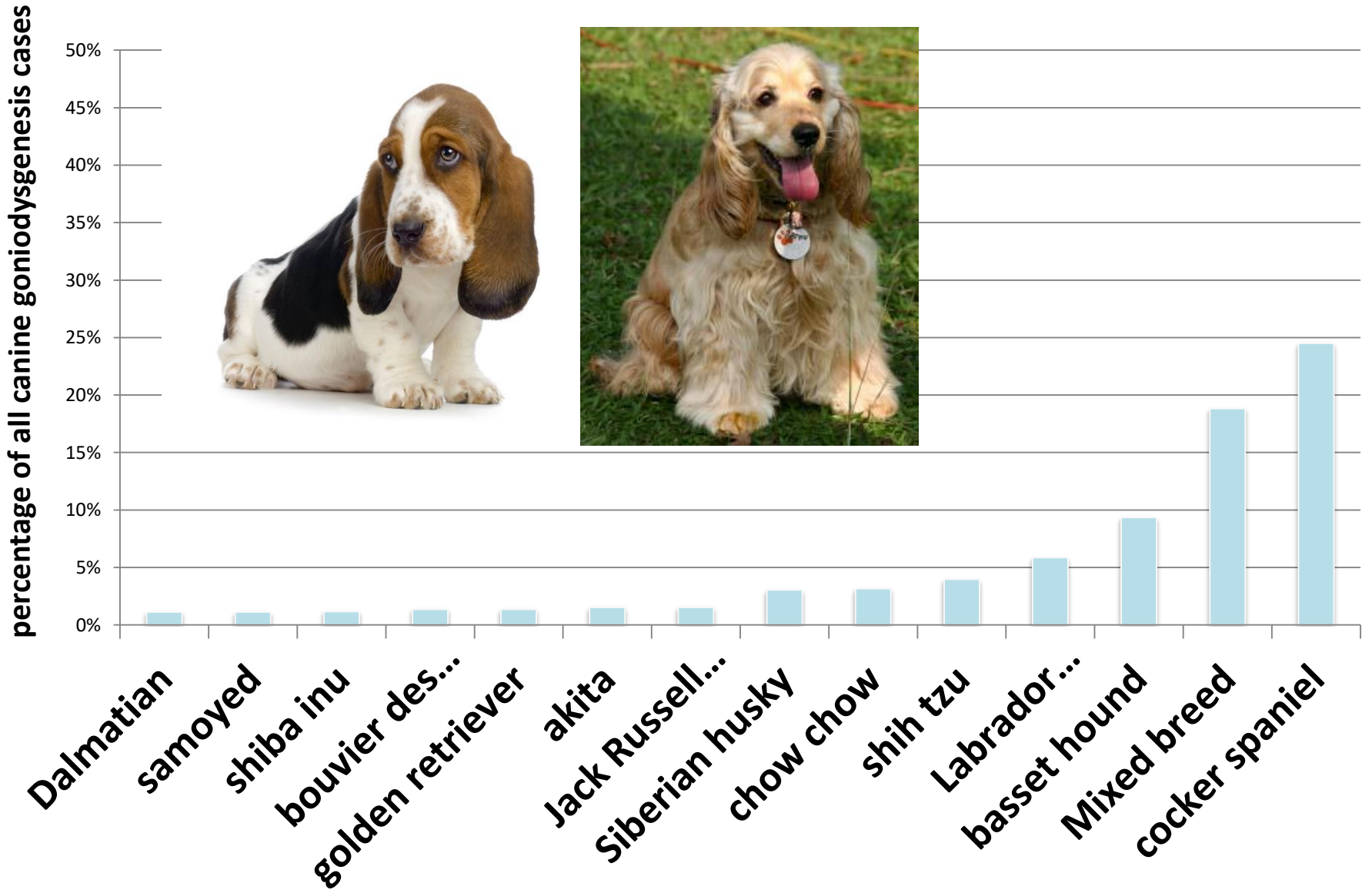
This scenario fits what we see in cats fairly well but it does not fit the pathology seen in most dog glaucoma. I will attempt to show why.

# Canine Primary Glaucoma

- Goniodysgenesis
- Pectinate ligament dysplasia
- Mesodermal dysgenesis
- Open-angle, closed-cleft glaucoma (Peiffer)
- Acute angle-closure glaucoma (Miller)
- Who knows what else



# Goniodysgenesis by breed, n=1710

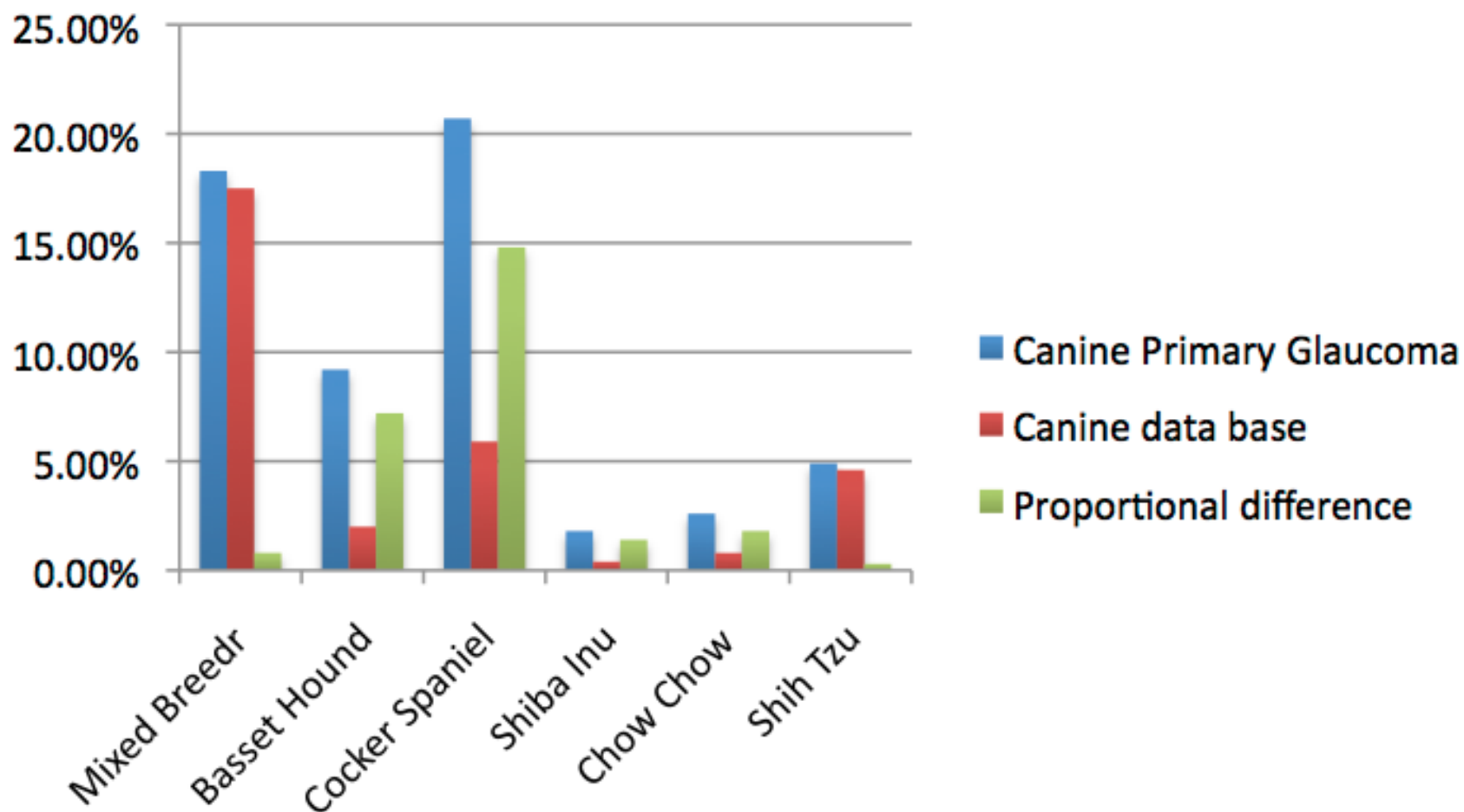


# Primary Glaucoma Breeds

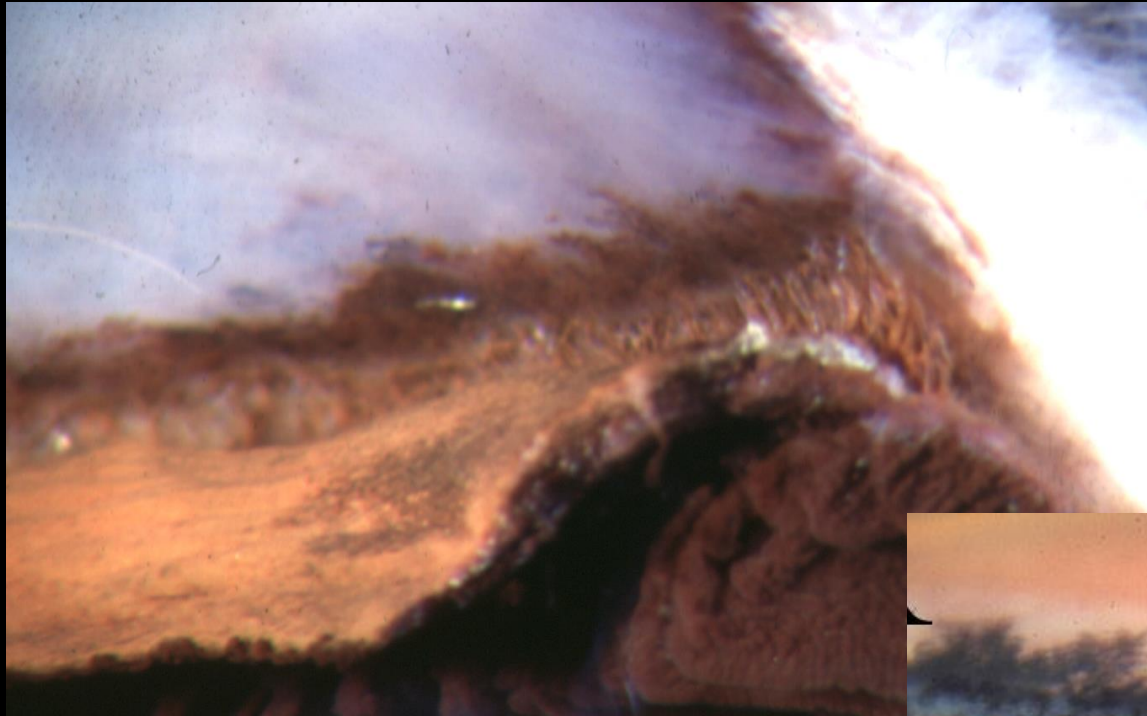
N = 2721

Canine Database

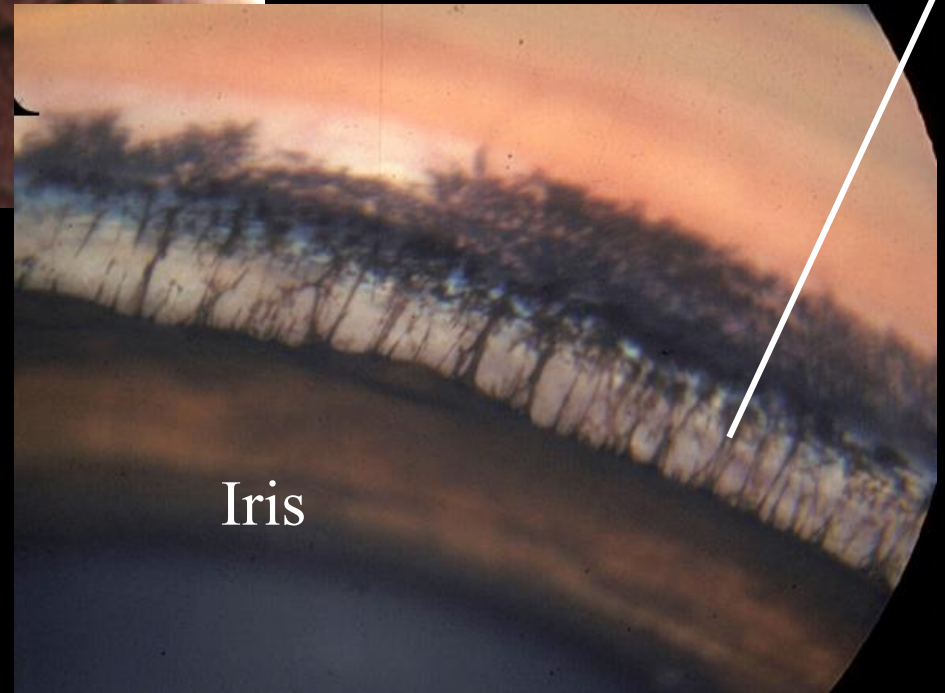
N = 29,822



# The Normal Canine Angle



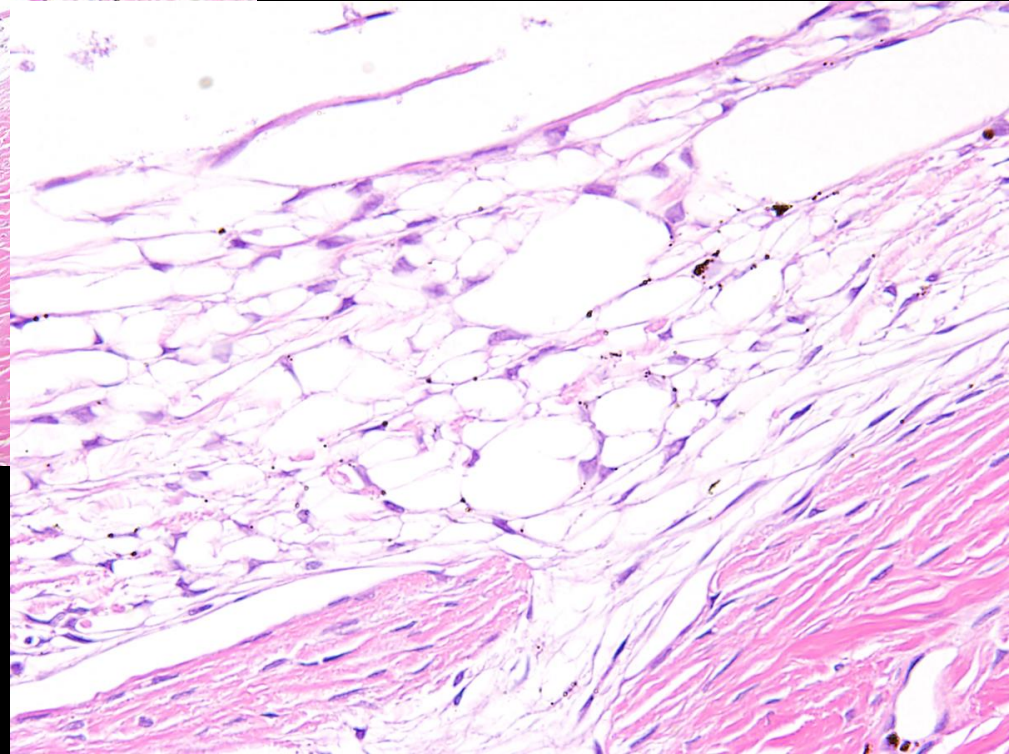
Pectinate Ligament



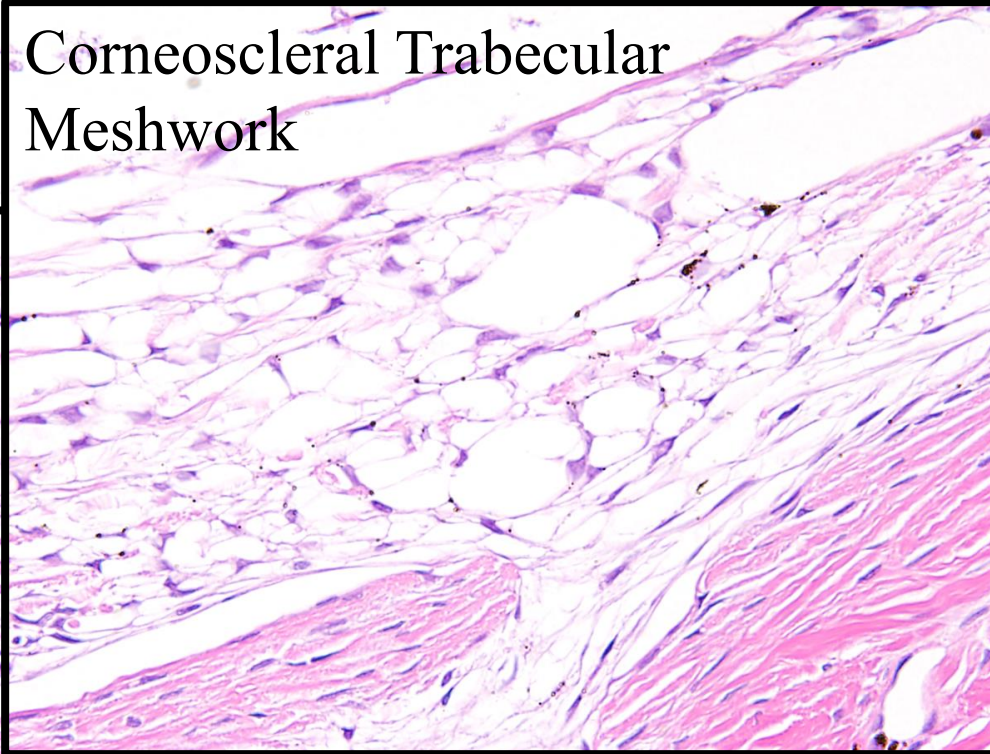
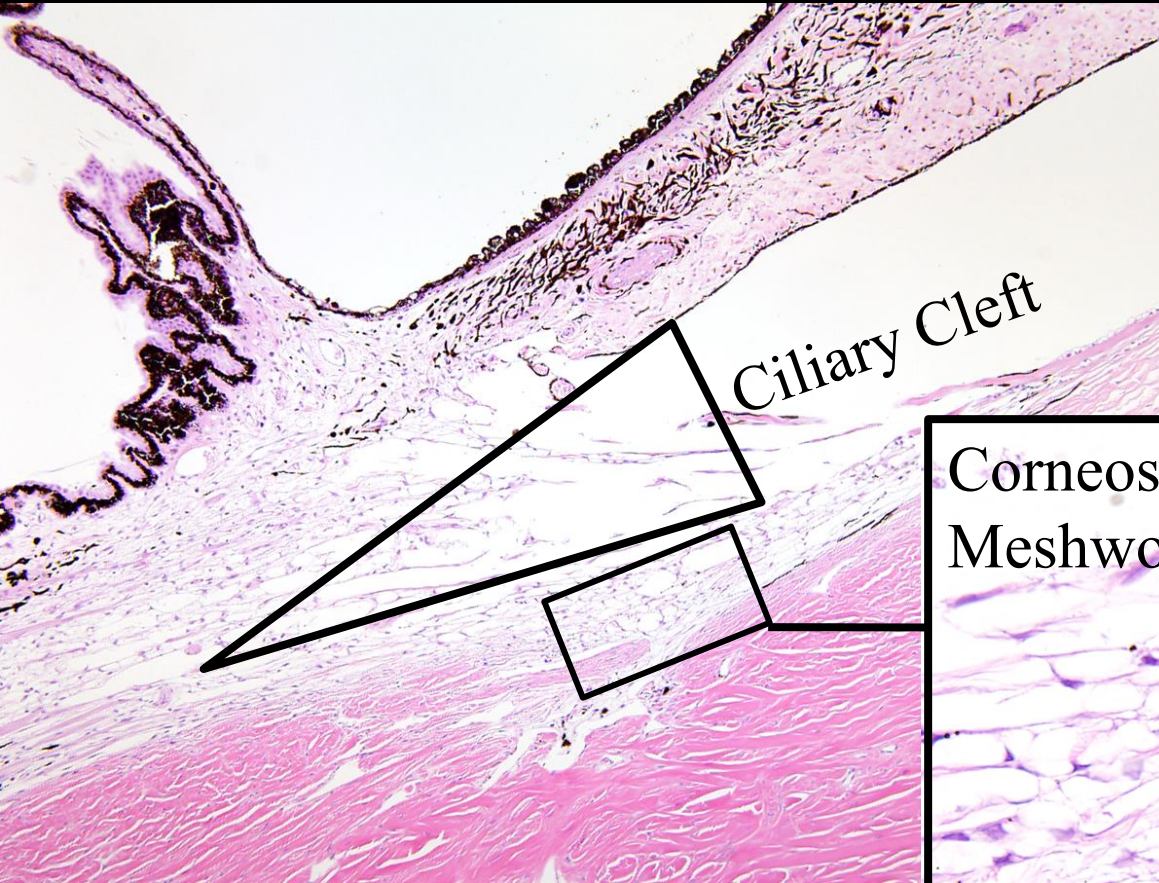
Iris

Dr Kerry Ketring

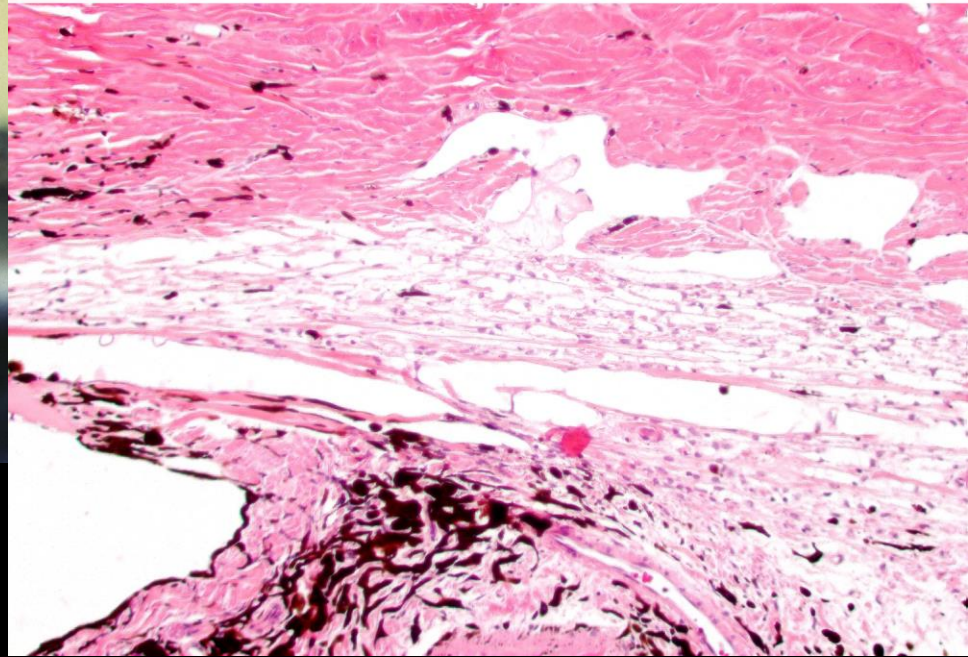
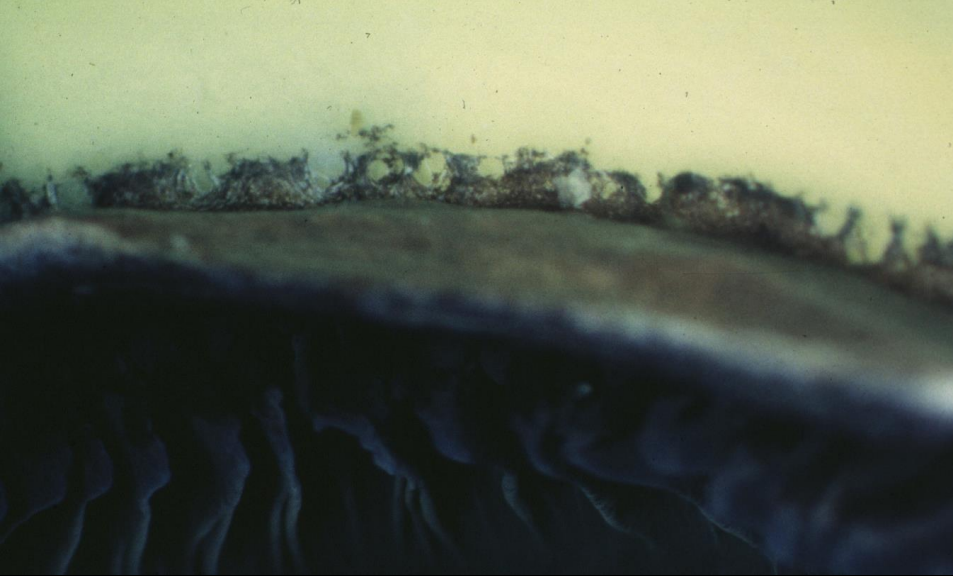
# The Normal Canine Angle



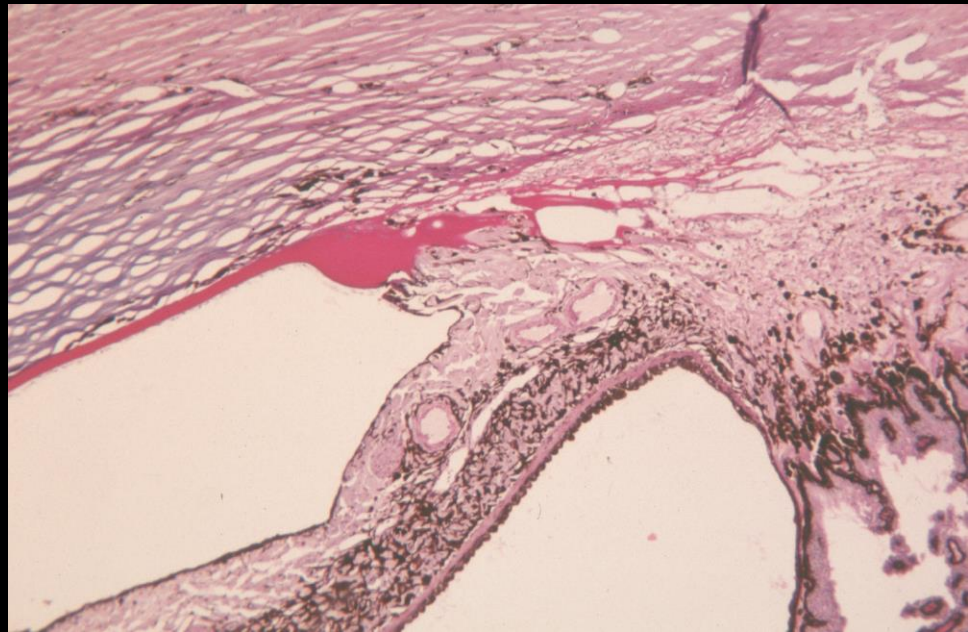
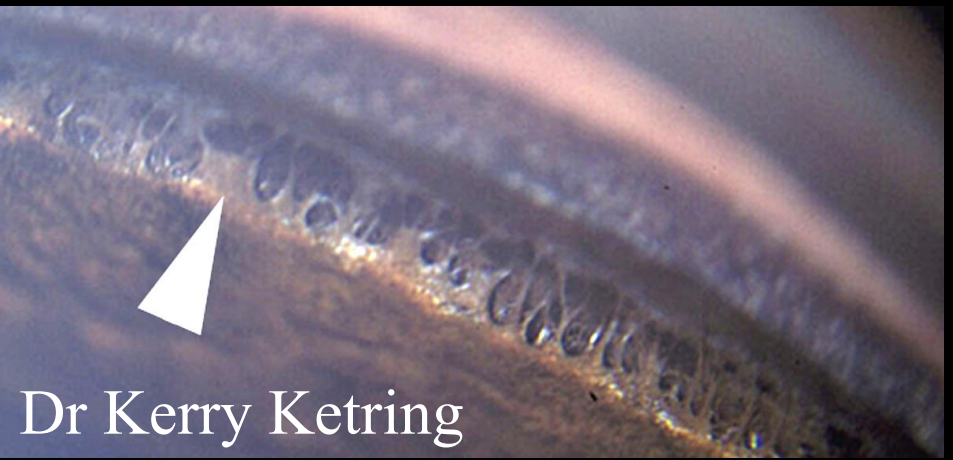
# The Normal Canine Angle



Normotensive Basset Hound with Goniodysgenesis



Goniodysgenesis  
Normal  
Pressure



Dr Kerry Ketring

# Canine Primary Glaucoma the Clinical Disease Syndrome

- Sudden onset of painful, red, often blind eye with very high pressures
  - In this talk, the time of disease is measured from when the owner first notices a painful red eye (Hour 0)
- The response to treatment is variable, but severe cases are blind from the start
- Enucleation is a common outcome
  - When dealing with the second eye, enucleation is often chosen very early (24 hours from the first signs of disease)

# Canine Primary Glaucoma the Histopathology

## Anterior Segment

Pigment dispersion

Ciliary cleft collapse

Neutrophilic infiltrate and stromal cell activation

Thinning of the sclera at the limbus

## Posterior Segment

Optic nerve head necrosis and malacia, infarction

“Red dead” ganglion cells

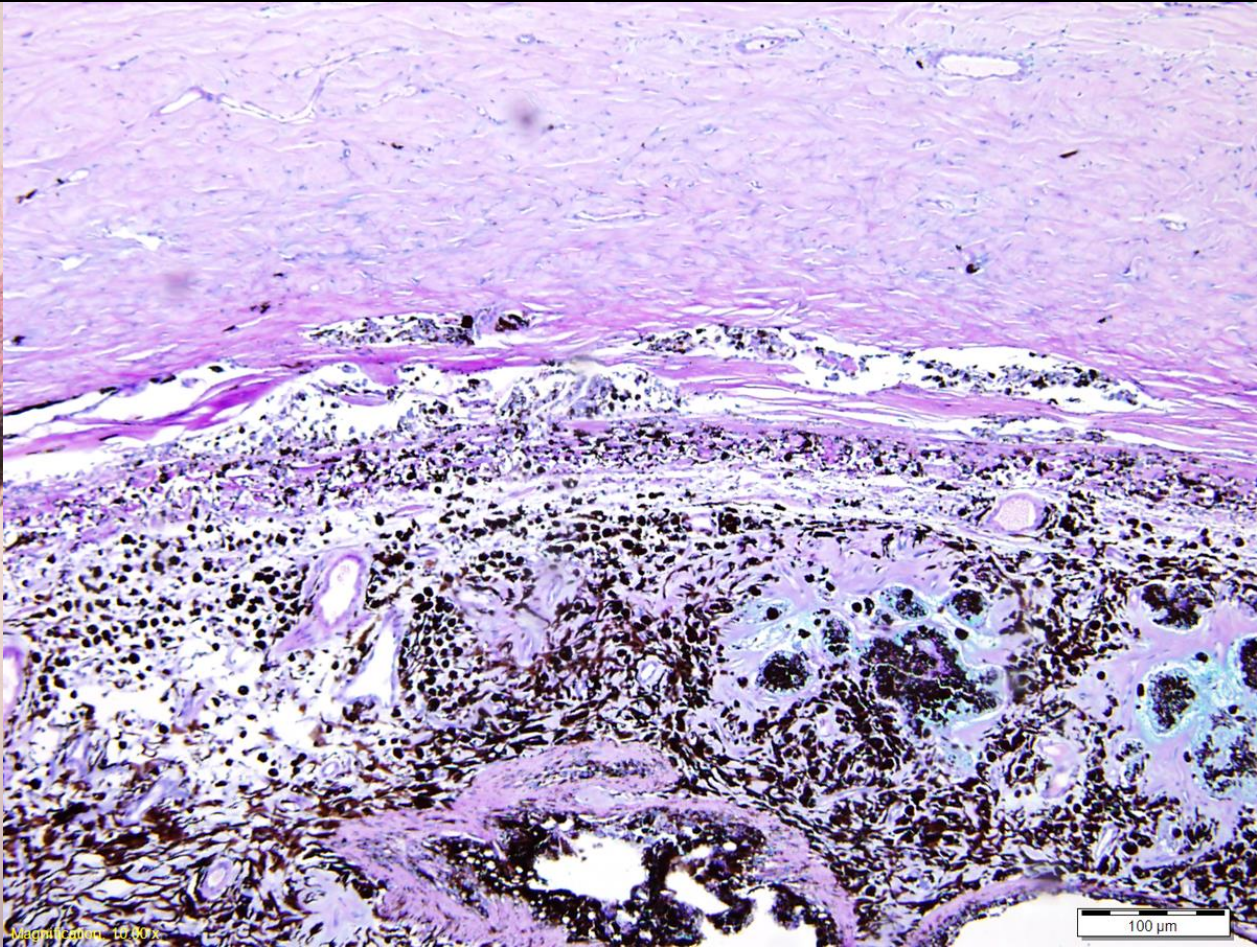
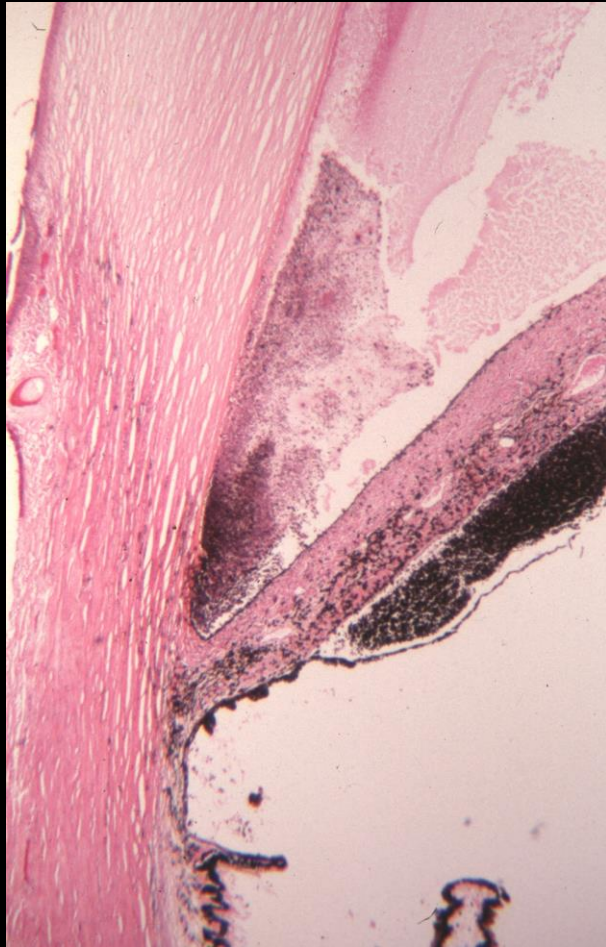
Apoptosis of all layers of the retina

Formation of a deep optic cup (Schnabel's cavernous atrophy)

A progressive loss of axons



# Pigment Dispersion and Neutrophilic Inflammation



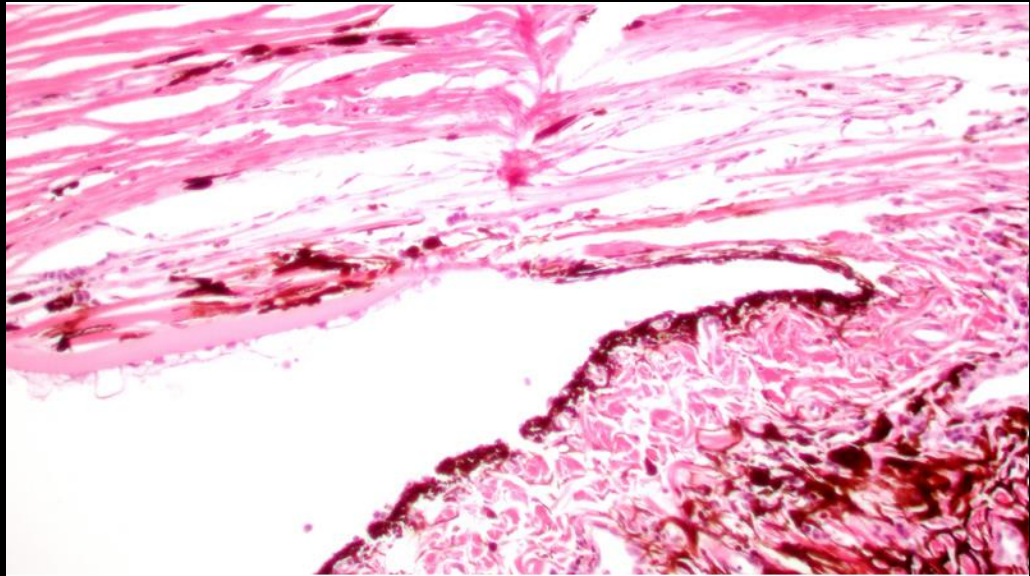
# Pigment Dispersion in Primary Glaucoma

- Distinguish superior from inferior angle by pigment alone
  - 1 to 3 Days: 92%
  - 4 to 7 Days: 95%
  - Chronic: 79%
- Cells Stripped from Iris
  - 1 to 3 Days: 43%
  - 4 to 7 Days: 75%
  - Chronic: 55%
- Pigmented Cells in the Angle
  - 1 to 3 Days: 64%
  - 4 to 7 Days: 95%
  - Chronic: 50%

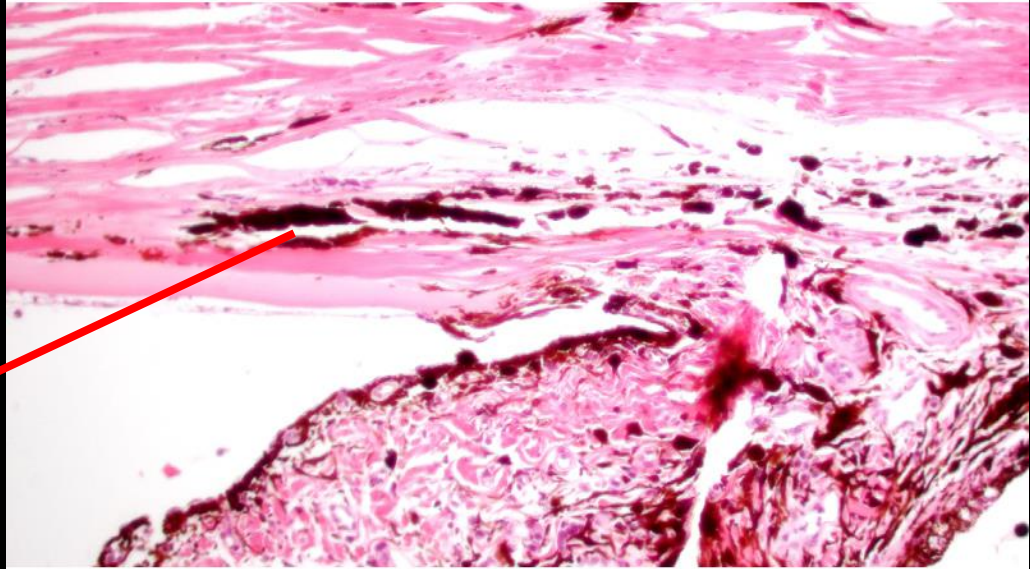
Reilly CM et al. (2005)  
Canine goniodysgenesis-related glaucoma: a morphologic review of 100 cases looking at inflammation and pigment dispersion. *Vet. Ophthalmol.*

# Neutrophilic Inflammation

- 1 to 3 Days: 86%
- 4 to 7 Days: 50%
- Chronic: 15%



Upper Angle



Lower Angle

Pigment Dispersion





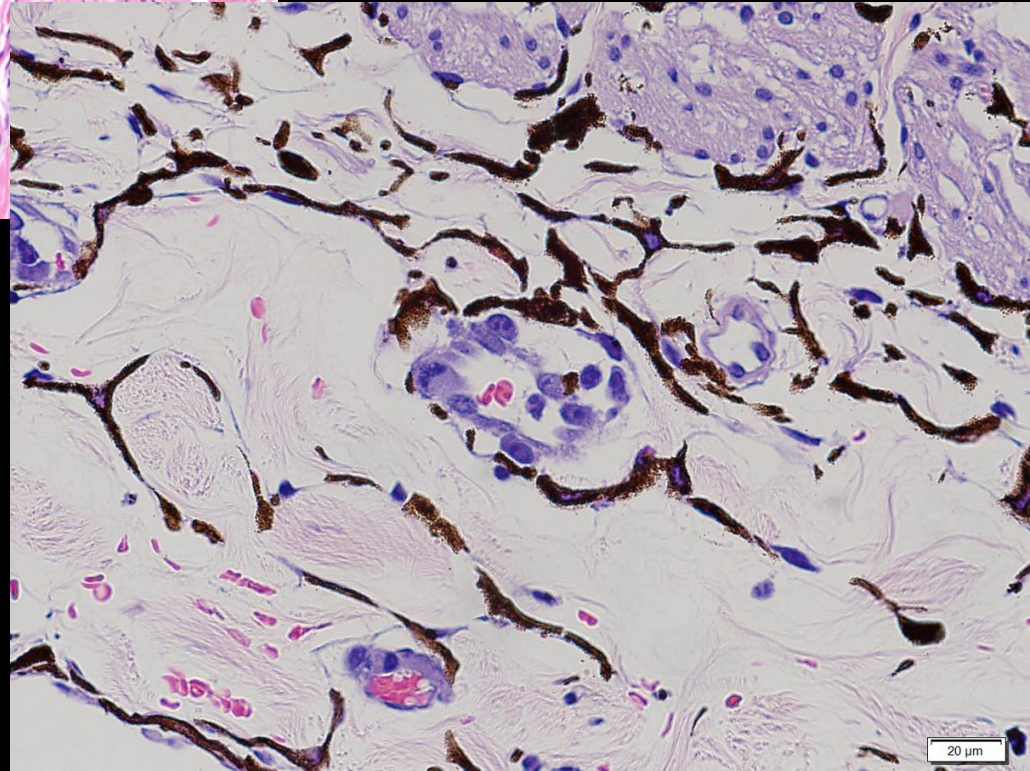
Neutrophils

This histological section shows the iridocorneal angle. The upper portion features a dense, purple-stained area representing a collection of neutrophils. Below this, the tissue layers of the angle are visible, including the endothelium and stroma, stained in shades of pink and purple.

Early Changes in the  
Iridocorneal Angle

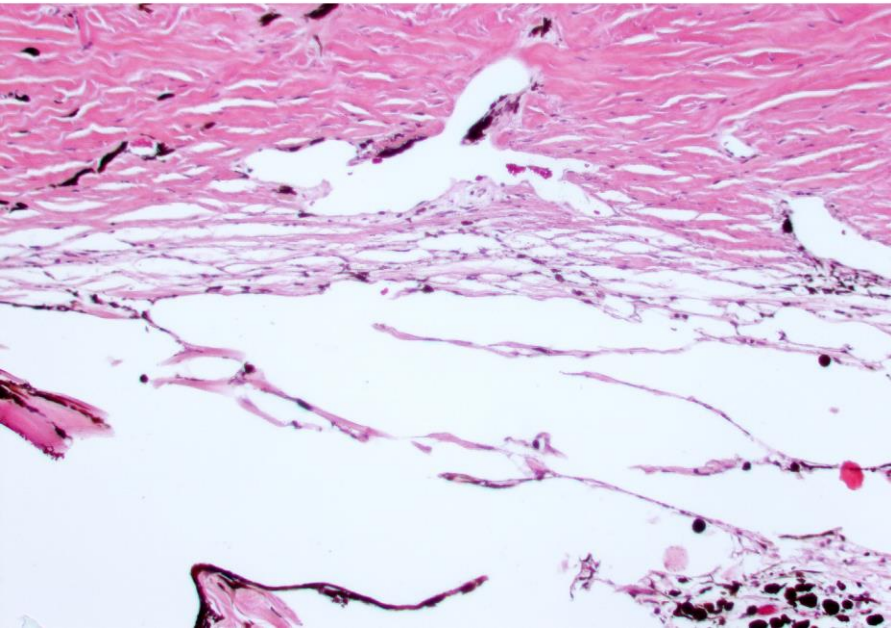
30 hour Glaucoma

Neutrophils and stromal  
and endothelial  
cell Proliferation



# Evidence of Gradual Atrophy of the Corneoscleral Trabecular Meshwork

Normal Cocker Sp. 2 with Goniodysgensis



Normal

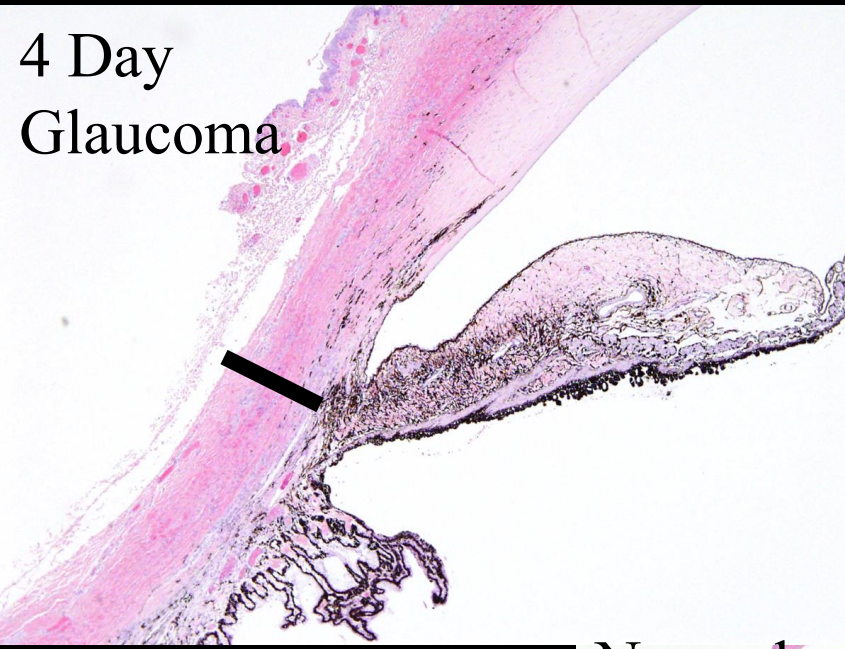


One Day Trabecular Meshwork

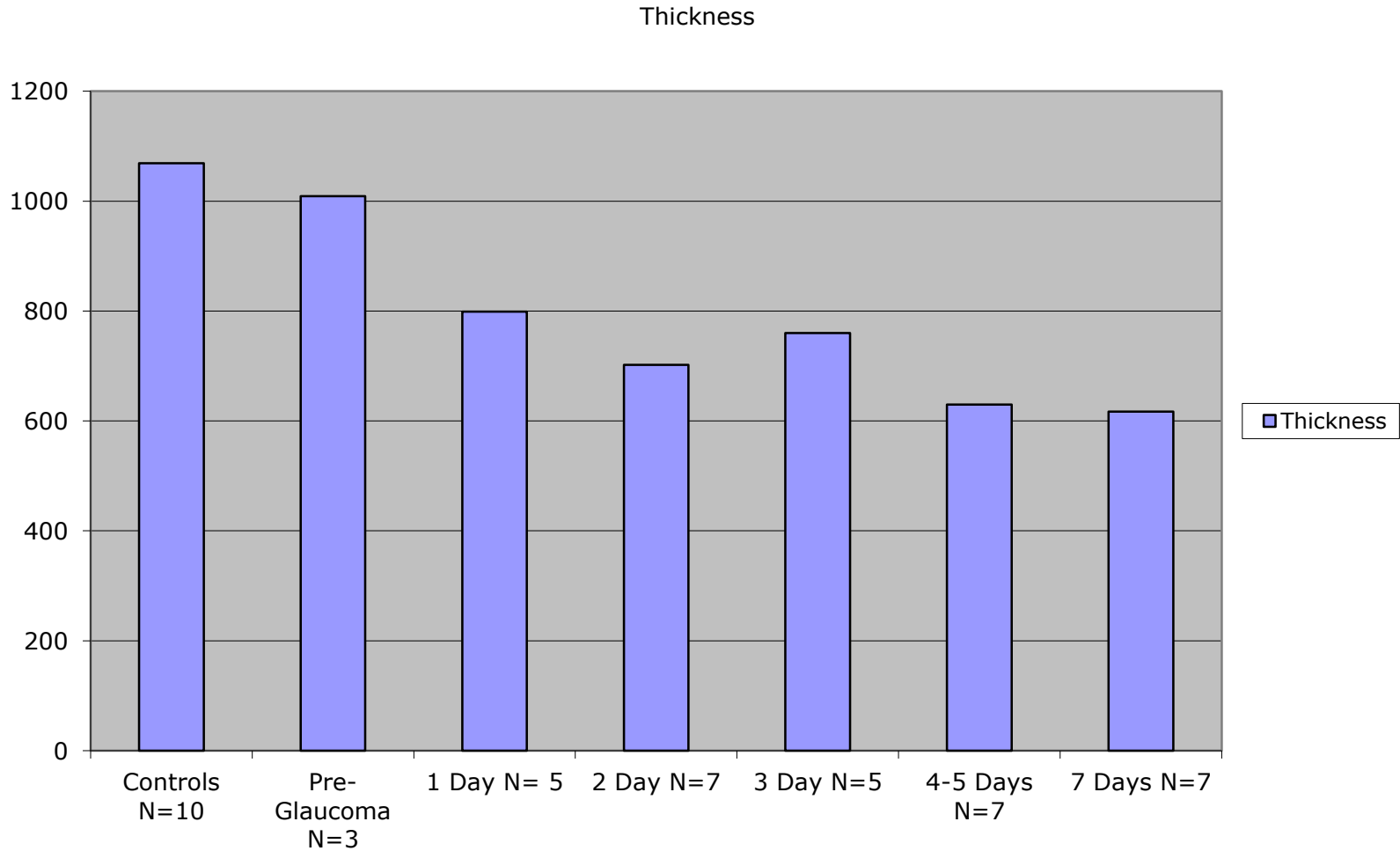
Atrophic

# Buphthalmos

## Scleral Thickness



# Average Scleral Thickness, $\mu$



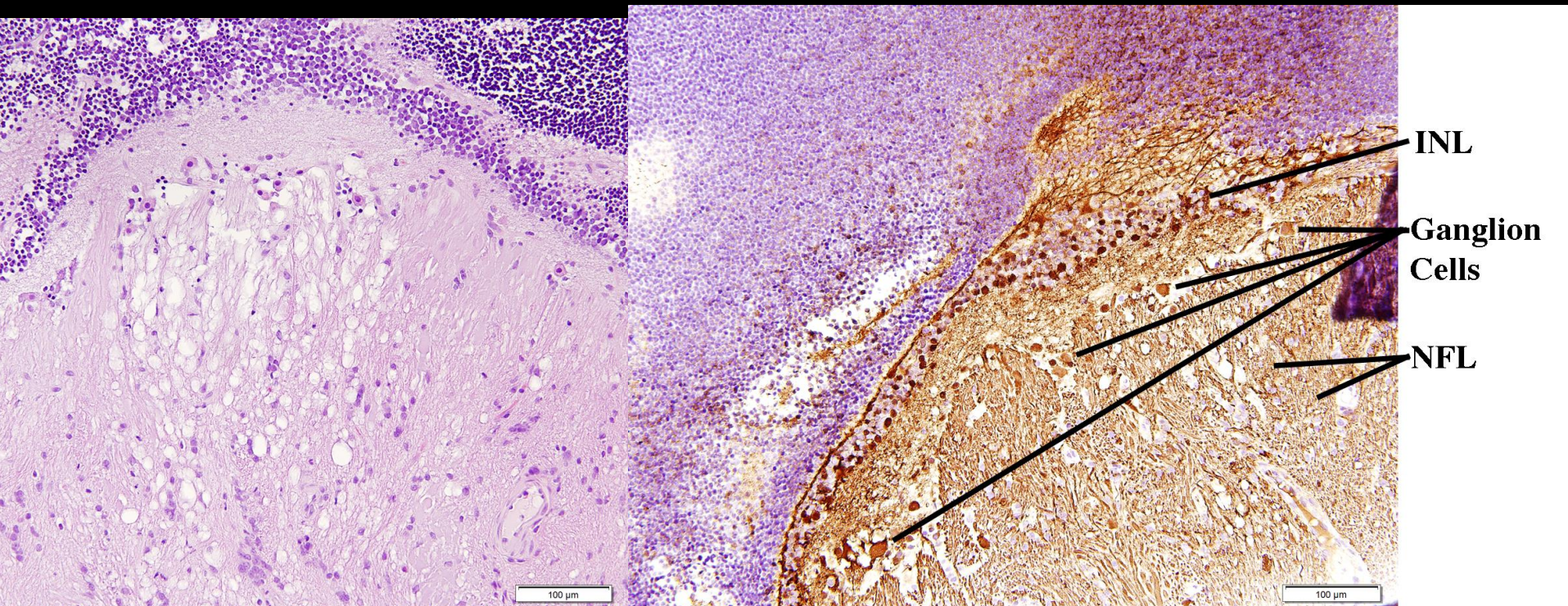


# Effects of Primary Glaucoma on the Optic Nerve and the Retina



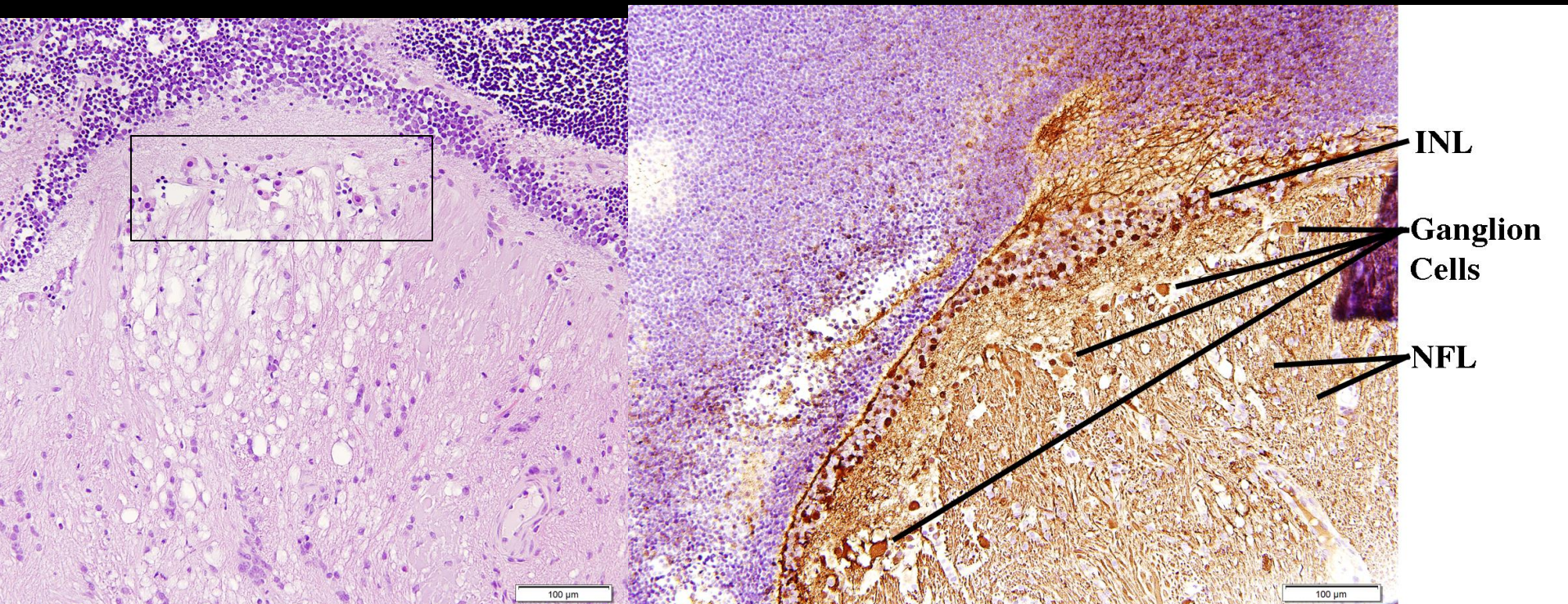
1-day Glaucoma

# Effects of Primary Glaucoma on the Optic Nerve and the Retina



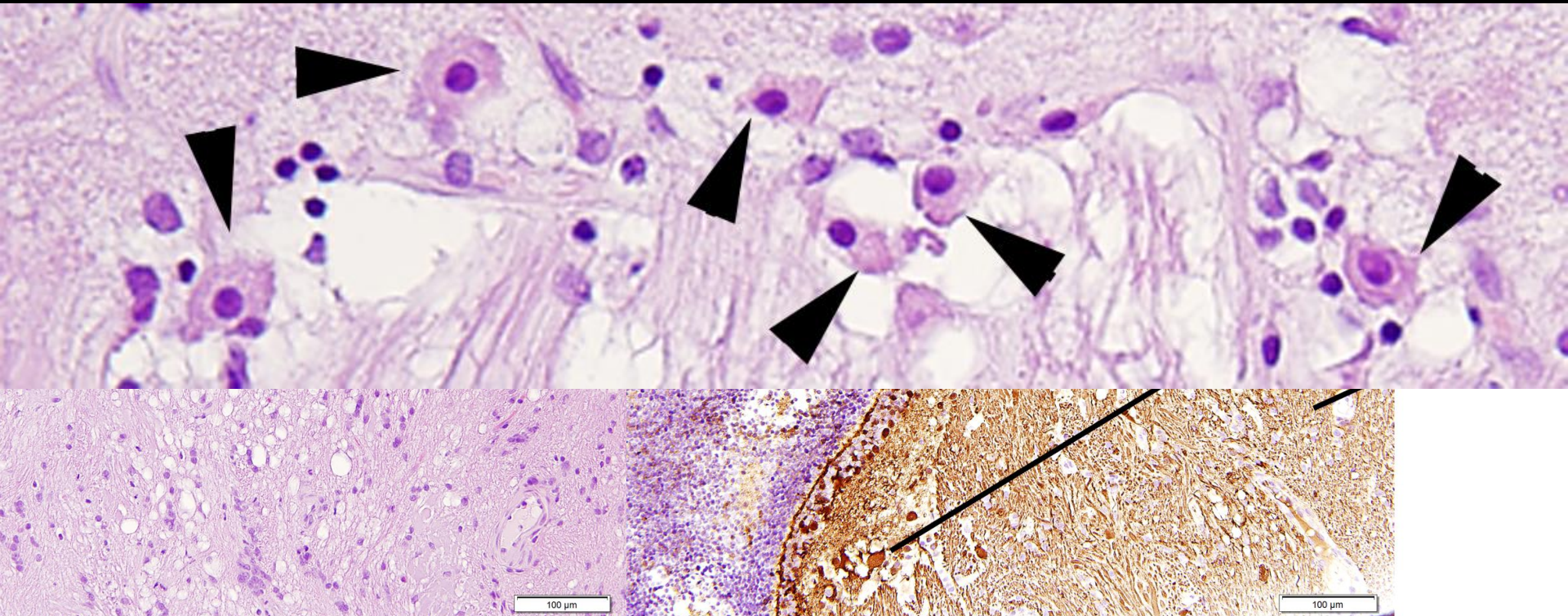
1-day Glaucoma

# Effects of Primary Glaucoma on the Optic Nerve and the Retina



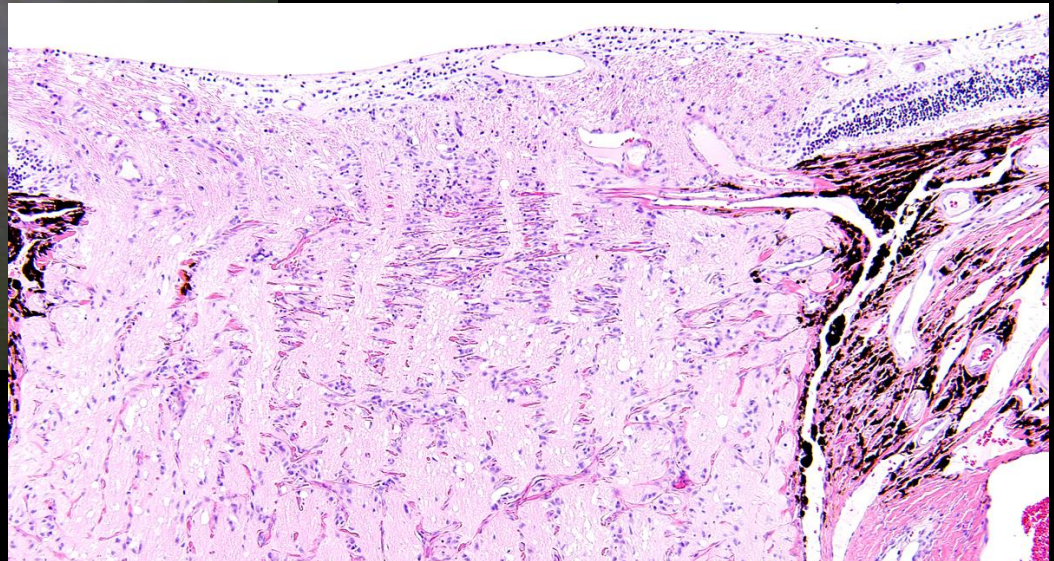
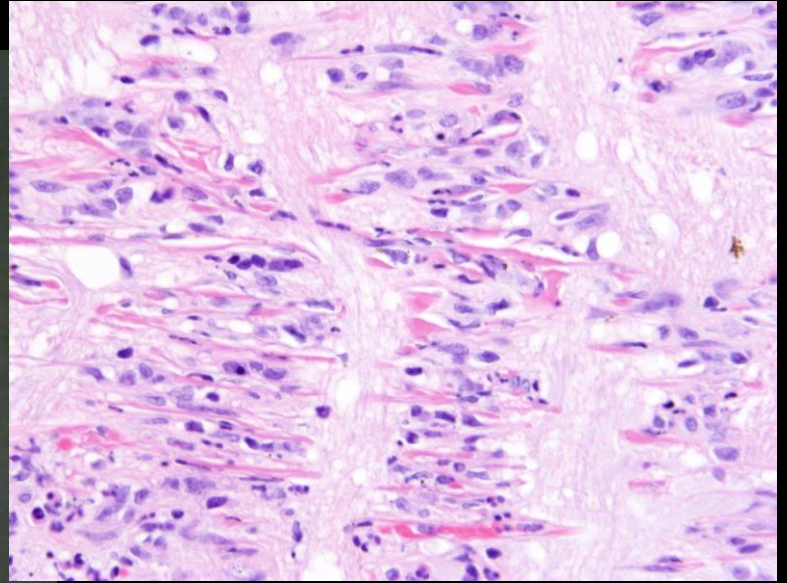
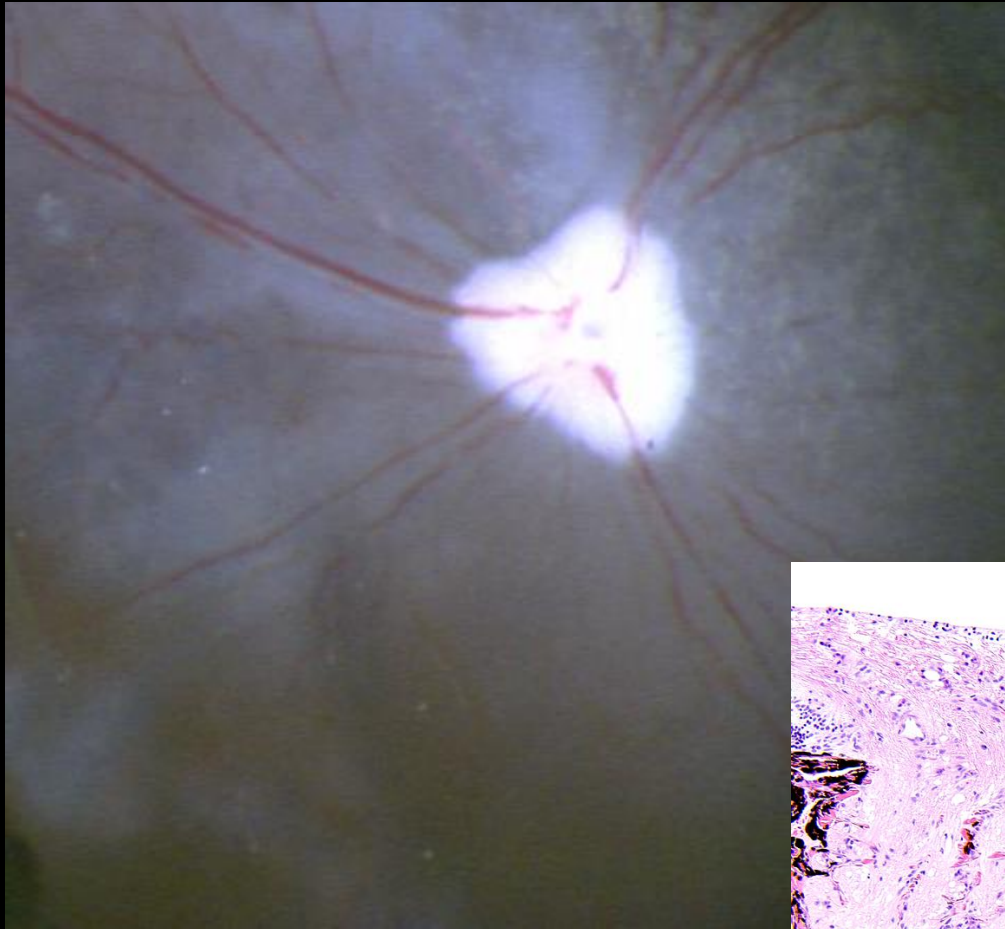
1-day Glaucoma

# Effects of Primary Glaucoma on the Optic Nerve and the Retina

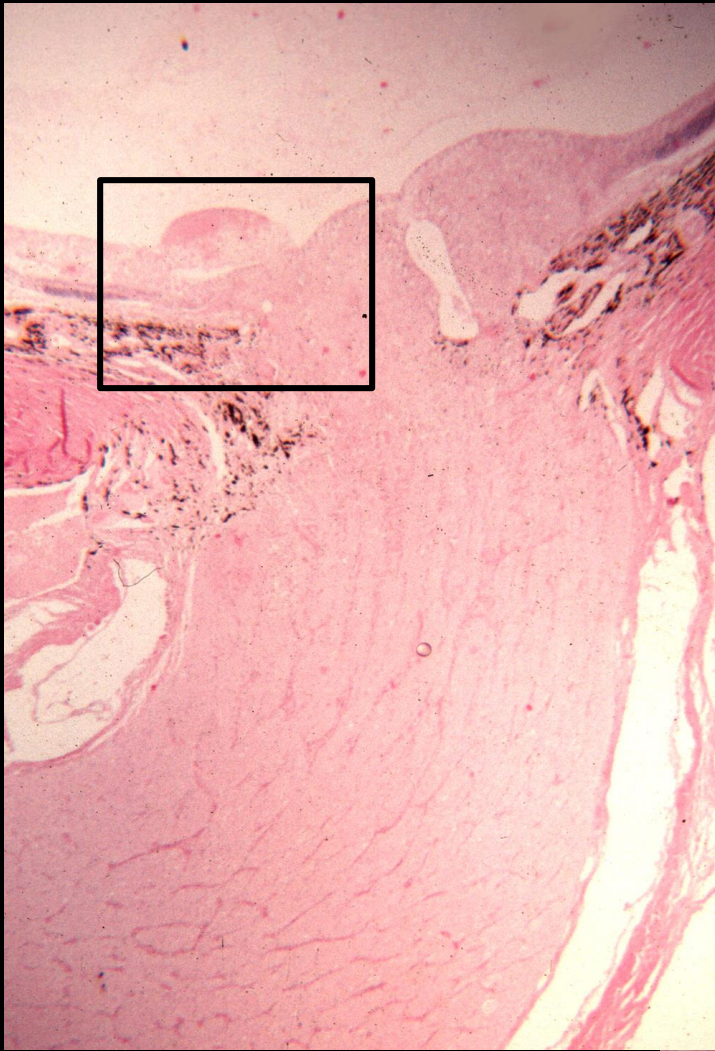


1-day Glaucoma

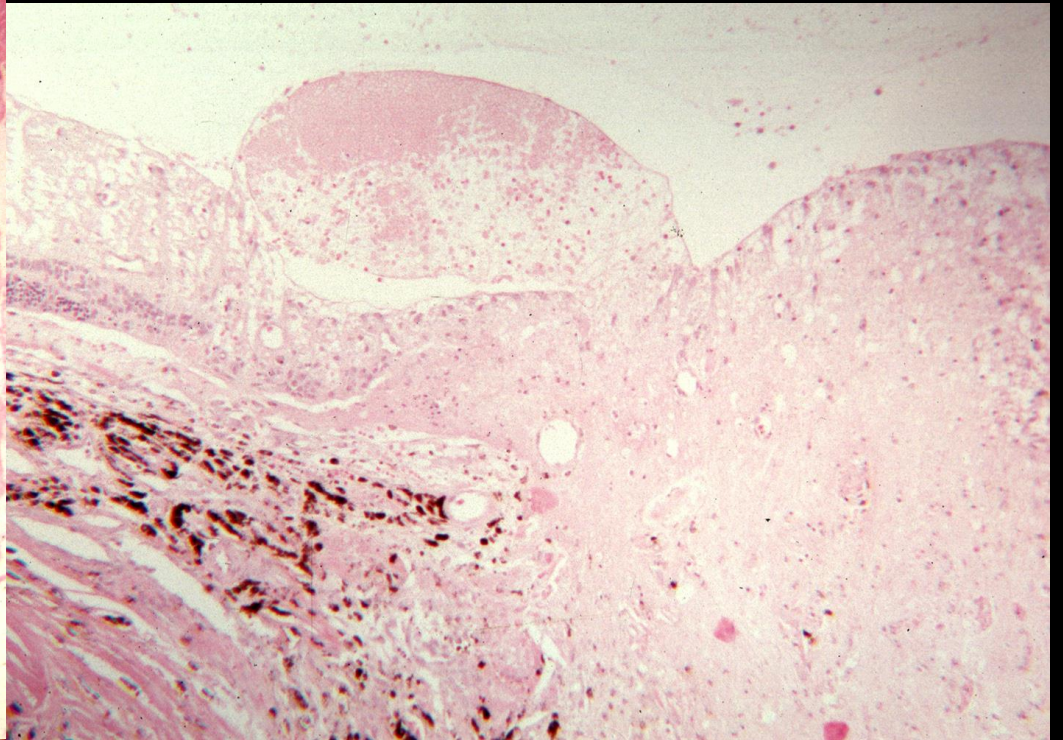
# 30 hour Glaucoma

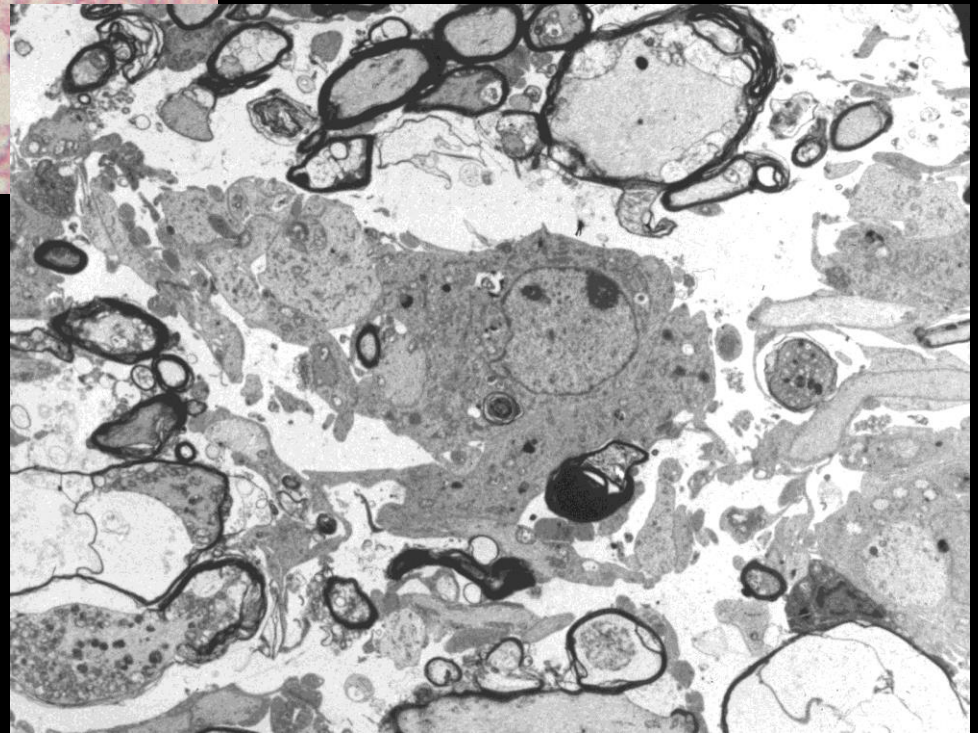
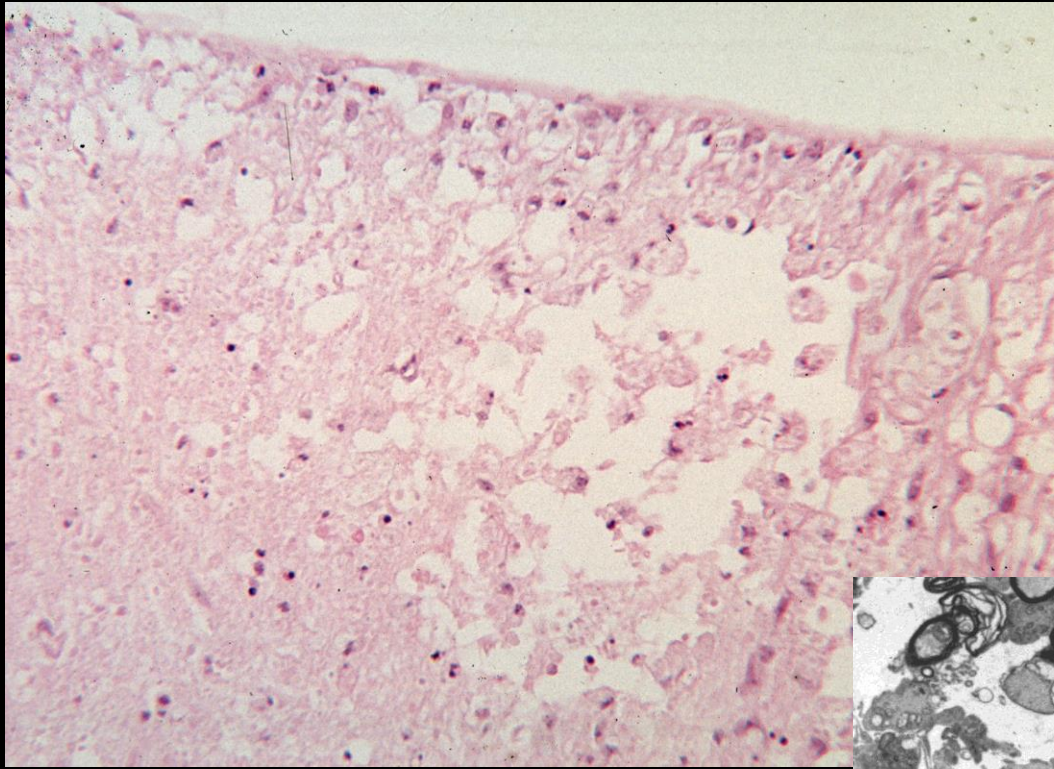


# Optic Nerve 2 to 4 Days



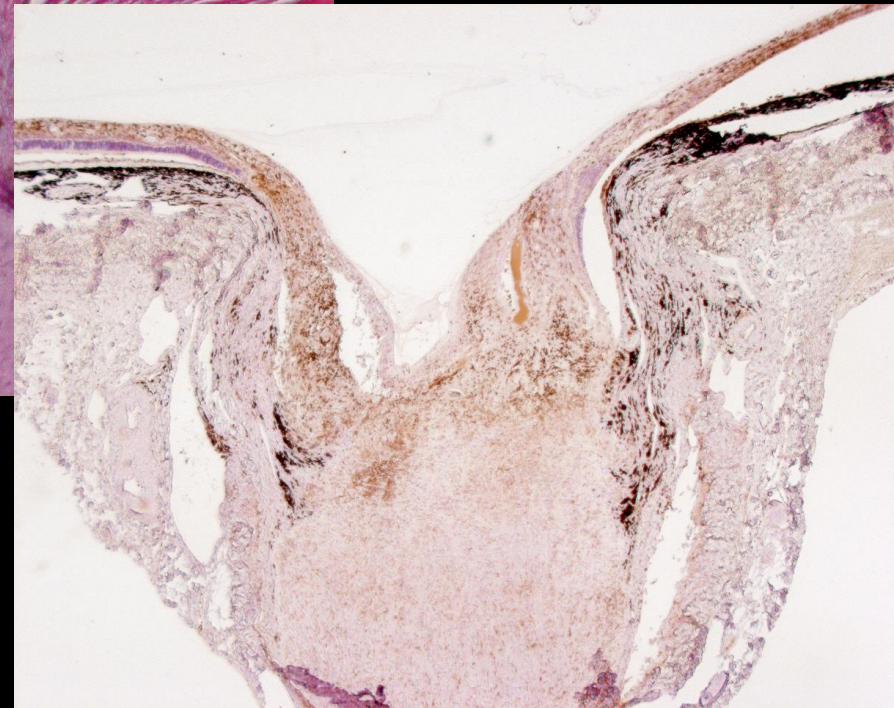
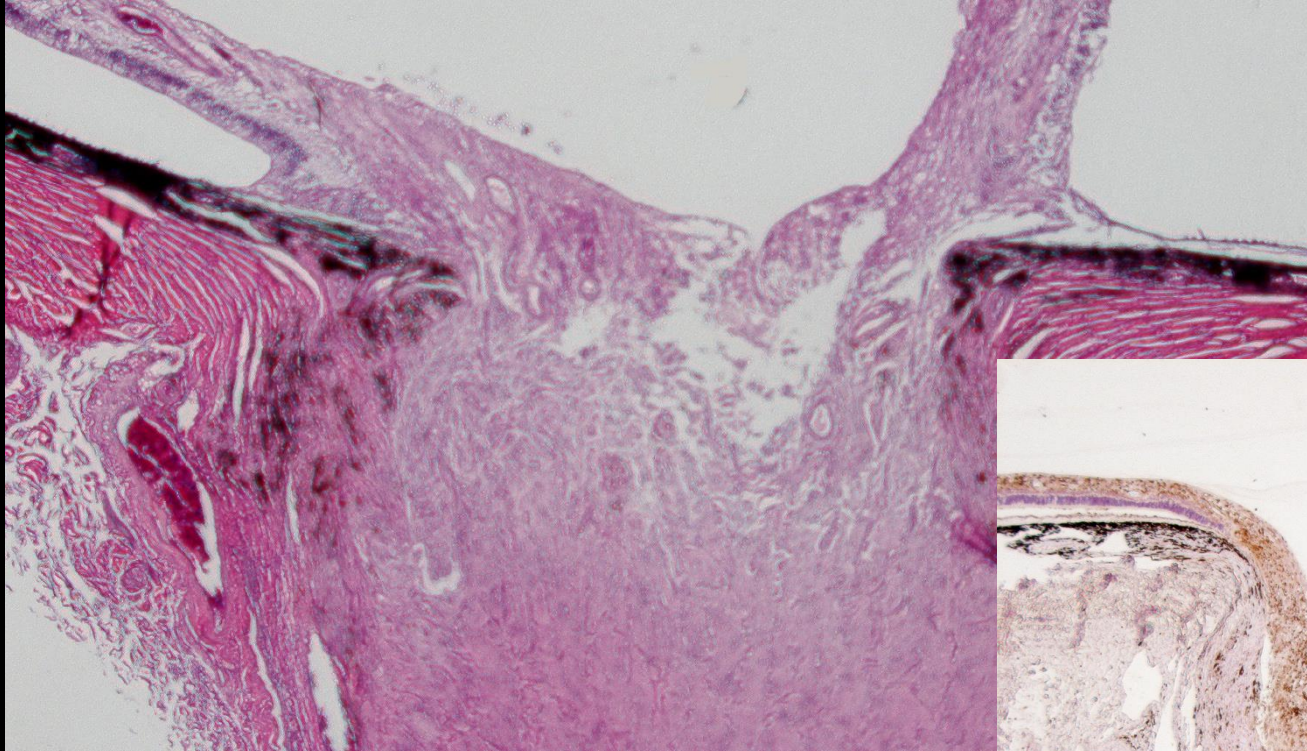
Necrosis of the neuropil





4 Day Optic Nerve Head  
Phagocytosis/Malacia

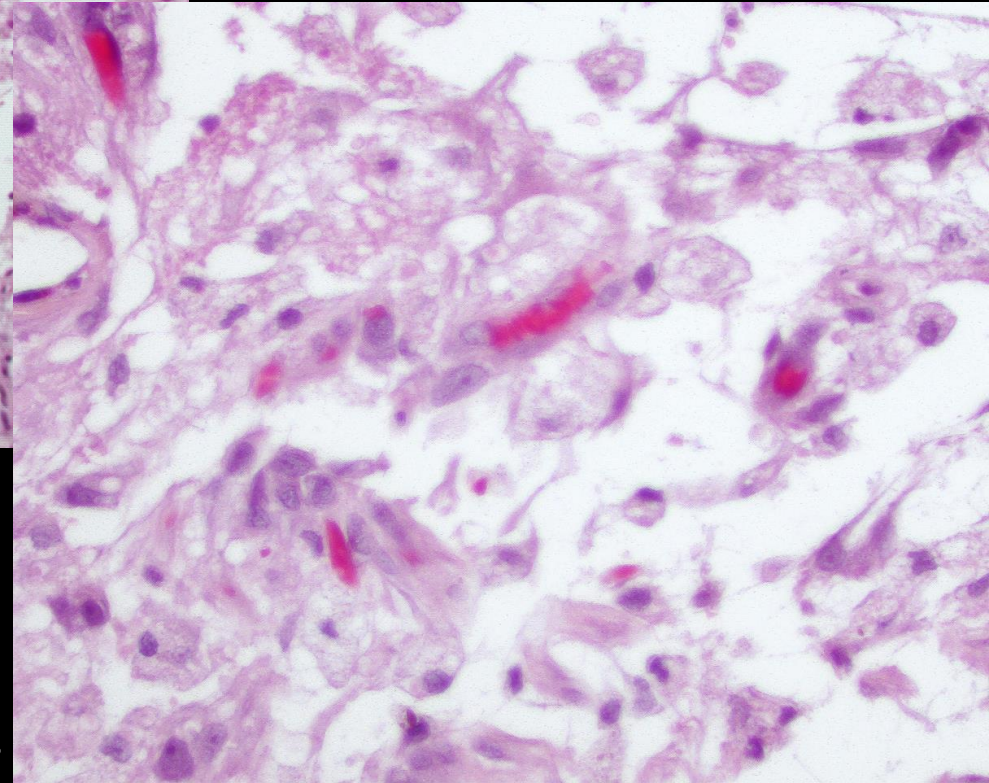
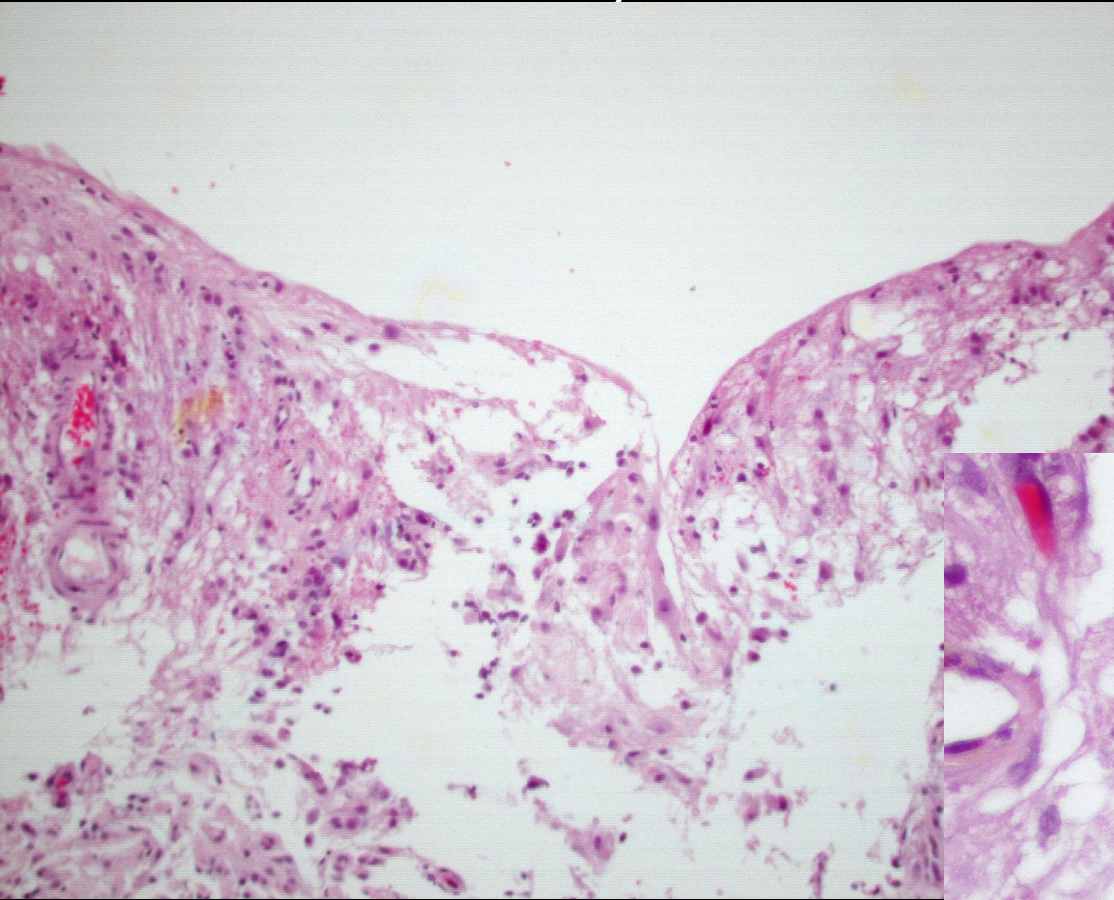
# Five day Canine Glaucoma



Stained for phagocytes

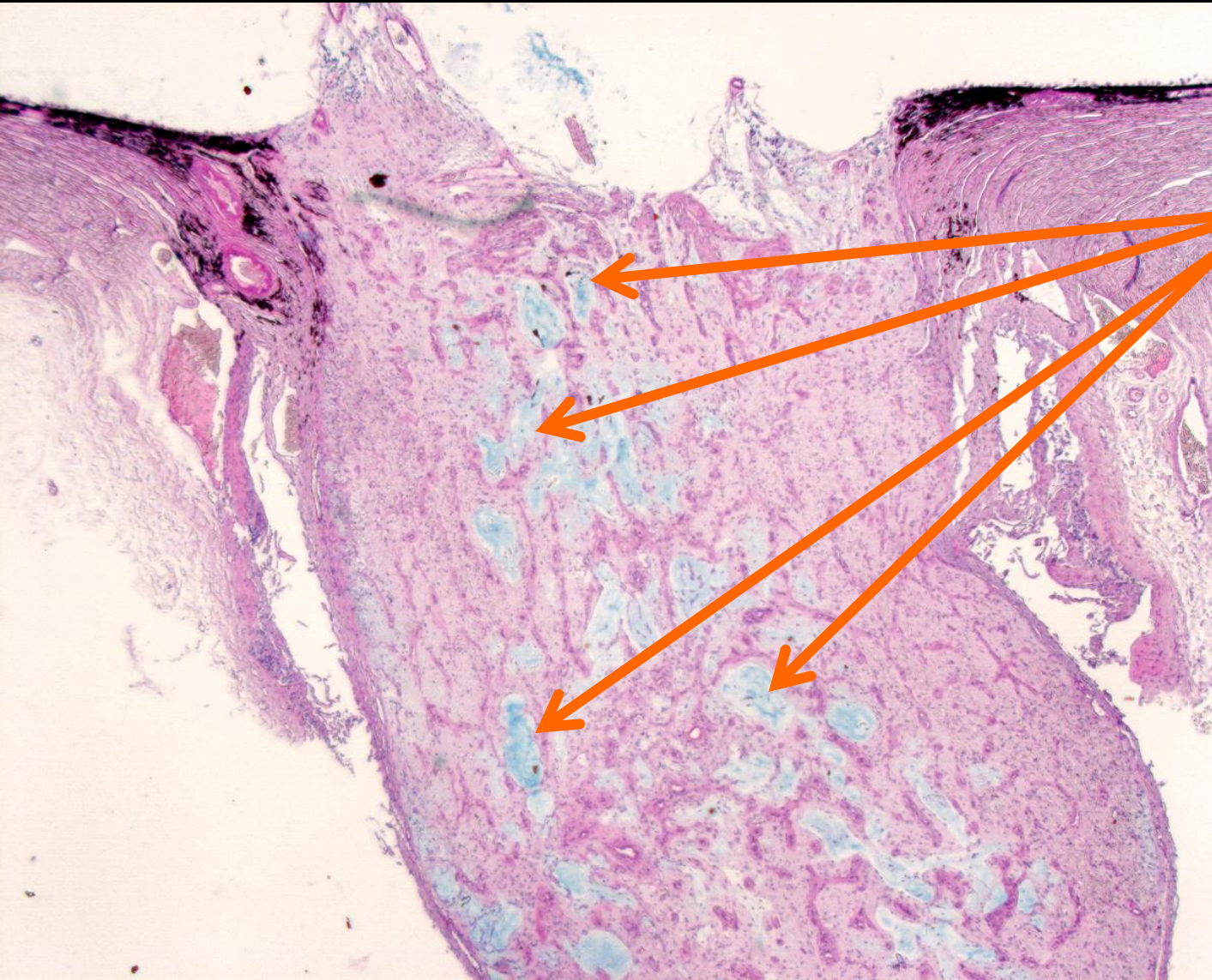


# 5 day Canine Glaucoma



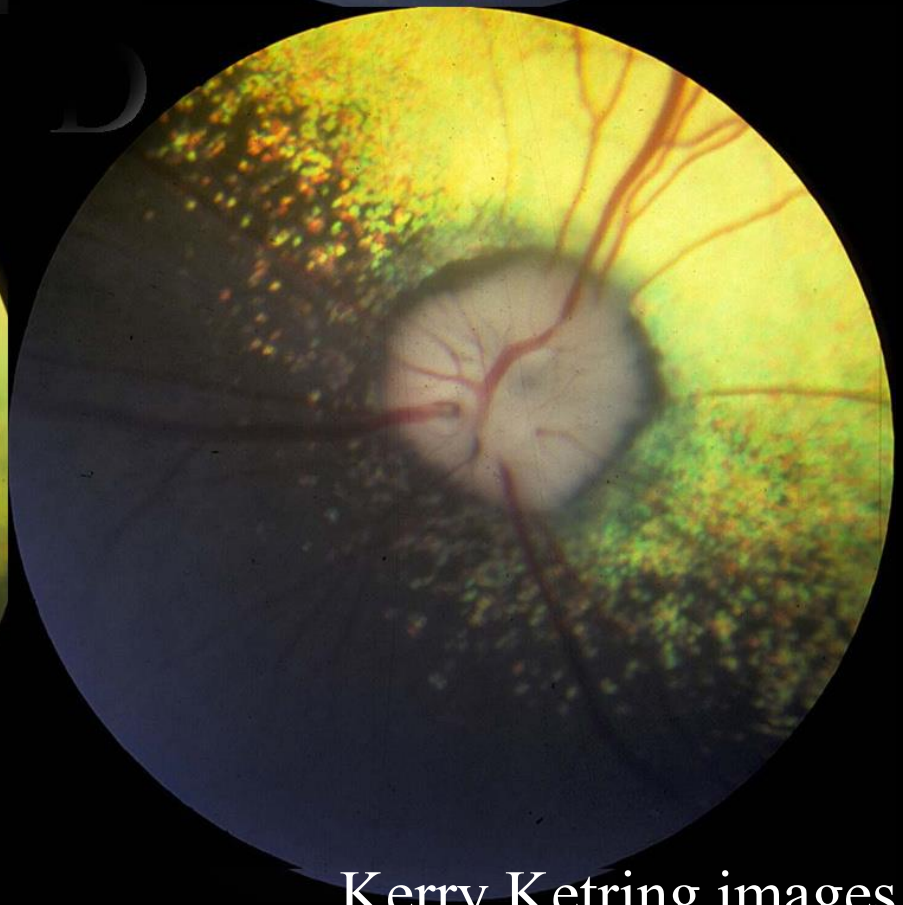
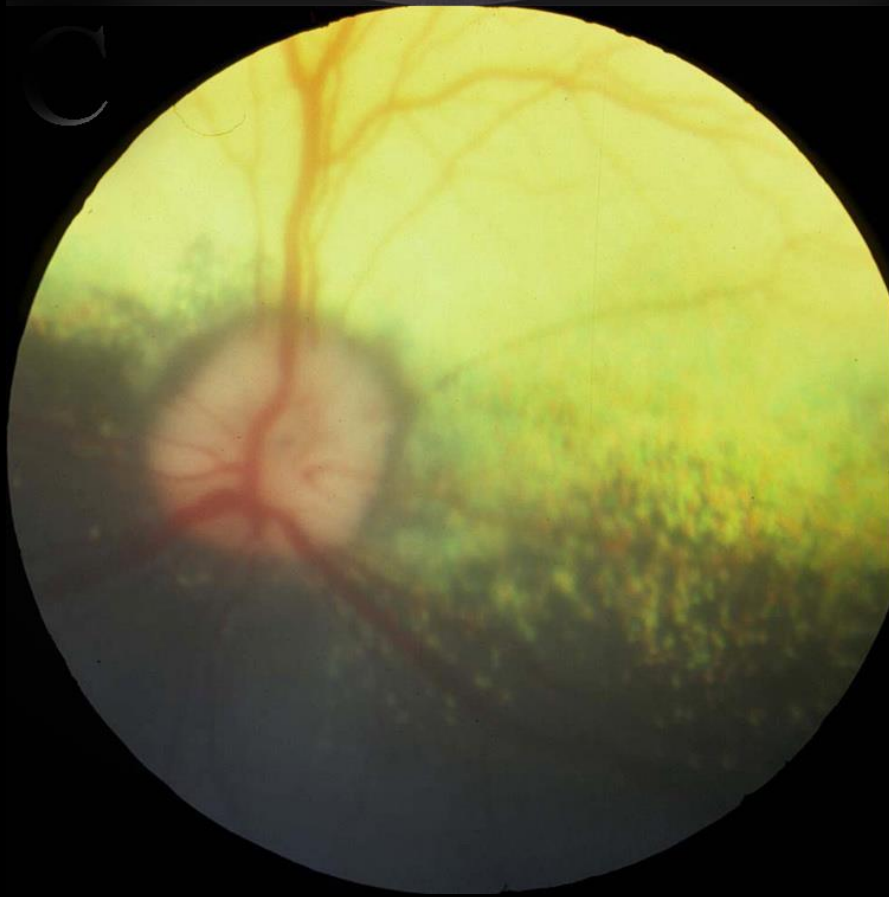
Gitter cell macrophages

# Schnabel's cavernous optic atrophy



Entrapped  
vitreous

# Early Progression of Retinal Disease



Kerry Ketring images

# 2 to 4 Day Glaucoma (Canine)



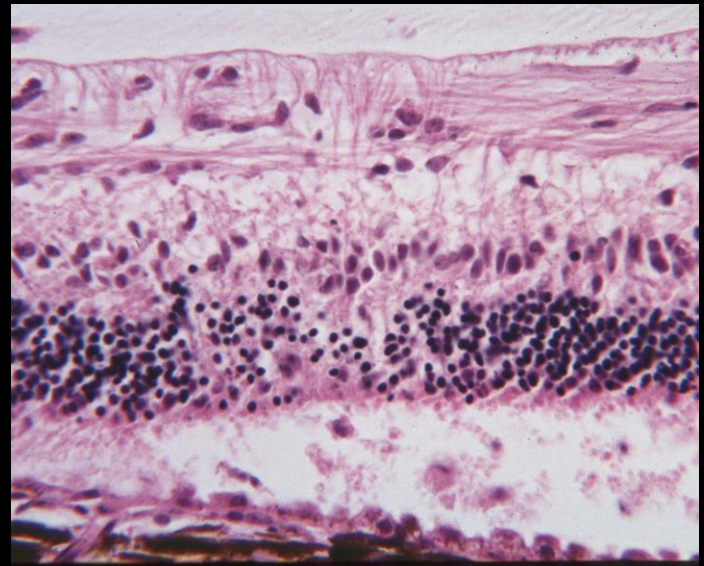
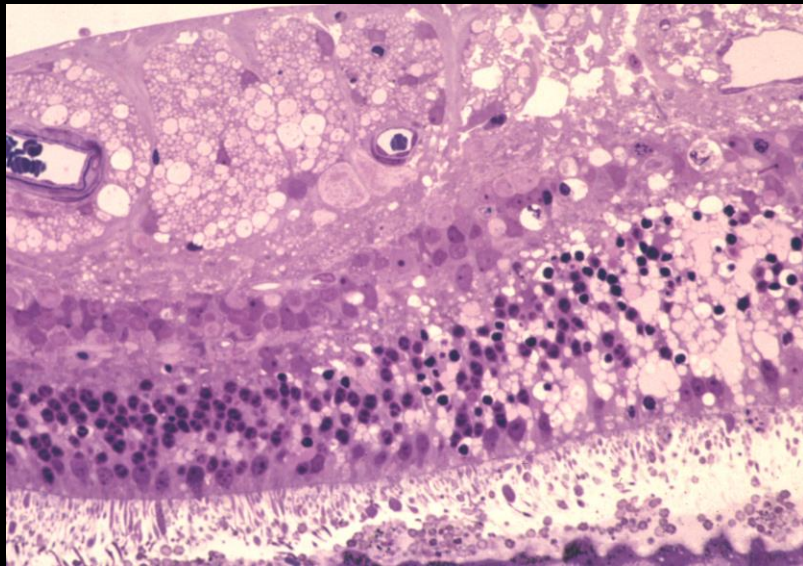
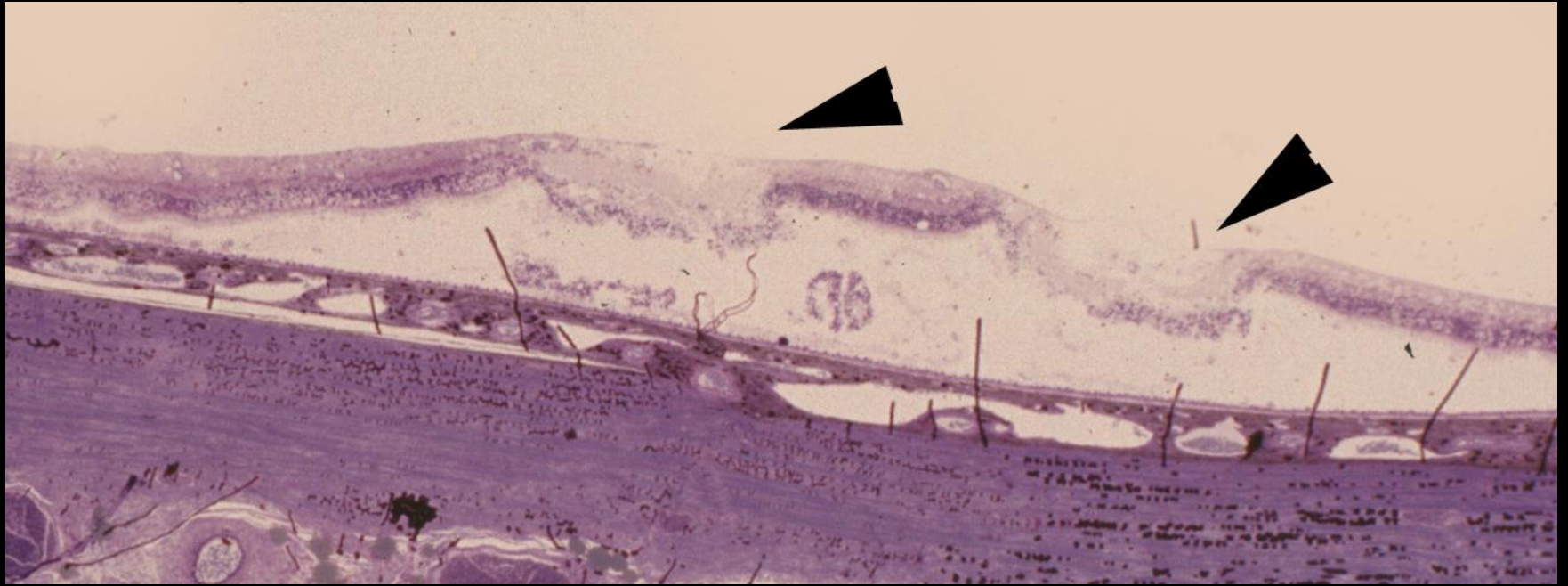
Four Day Glaucoma

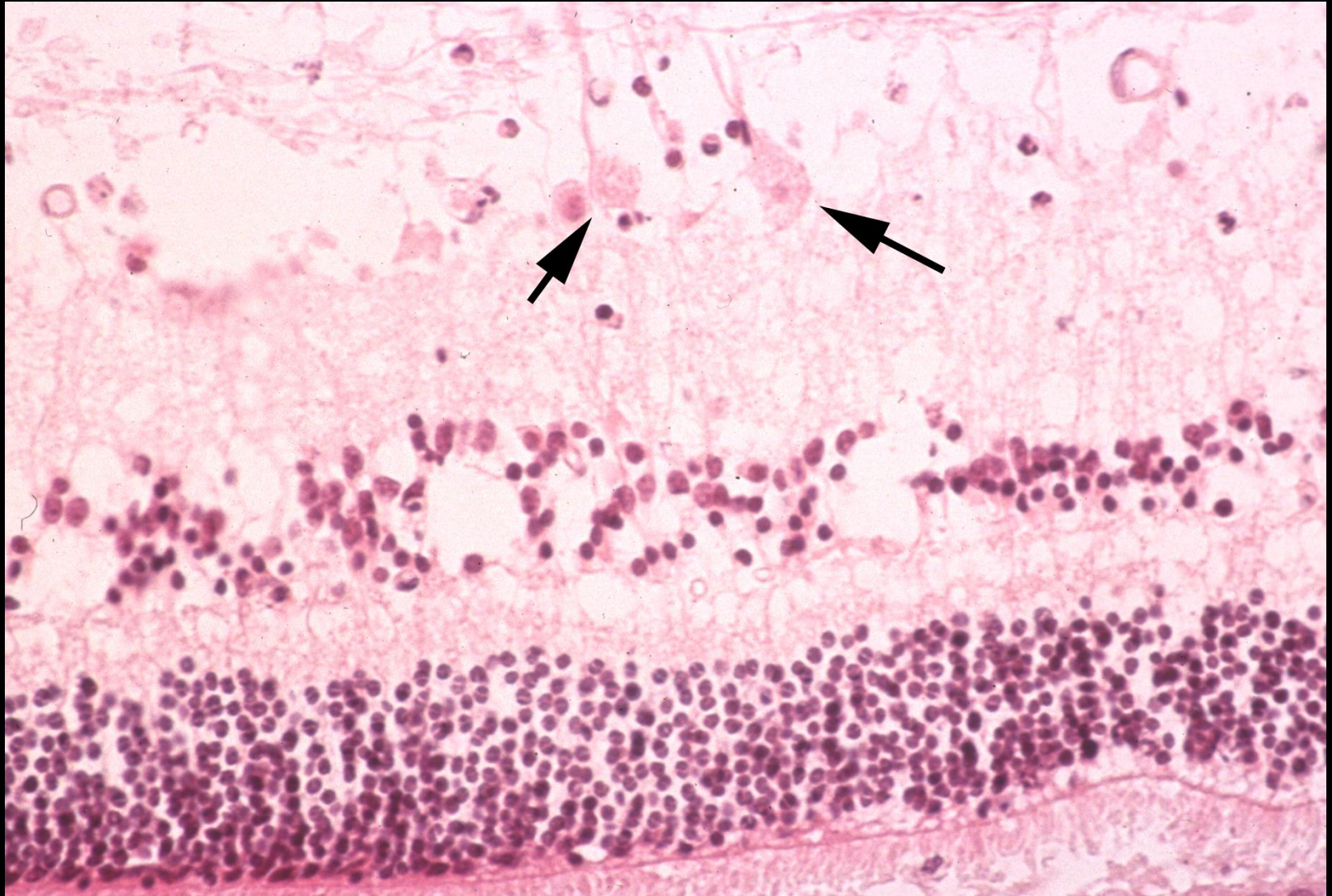
# 2 to 4 Day Glaucoma (Canine)



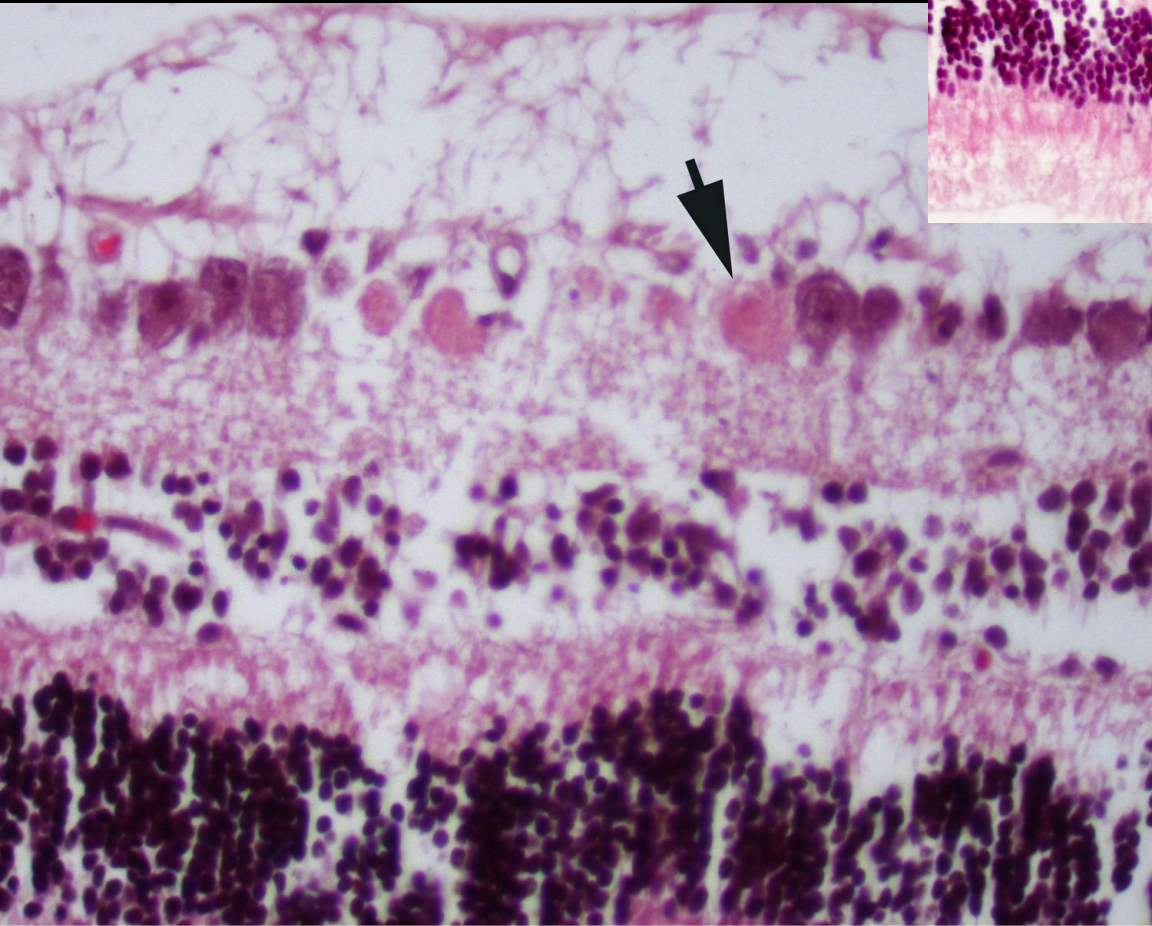
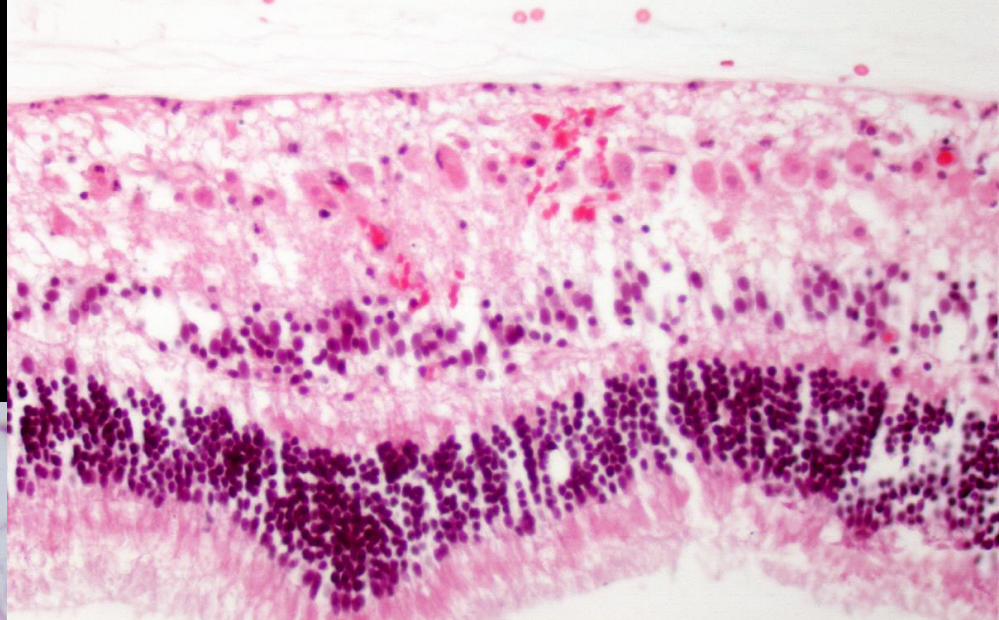
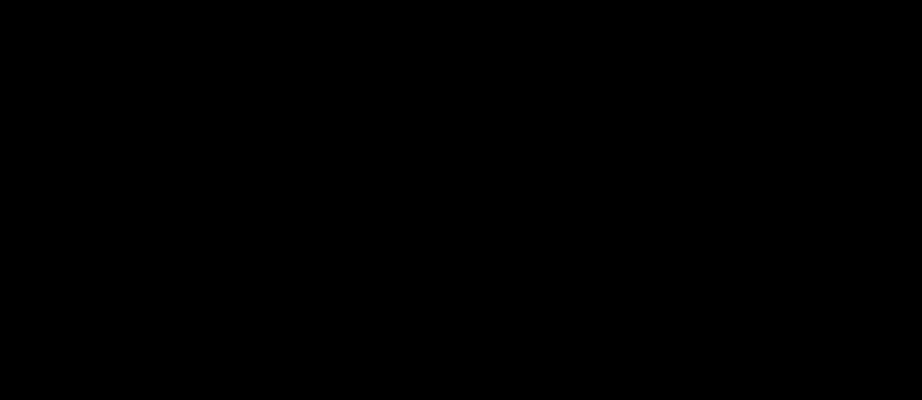
Sampled for  
Histopathology

Four Day Glaucoma





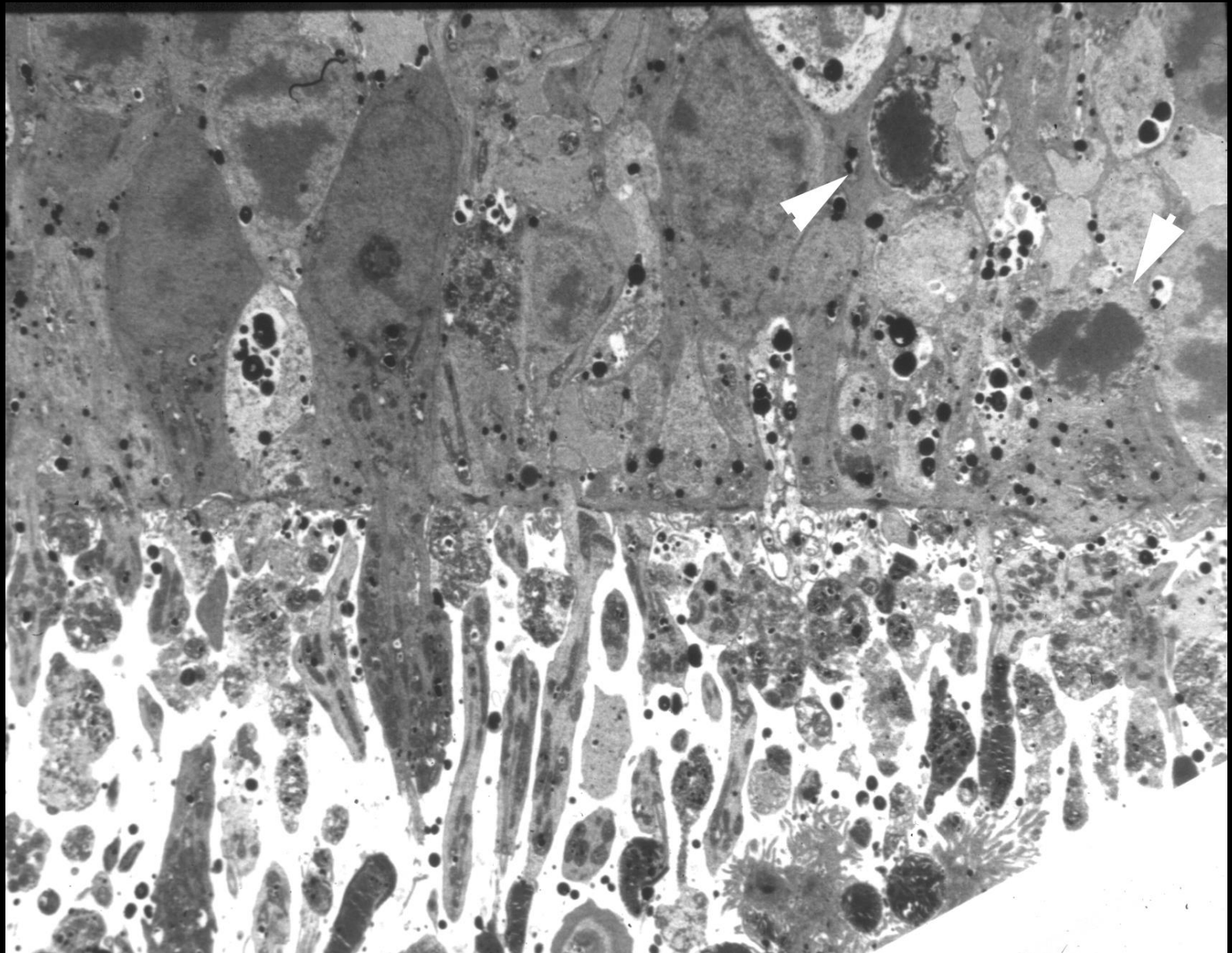
One Day Glaucoma  
Red-Dead Ganglion Cells



Proptosis, 3 days

Glaucoma 2 Days after Laser Ablation of Melanocytoma

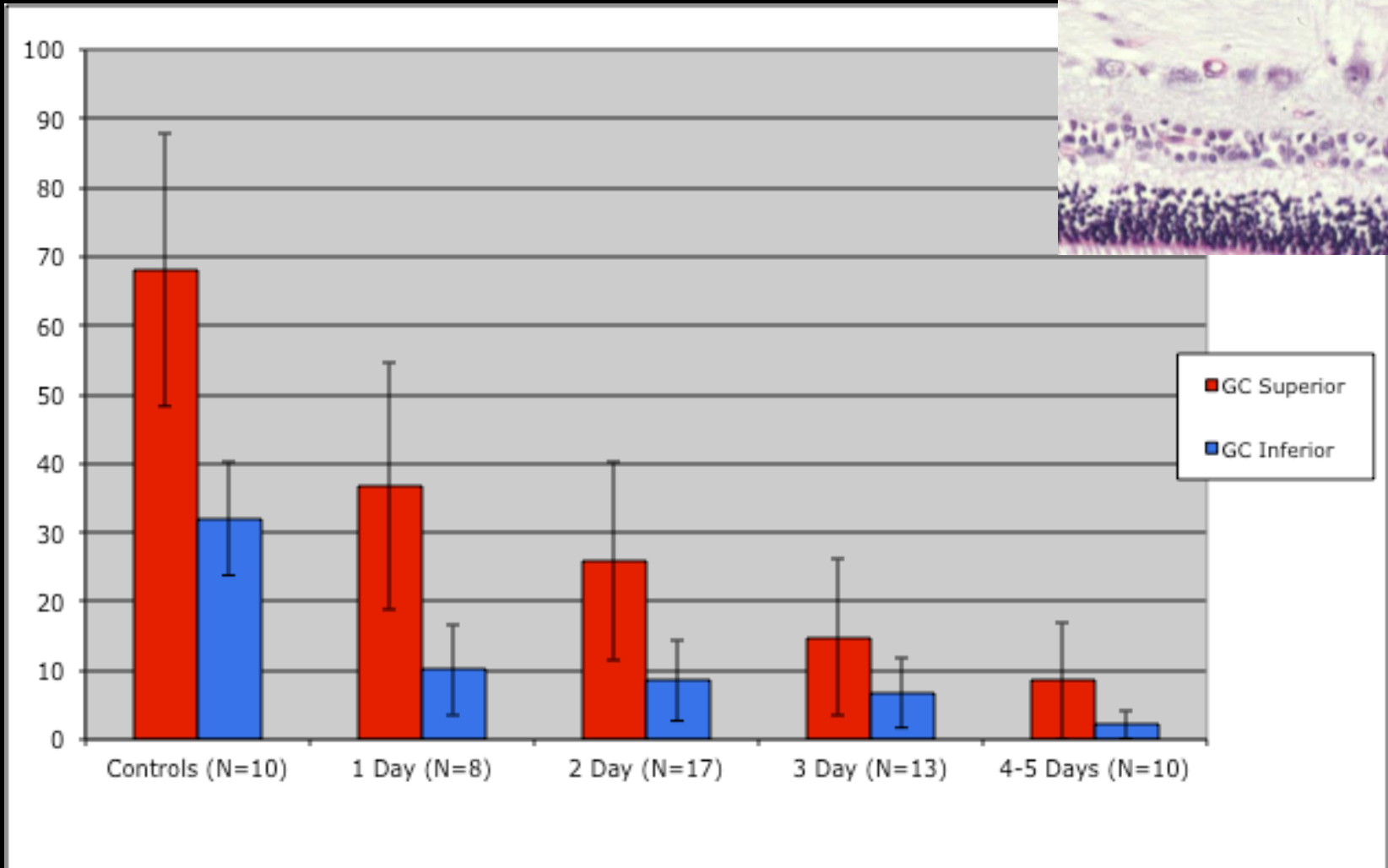
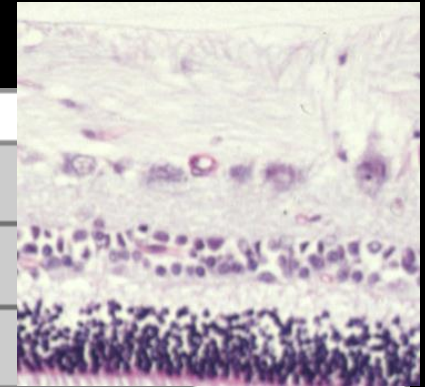




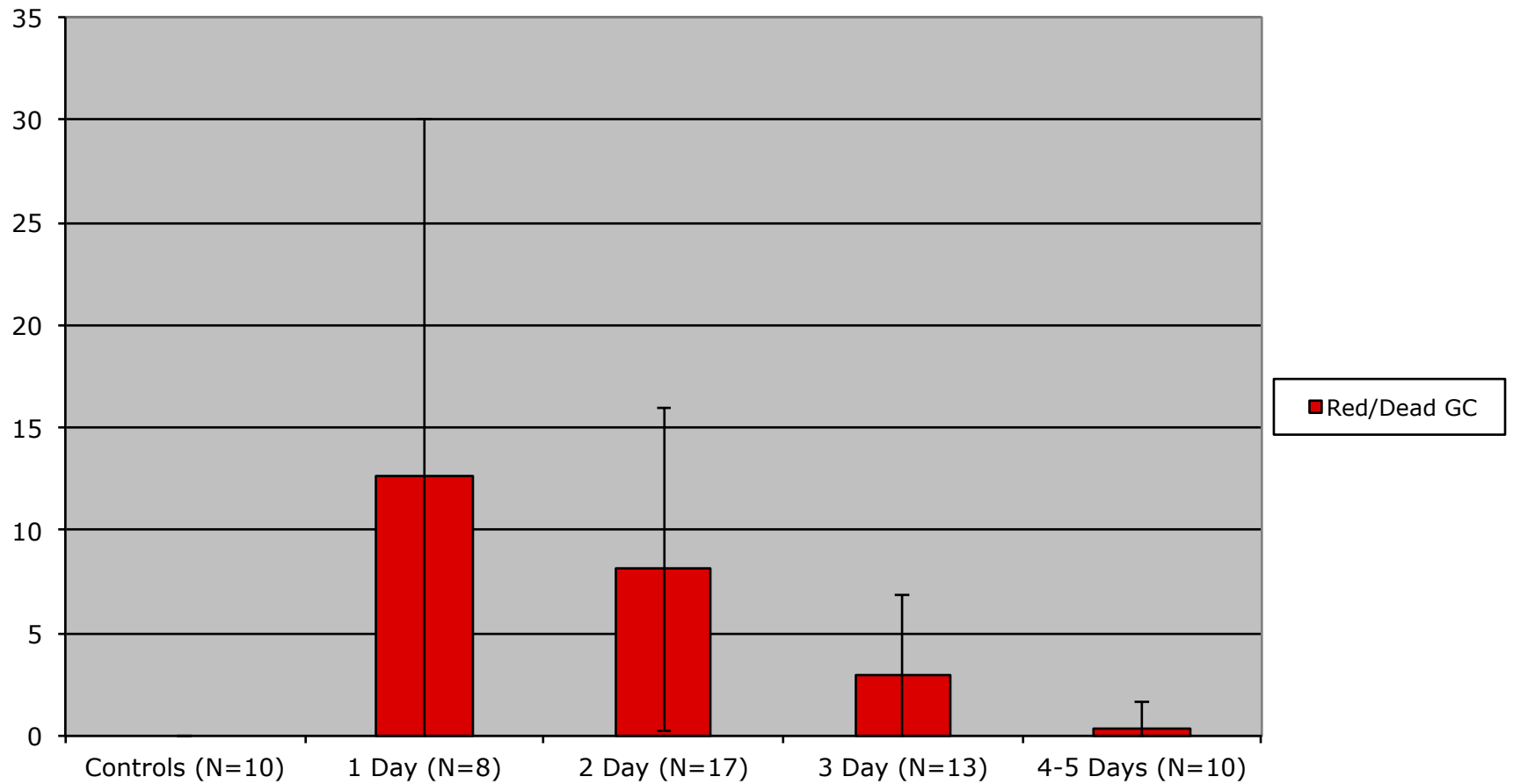
Electronmicrograph of 4-Day Glaucoma  
Apoptosis

# Average Ganglion Cell Counts

*This count includes "Red Dead" cells*

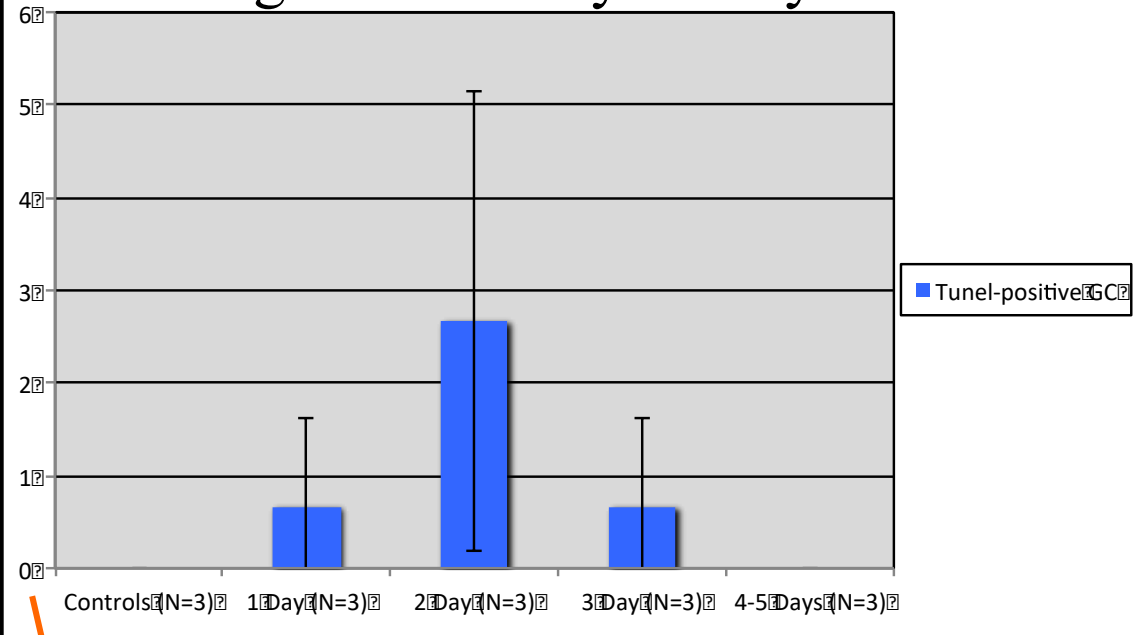


# “Red Dead” Ganglion Cells

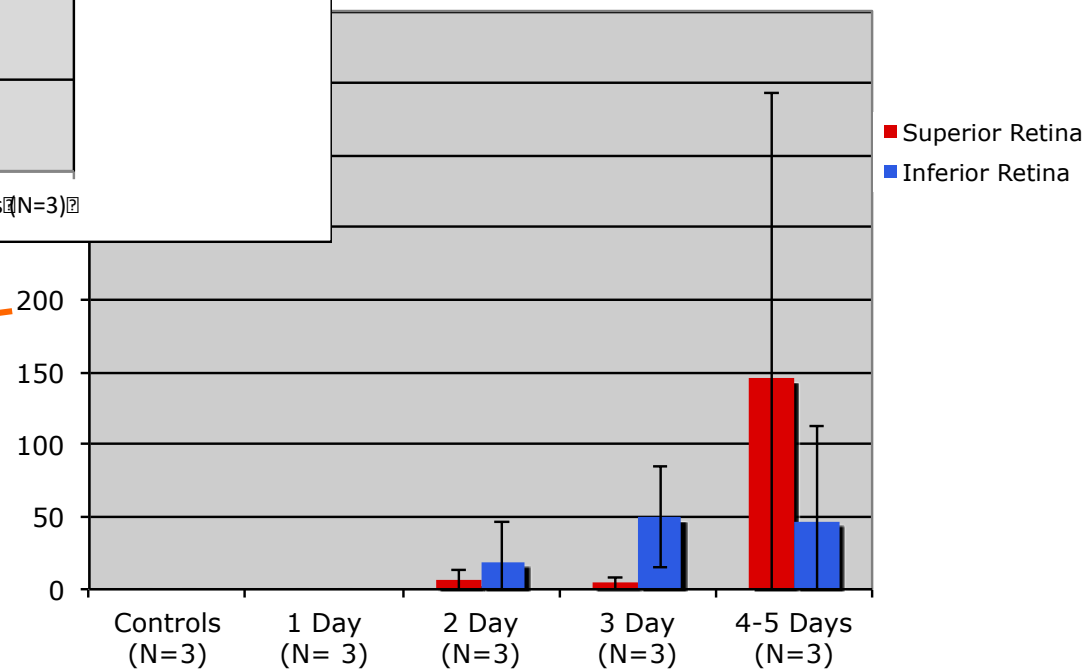


# TUNEL + cells by day

## Ganglion Cell Layer Only

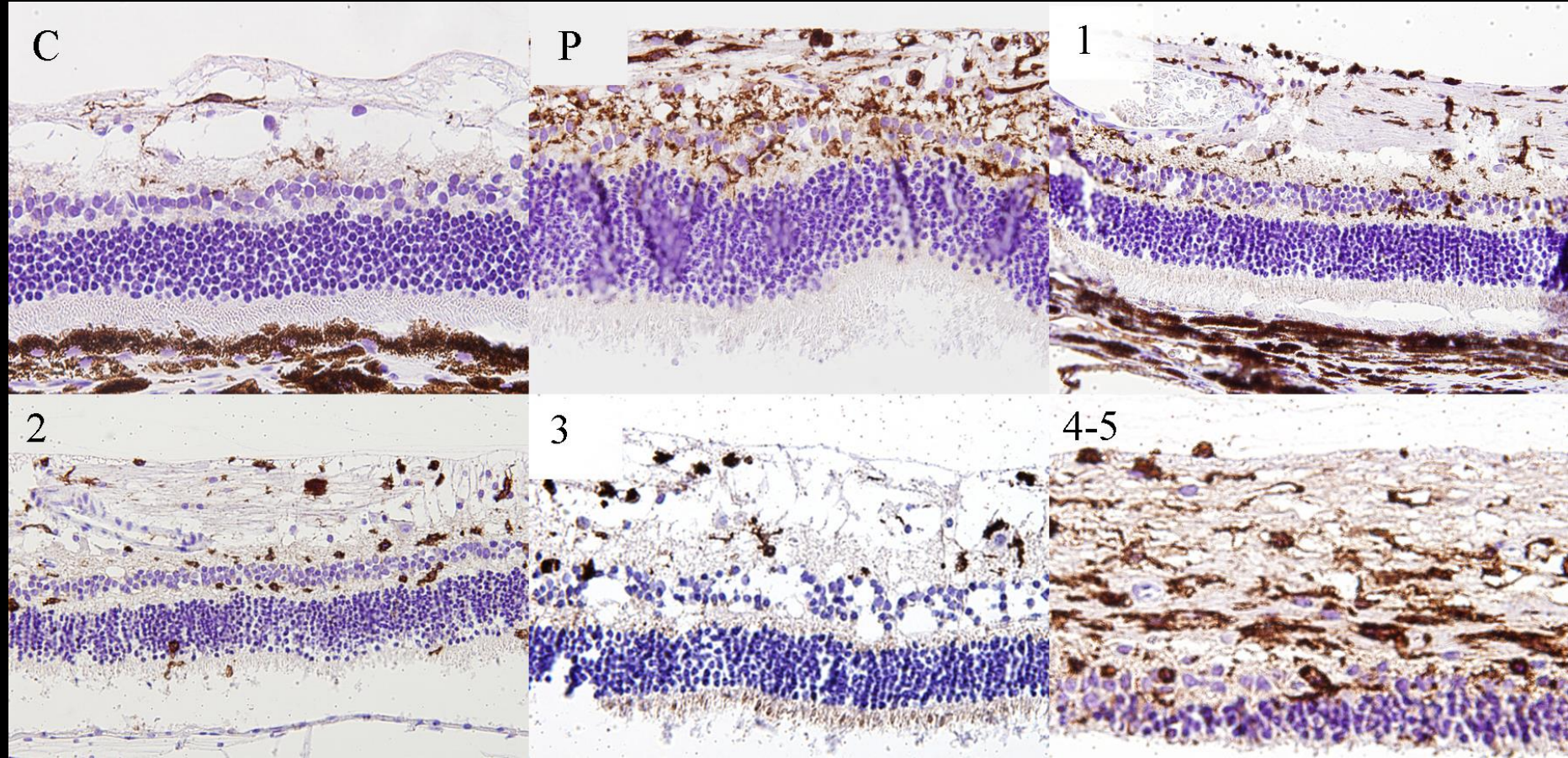


Notice the scale change



# Retinal MHC-2 Phagocytes

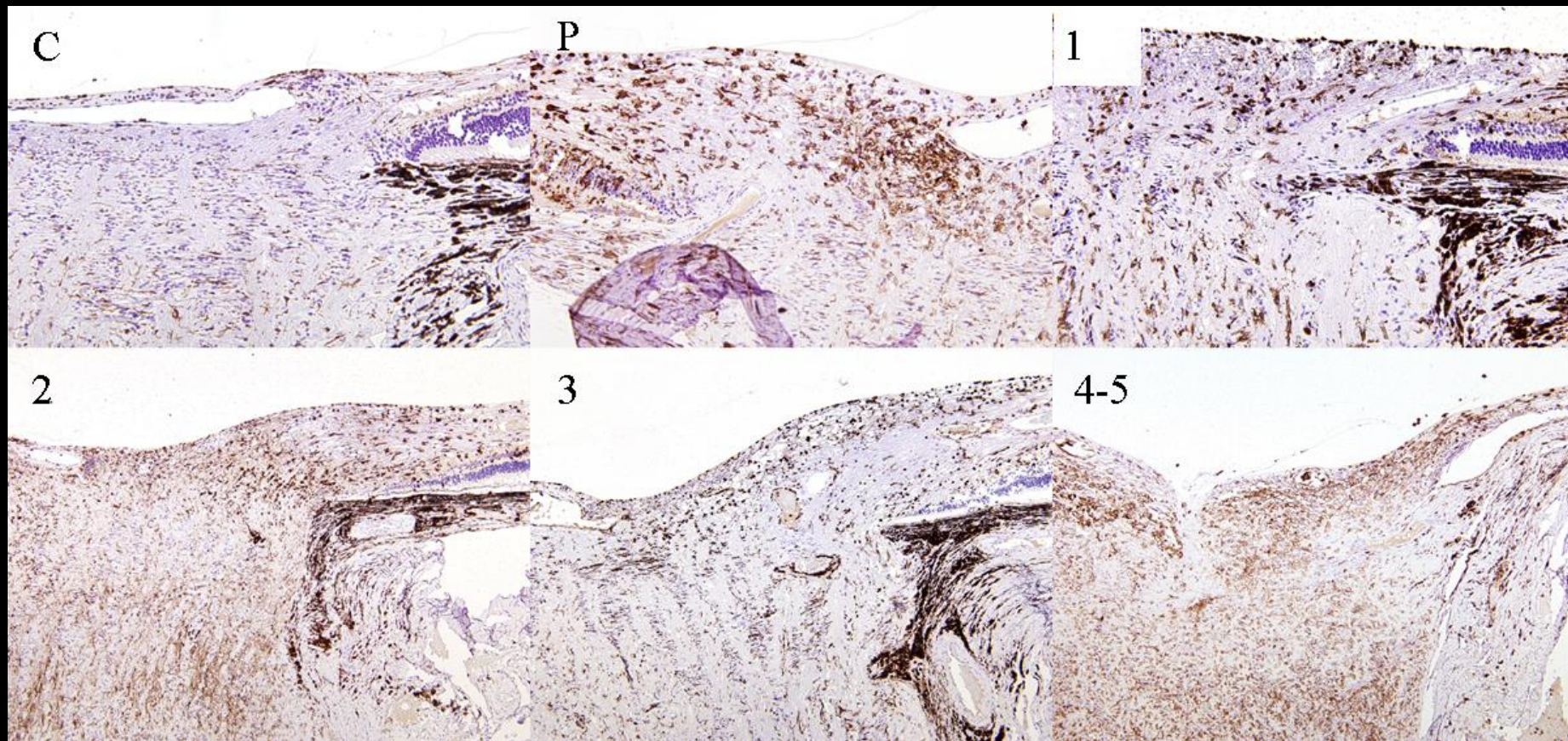
## Retina



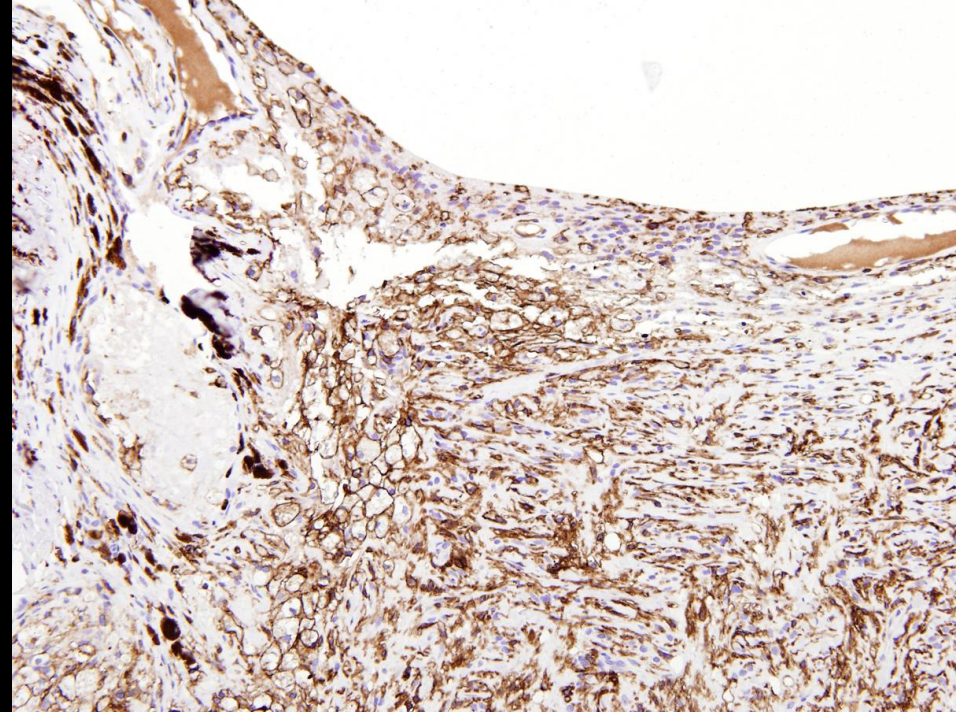
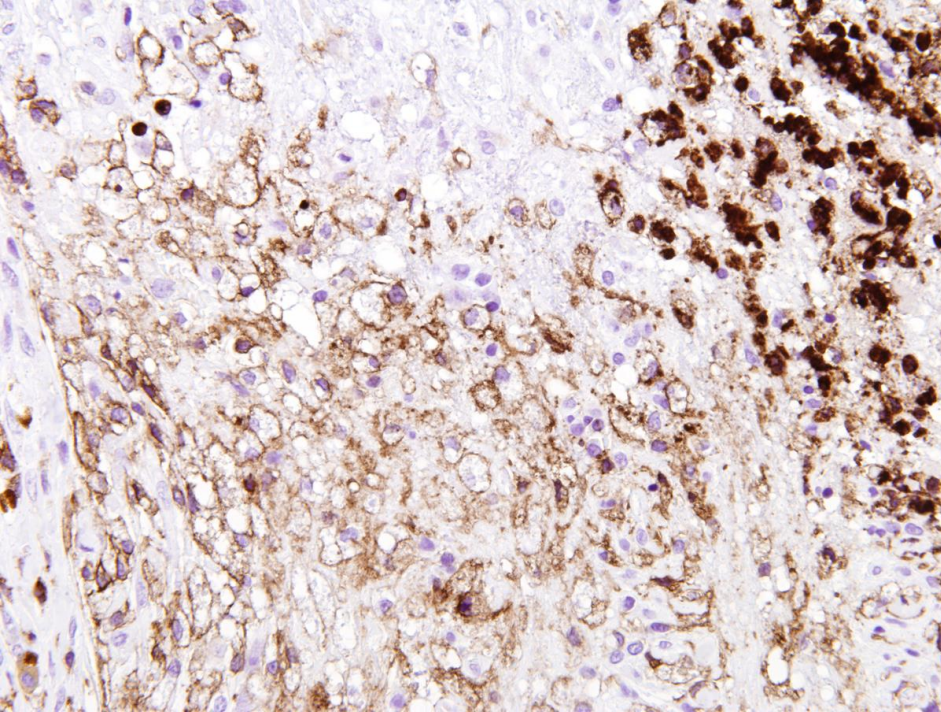
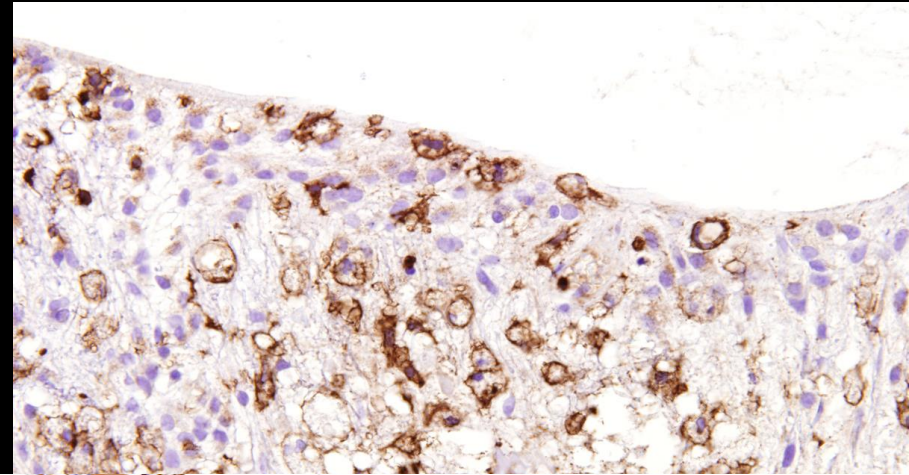
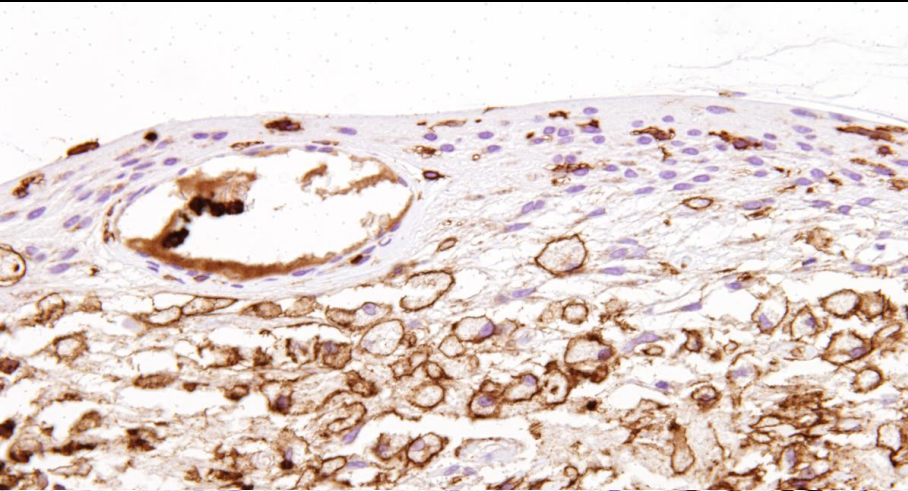
Phagocytic cells are the same at all time points

# Optic Nerve MHC-2 Phagocytes

## Optic Disk

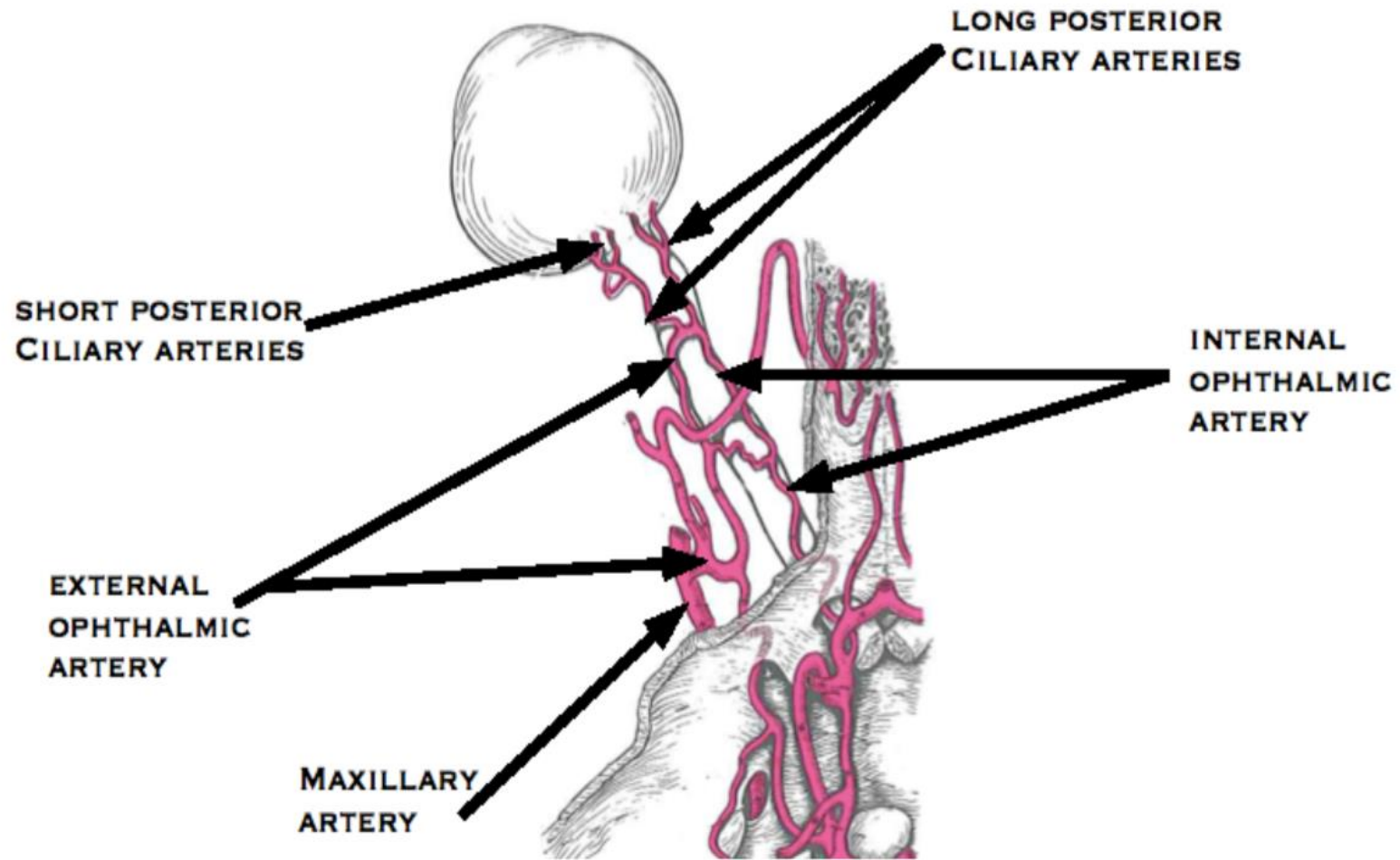


# MHC-2 on 4-5 Day Glaucoma Optic Nerve



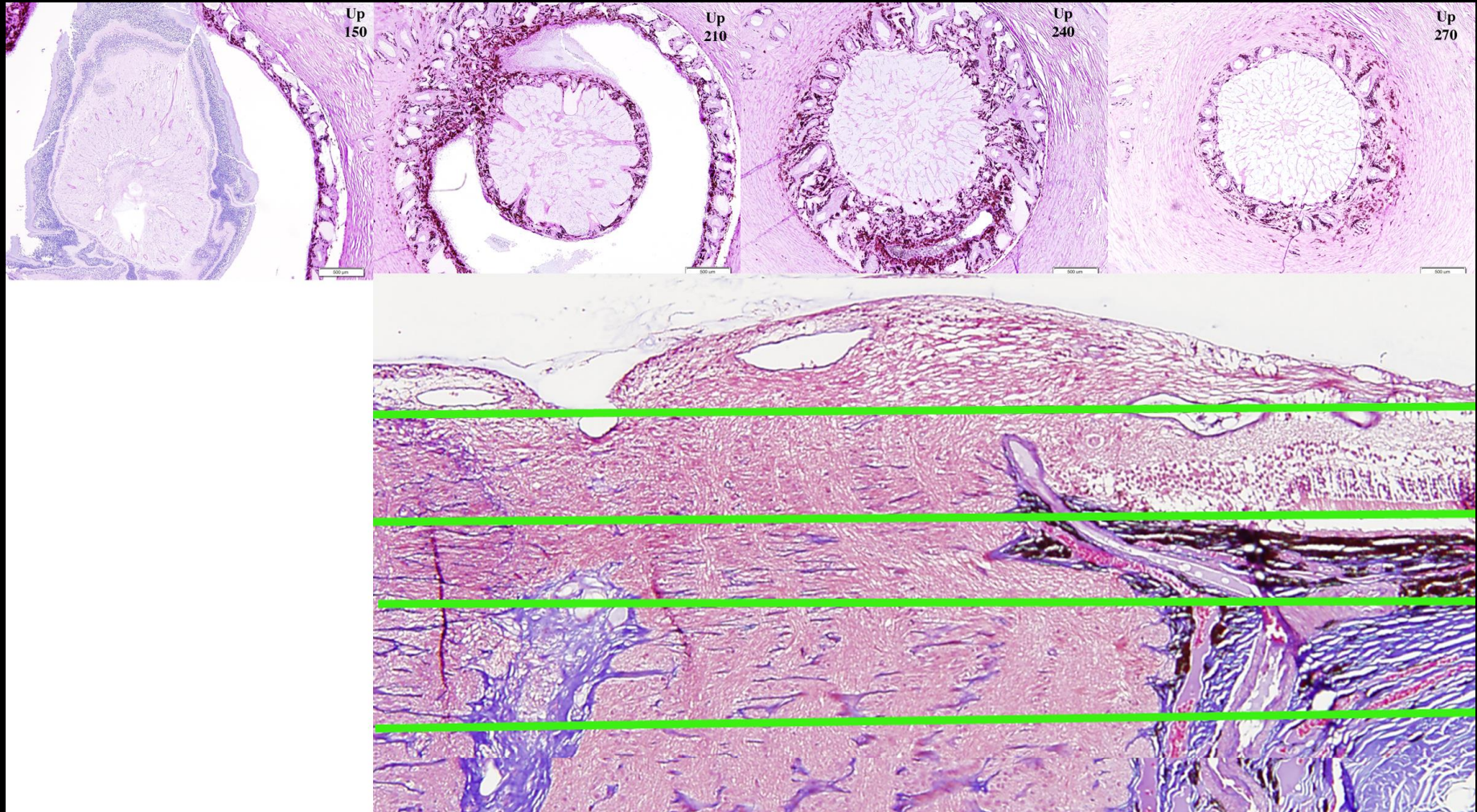
# Why is Acute Canine Glaucoma an Ischemic Disease?

## Vascular Anatomy of the Posterior Segment

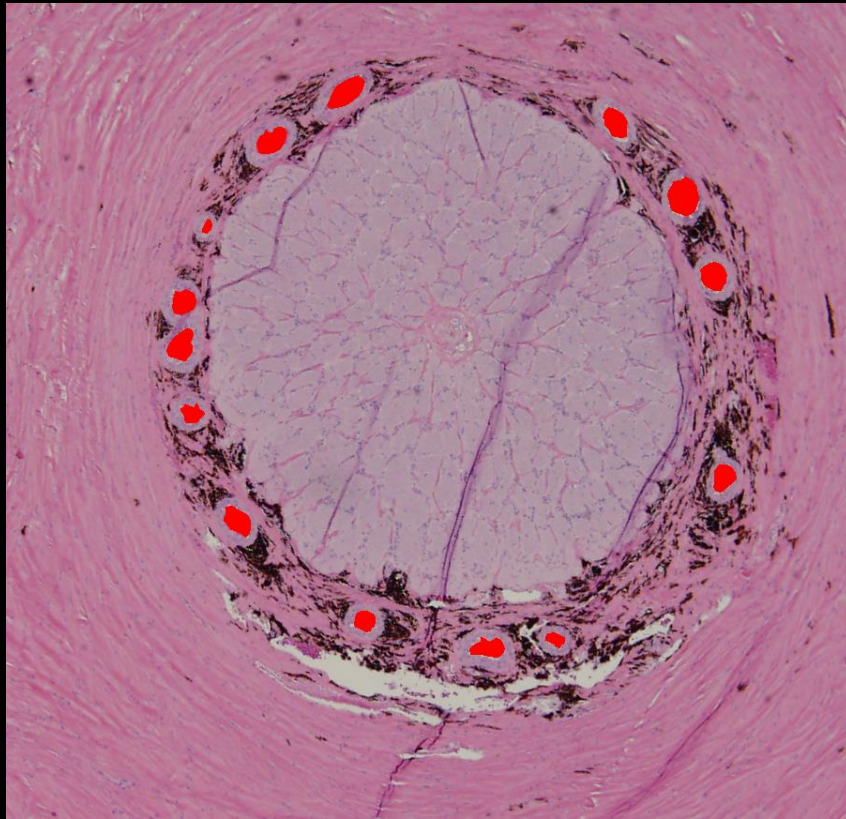




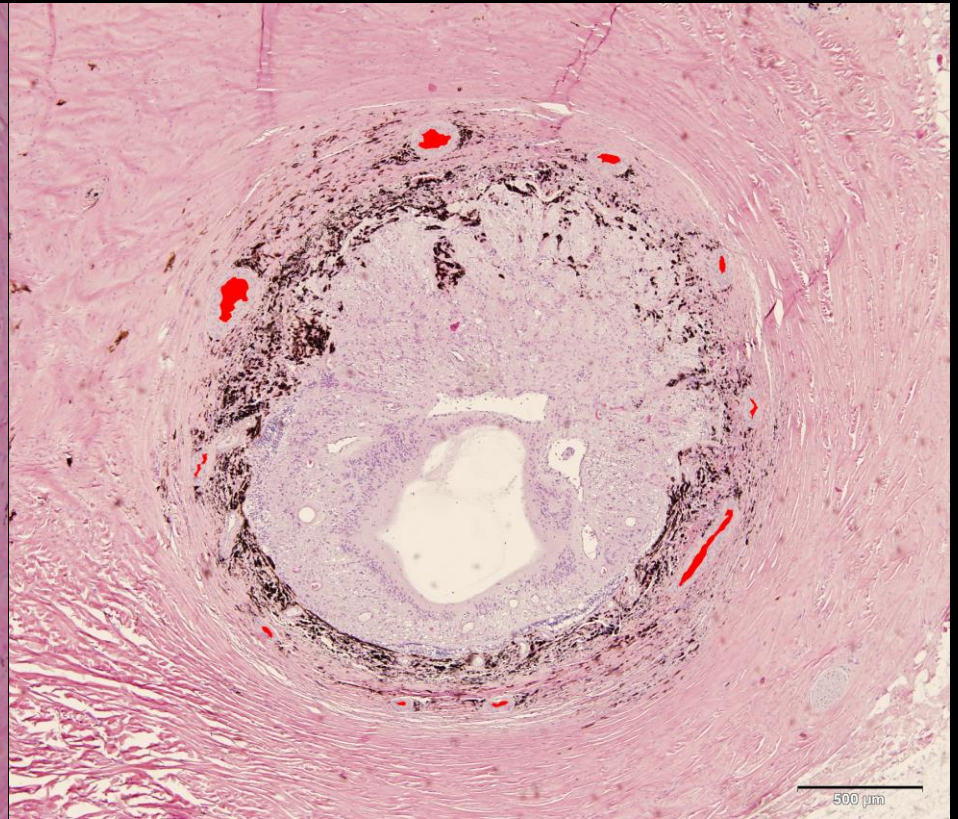
# Why is Acute Canine Glaucoma an Ischemic Disease?



# Why is Acute Canine Glaucoma an Ischemic?



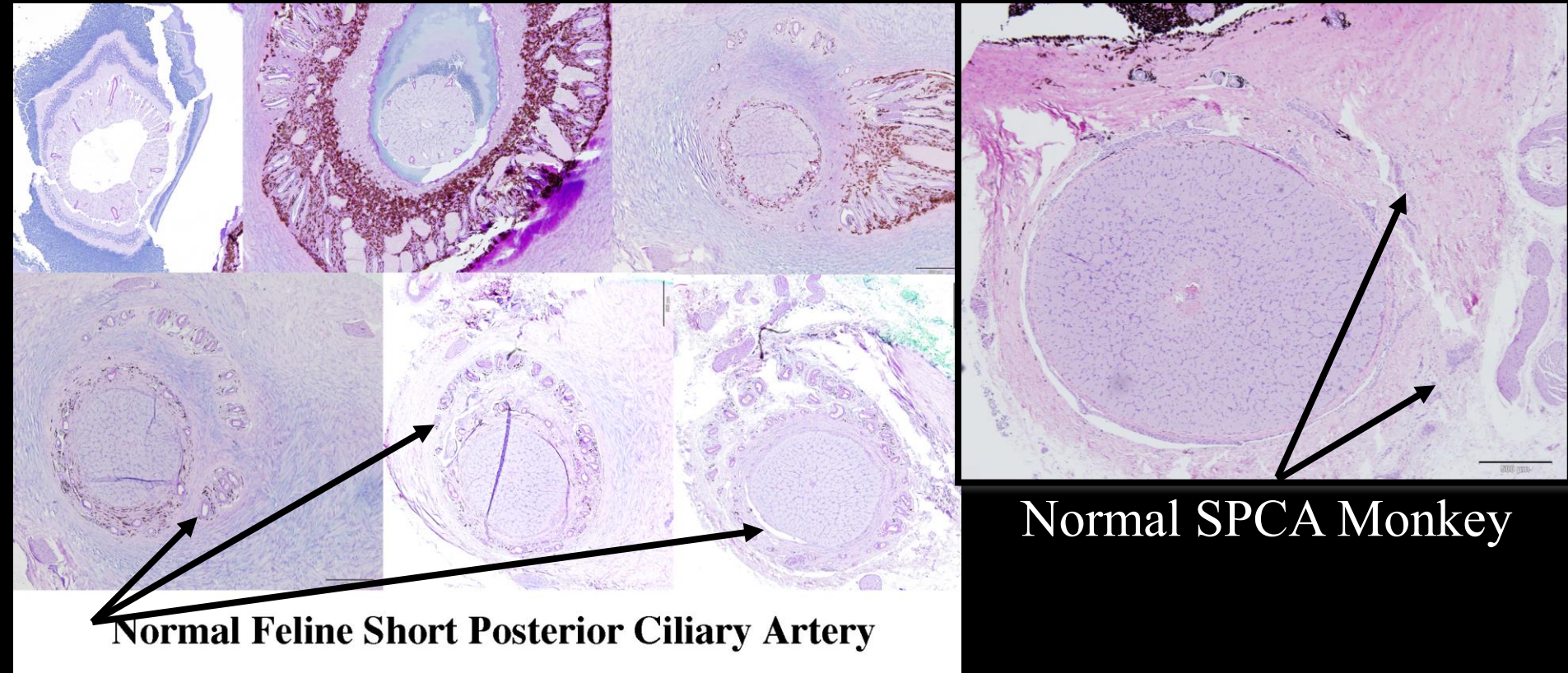
Normal

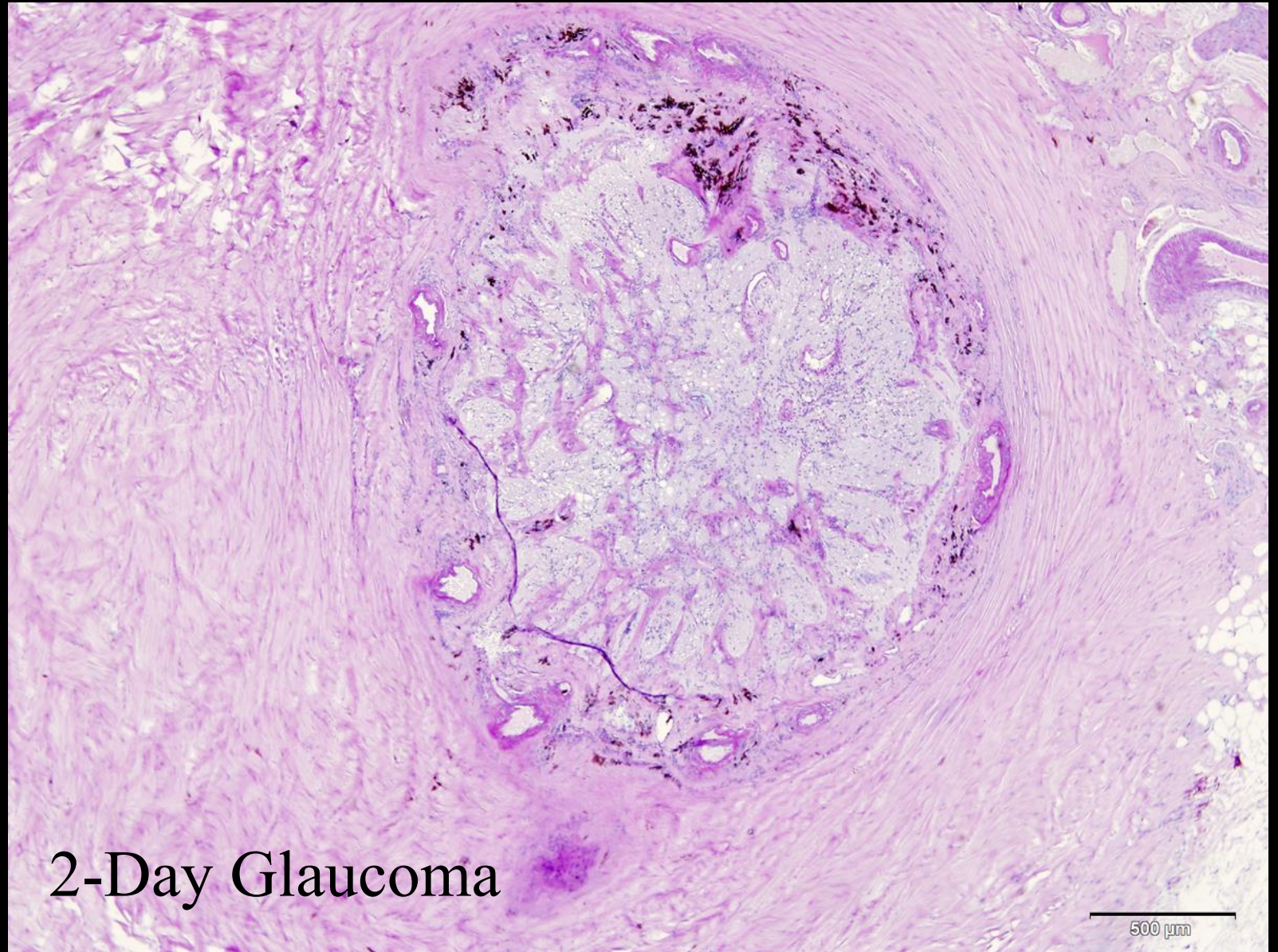


Acute Glaucoma

# Comparative Anatomy

## Short Posterior Ciliary Artery

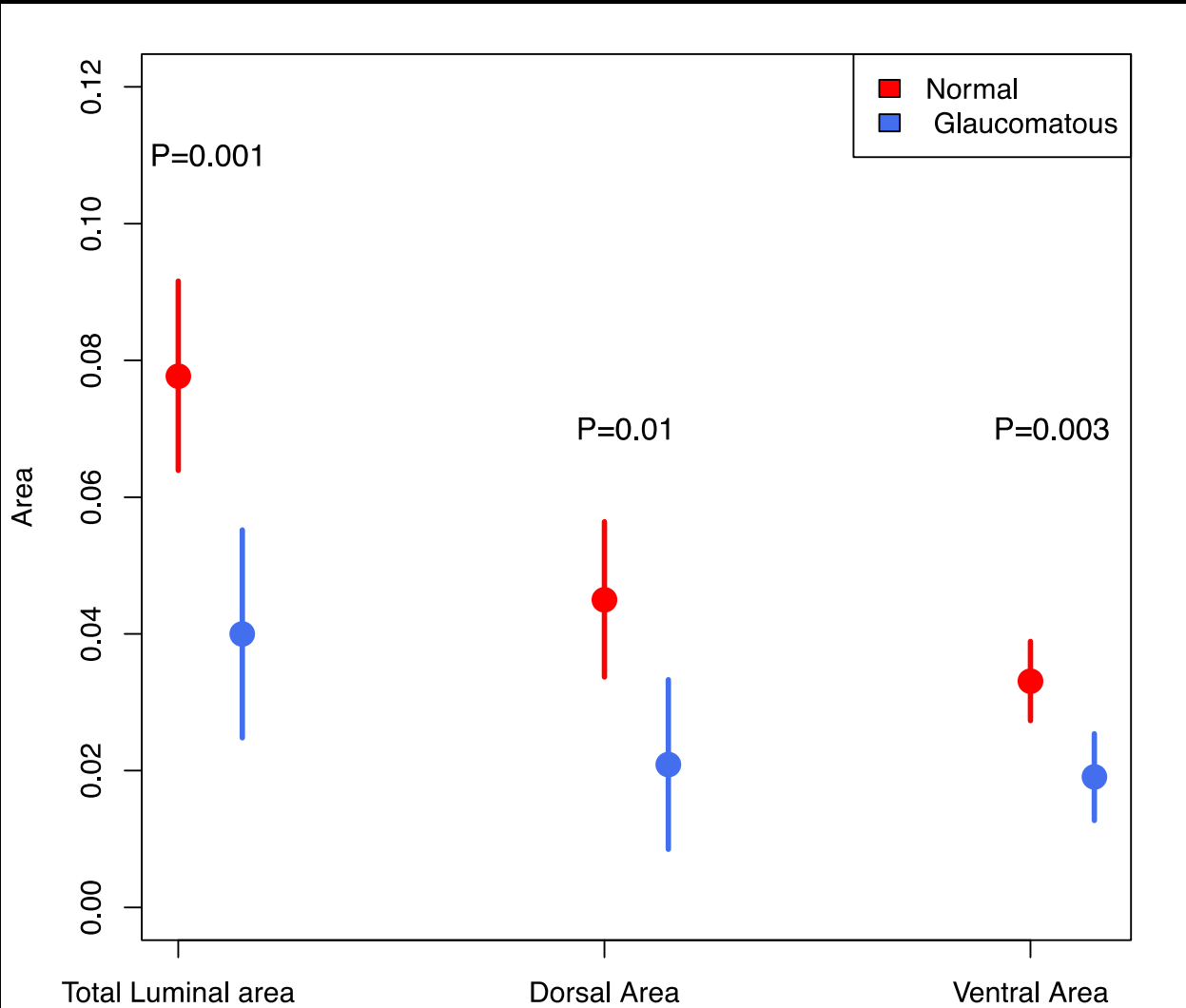




2-Day Glaucoma

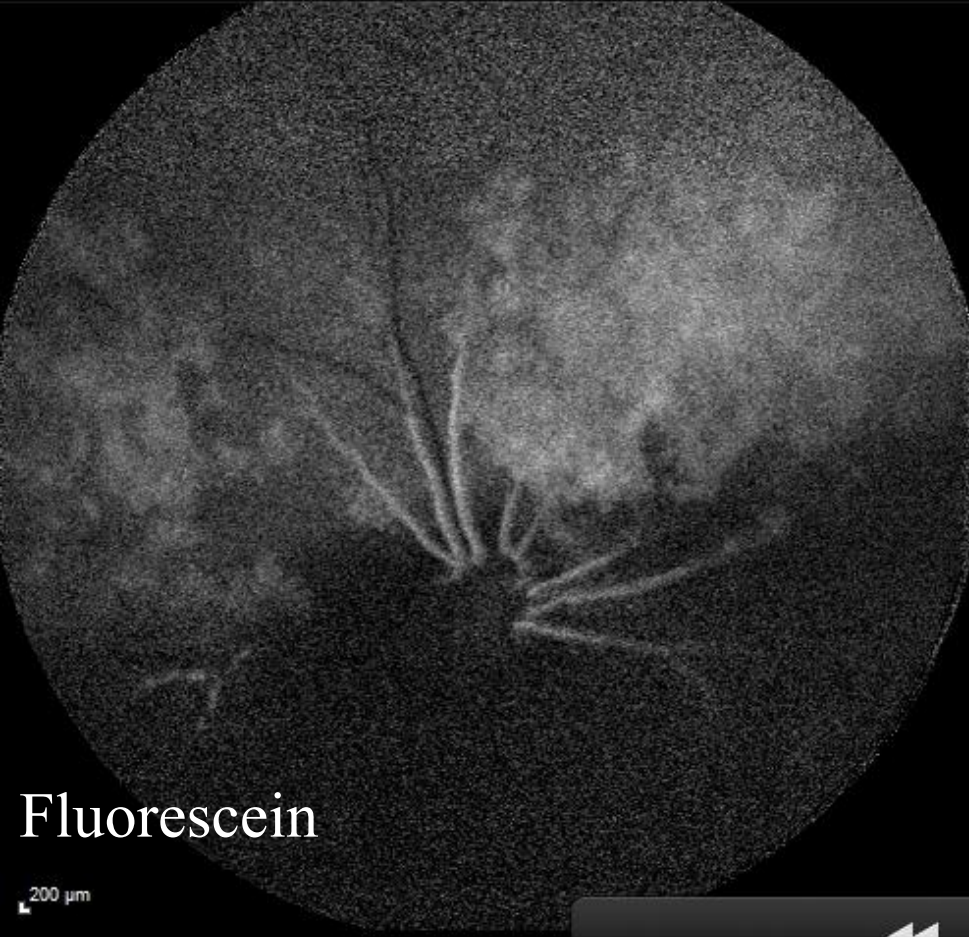
500  $\mu$ m

# Blood Vessel Area Normal vs Acute Glaucoma

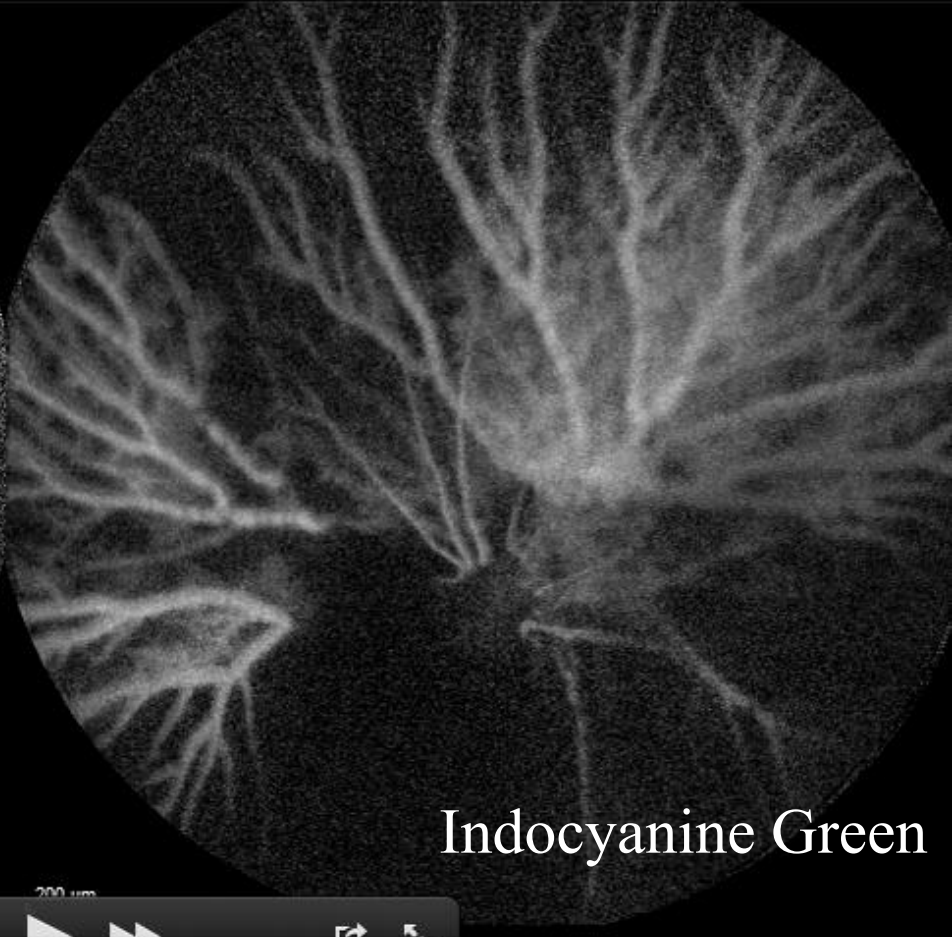


# 13 Second Angiogram

America 13rd2926.mov



Fluorescein



Indocyanine Green

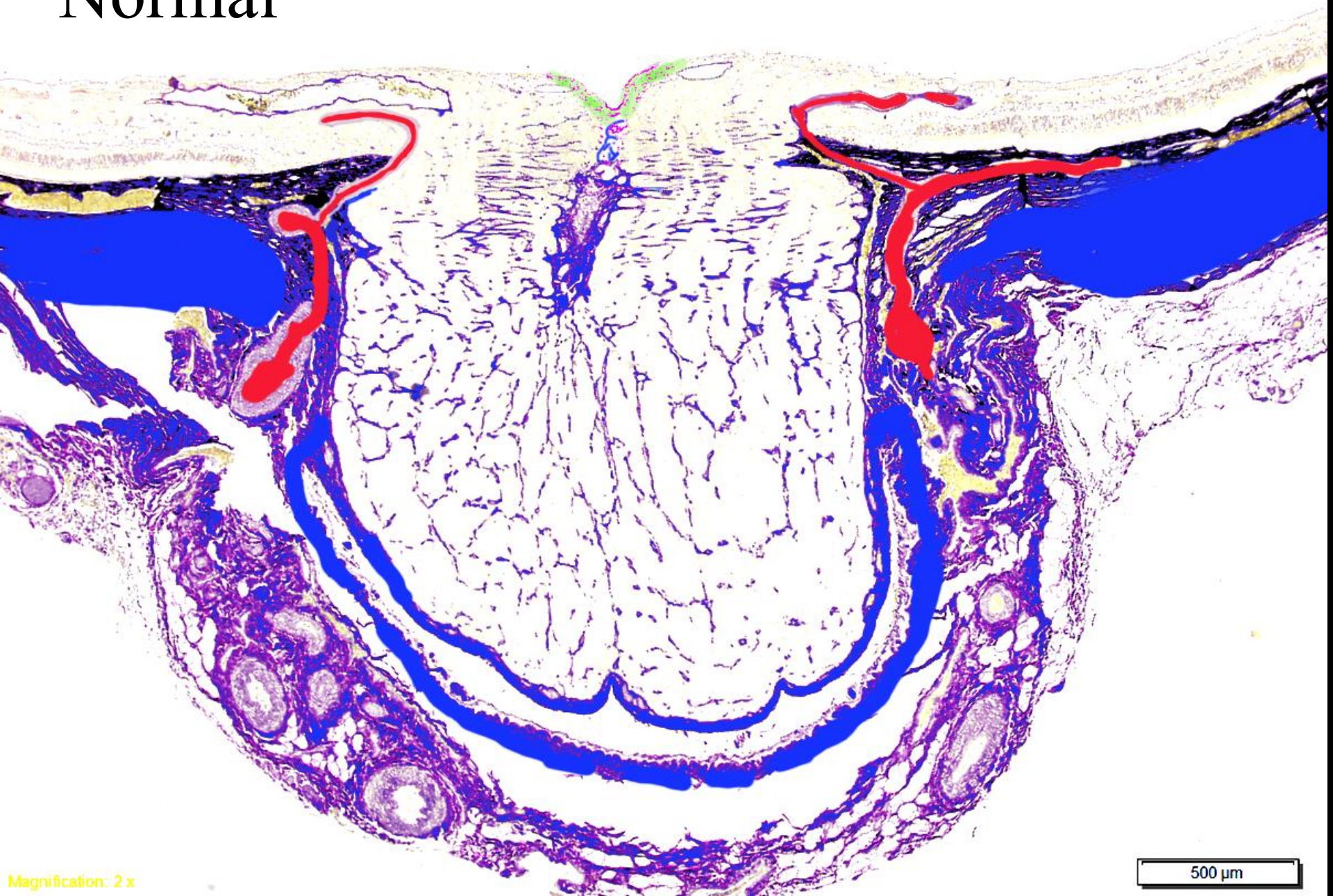
00:00:12 -00:00:43

POAG Affected, America, 6/19/2003

11/12/2013, OS

FA&ICGA 0:13.45 55° ART(10) 0:13.35 55° ART(10)

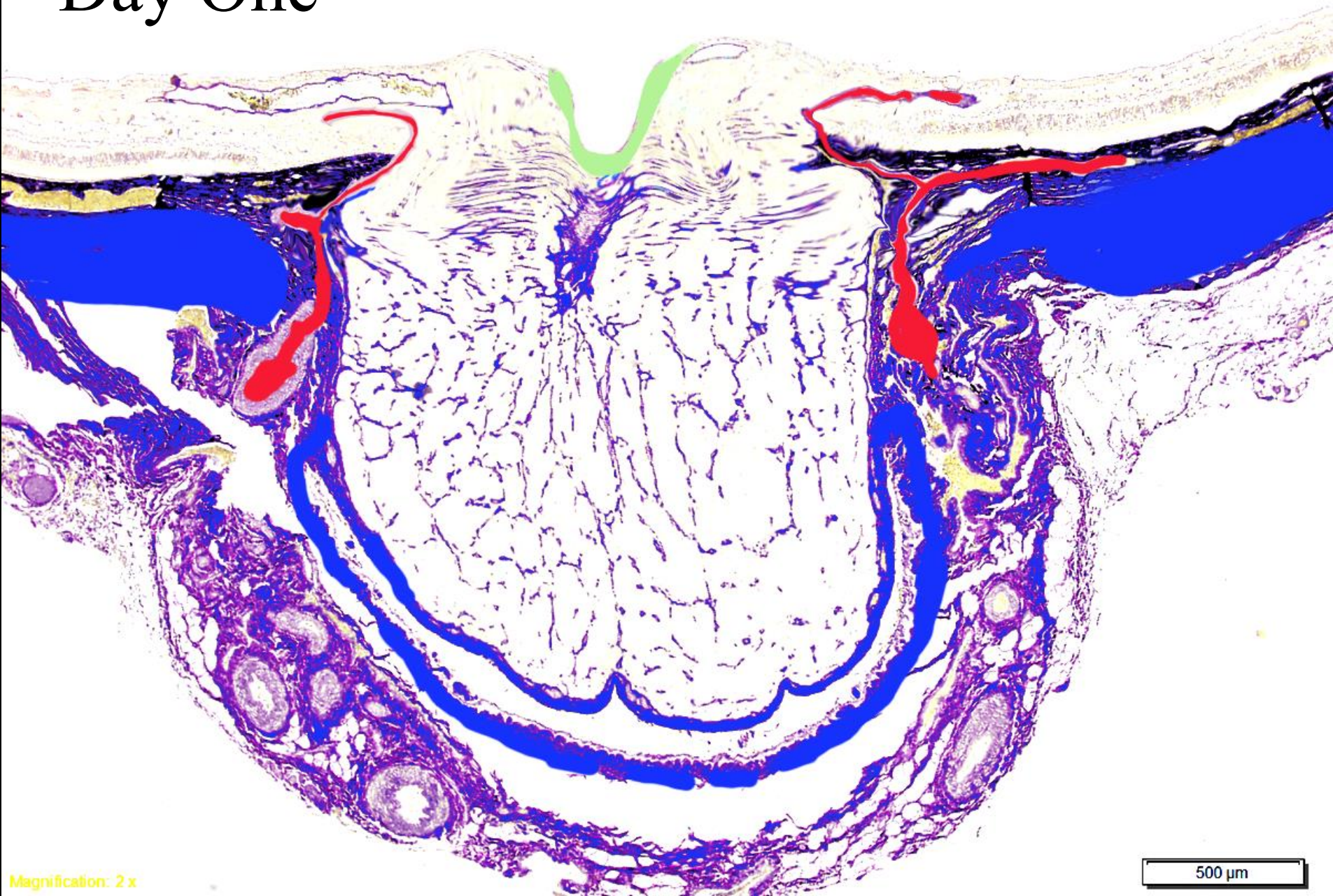
# Normal



Magnification: 2 x

500  $\mu$ m

# Day One

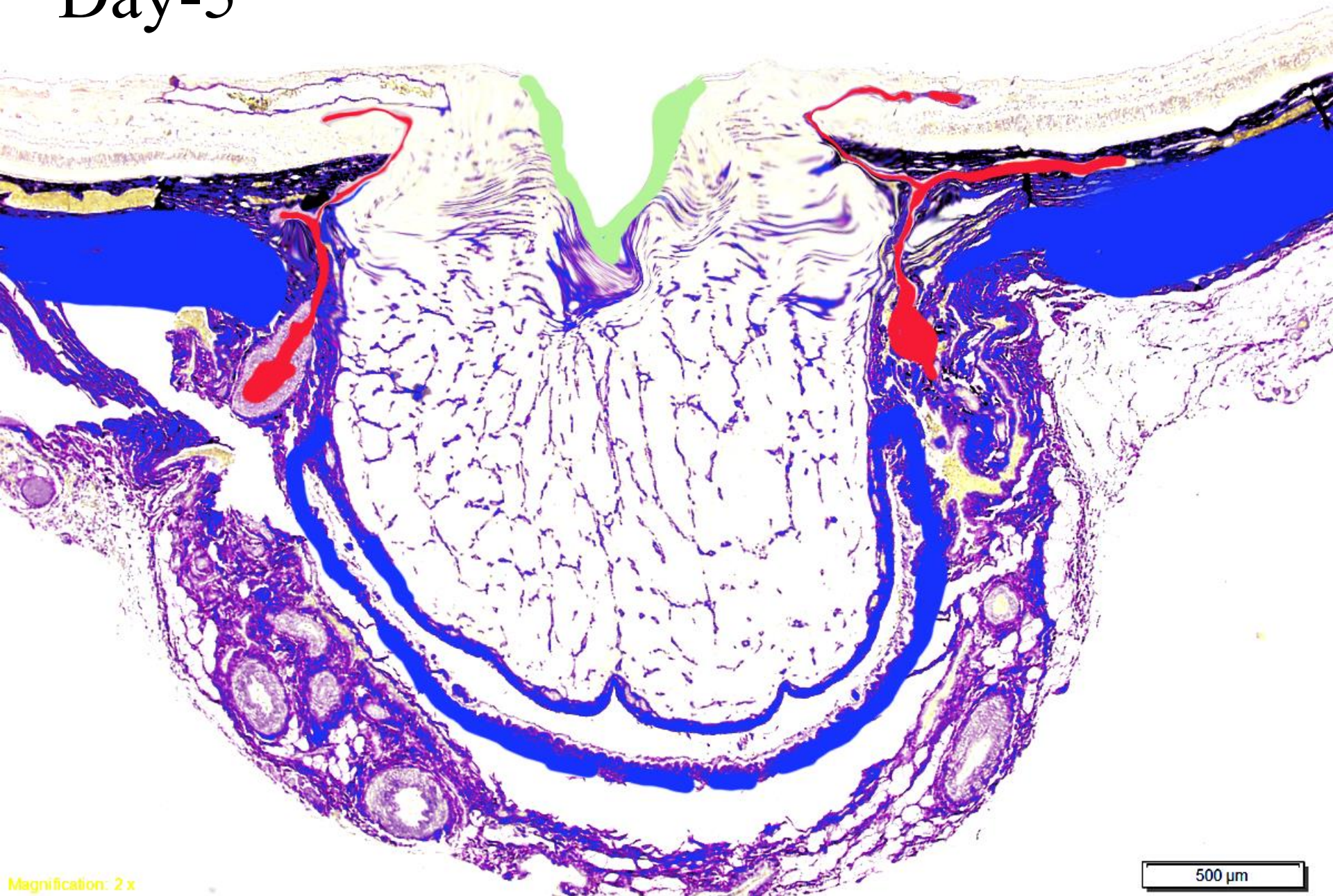


Magnification: 2 x

500 μm



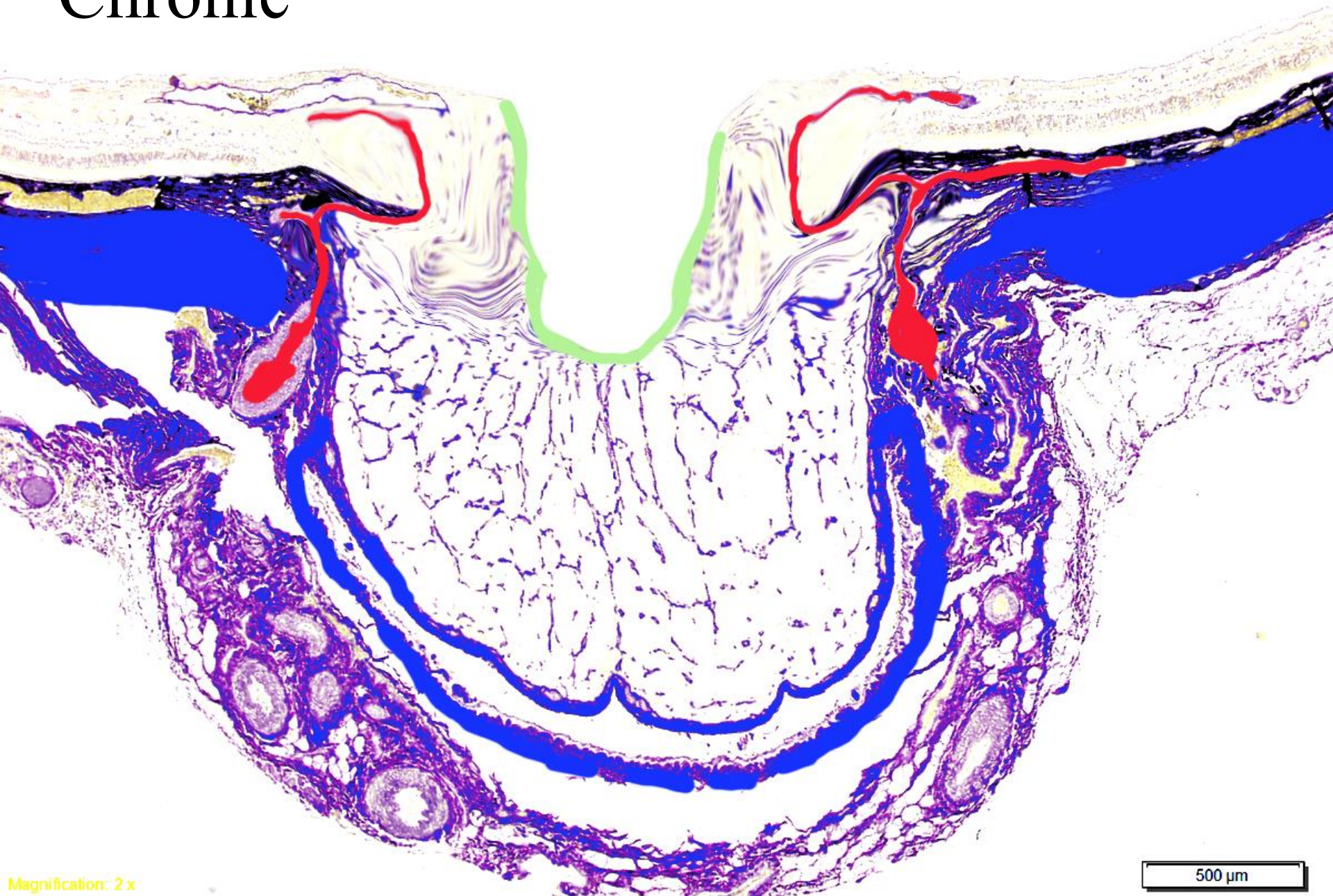
Day-5



Magnification: 2x

500 μm

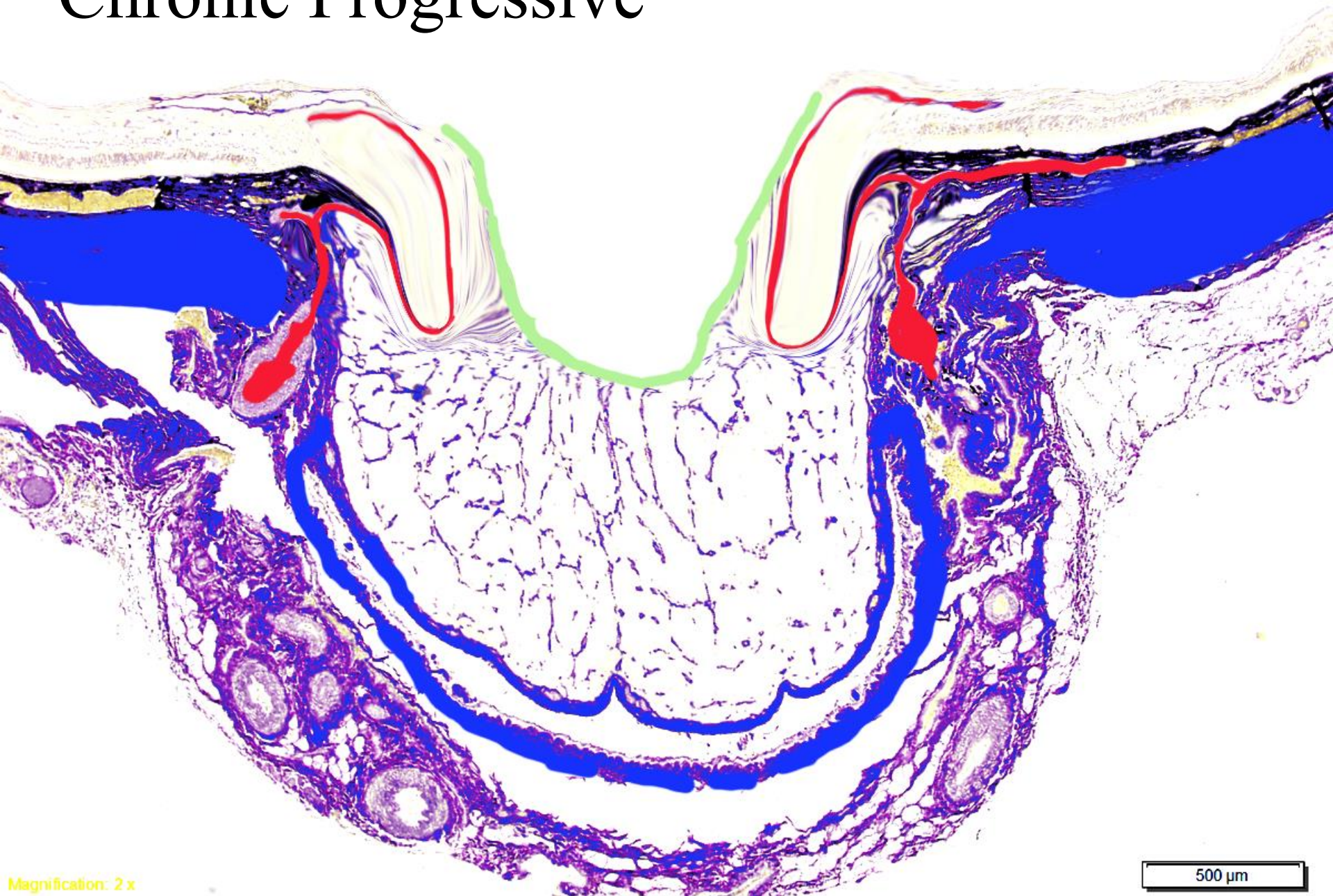
# Chronic



Magnification: 2 x

500  $\mu$ m

# Chronic Progressive



Magnification: 2 x

500  $\mu$ m

# Suggested Timeline

## Before the Owner Detects Pain

1. Young normotensive dog with goniodysgenesis
  1. Ciliary cleft open at first
2. The altered morphology has an effect on iris movement
  - a) Rubbing of iris on lens – Pigment dispersion
3. Gradual loss of ganglion cells
  - a) Likely bouts of pressure spikes
4. Gradual atrophy of the corneoscleral trabecular meshwork
5. Collapse of the ciliary cleft
  - a) Detected with ultrasound biomicroscopy

# Suggested Timeline

## After the Owner Detects Pain

1. Sudden painful crisis and compression of SPCA - Infarction
  - a) Pathology suggests an event 2-3 days before owner detects
2. Stepwise rapid necrosis of the optic nerve and retina
  - a) Neutrophils, dead ganglion cells, apoptosis, and finally phagocytosis
3. The second eye progresses through the same cycle