euretina InSight

Management of Progressive ROP

Current Management of ROP & Paediatric Vitreoretinal Diseases

Click Next button to begin module

Andrés Kychenthal, MD

The editor for this module is:

Andrés Kychenthal, MD
KYDOFT Foundation,
Santiago,
Chile.

Click each tab below to see Copyright Notices and Financial Disclosures

Copyright Notices | Financial Disclosures

Objectives

This module examines the **management of progressive ROP** in two very different clinical situations: firstly with persistent plus disease and an attached retina, and secondly with retinal detachment. The focus is on identifying best treatment options dependent on certain factors such as zone of disease, stage of disease, vascular activity, etc.

Having completed this module, you will be able to:

- ✓ List the secondary treatment options available during the management of progressive ROP when there is persistent plus disease with an attached retina, and describe the factors that inform the correct treatment approach.
- ✓ Identify characteristics of laser treatment and anti-VEGF treatment, and list some benefits of anti-VEGF treatment over laser treatment.
- ✓ Describe the factors that may explain the high number of re-treatments required, following the use of anti-VGF as the primary treatment in certain studies.
- ✓ Identify the treatment options available during the management of progressive ROP where there is a retinal detachment, and describe the key factor that informs the correct treatment approach.
- ✓ Identify the recommended treatment approach for patients that receive no primary treatment and subsequently develop stage 5 ROP, and describe why this treatment is recommended.
- ✓ Identify a treatment option for patients that are referred following vitrectomy failure, and who have retinal detachment with a lot of residual traction.

Introduction

This module examines the **management of progressive ROP**, where two very different clinical situations need to be considered:

- With the **retina attached and persistent plus disease**
- With **retinal detachment**

Primary treatments for type I ROP typically include:

- **Laser**
- **Anti-VEGF**
- **Vitrectomy** (*in cases of retinal detachment*)

Following primary treatment for ROP, factors that must be considered when deciding the next step in the management of progression, include:

- **Type of primary treatment**
- **Zone of disease**
- **Stage of disease**

Overview

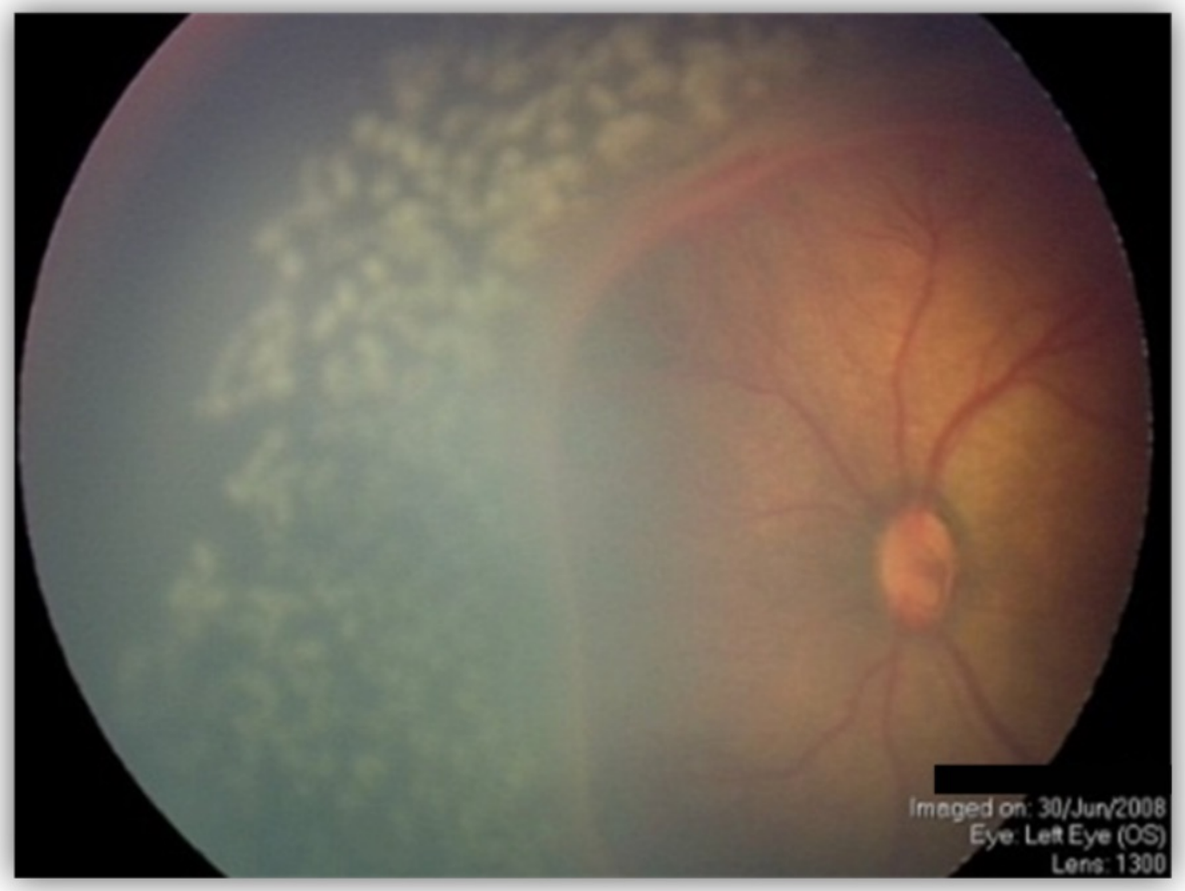
This module is divided into the topics listed below; each is followed by a quiz if you chose this option on the first screen. Click next to begin. Revisit any section by clicking it here.

- **Persistent Plus Disease, Attached Retina**
- **Retinal Detachment**
- **Summary**
- **Knowledge Check**

Click the buttons above to visit a specific topic or the next button below to visit all topics in order

Overview

This module is divided into the topics listed below; each is followed by a quiz if you chose this option on the first screen. Click next to begin. Revisit any section by clicking it here.

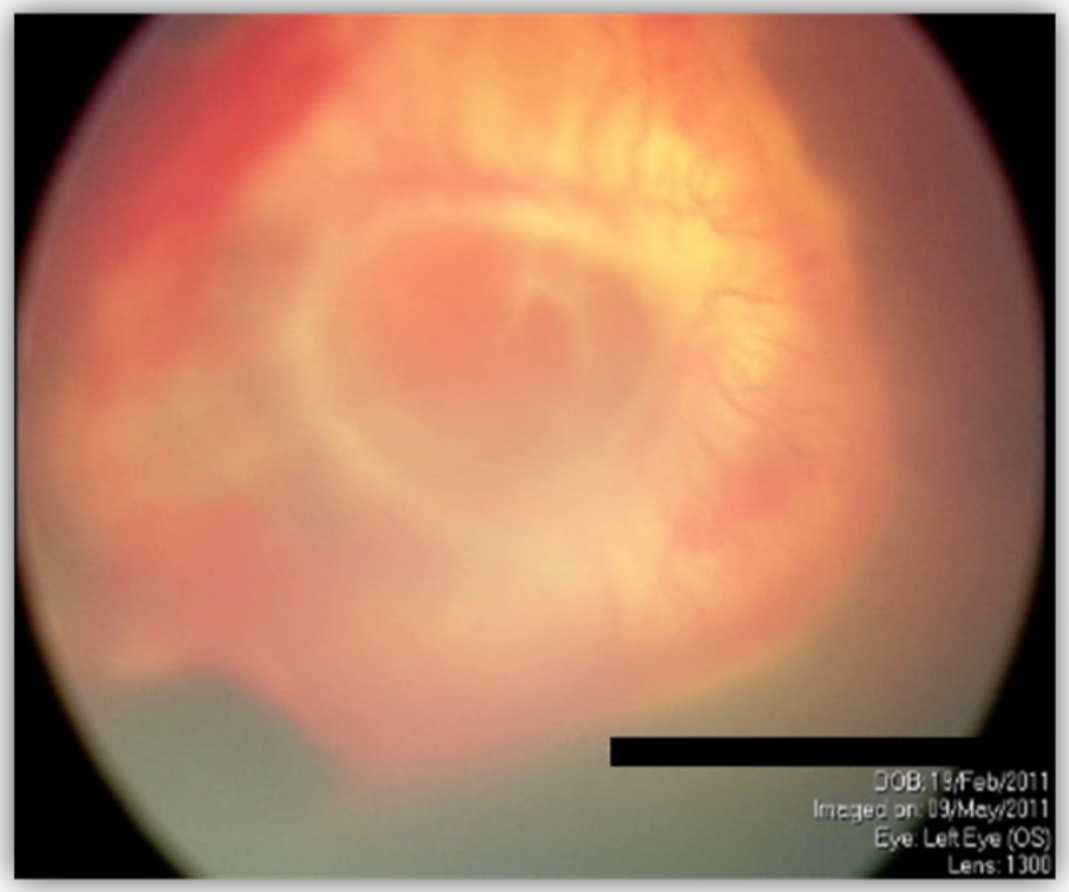


Click the buttons above to visit a specific topic or the next button below to visit all topics in order

Overview

This module is divided into the topics listed below; each is followed by a quiz if you chose this option on the first screen. Click next to begin. Revisit any section by clicking it here.

- Persistent Plus Disease, Attached Retina
- Retinal Detachment
- Summary
- Knowledge Check



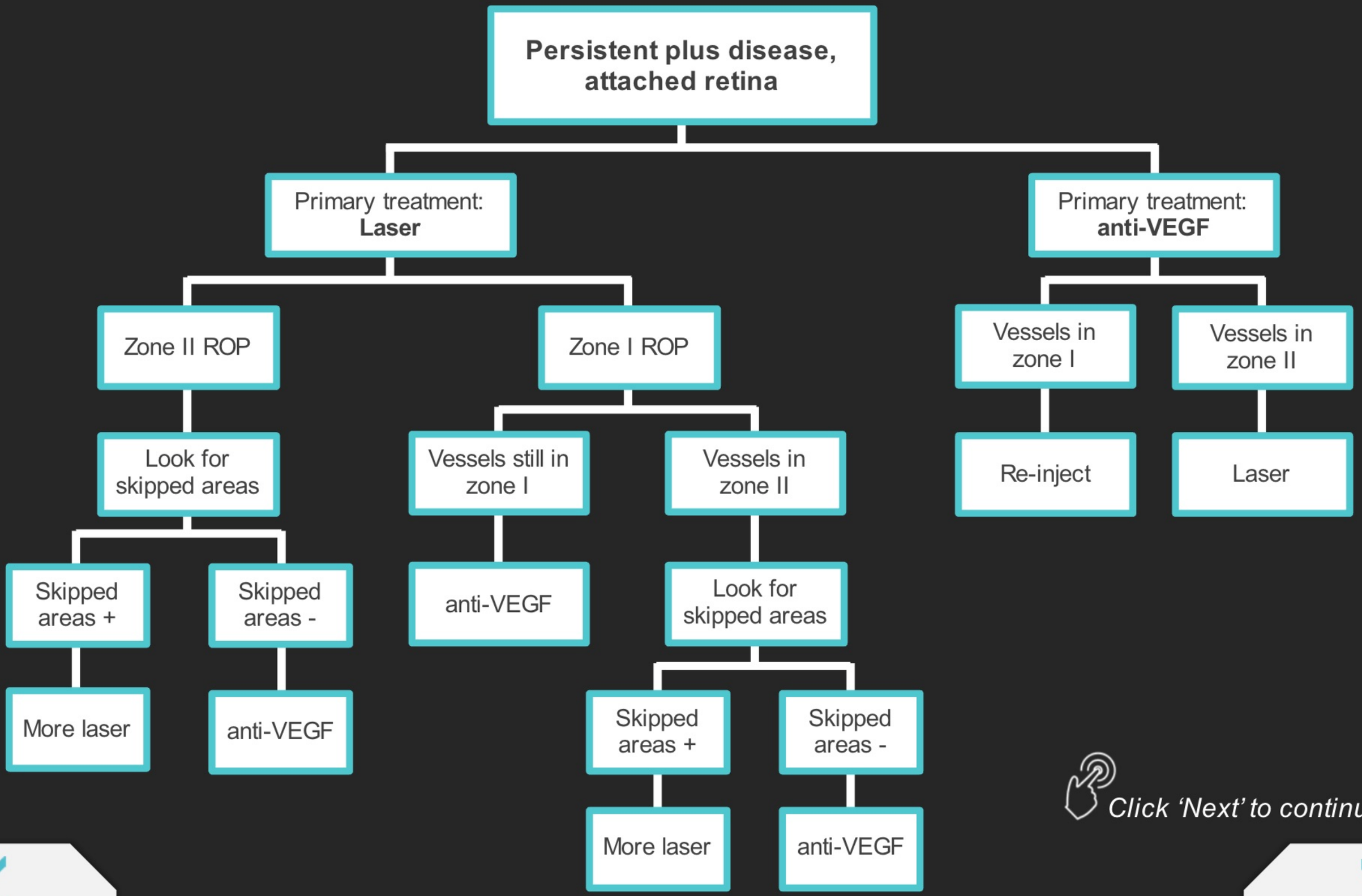
Click the buttons above to visit a specific topic or the next button below to visit all topics in order

Module Progress:

Persistent Plus Disease, Attached Retina

Management of Progressive ROP

Persistent Plus Disease & Attached Retina



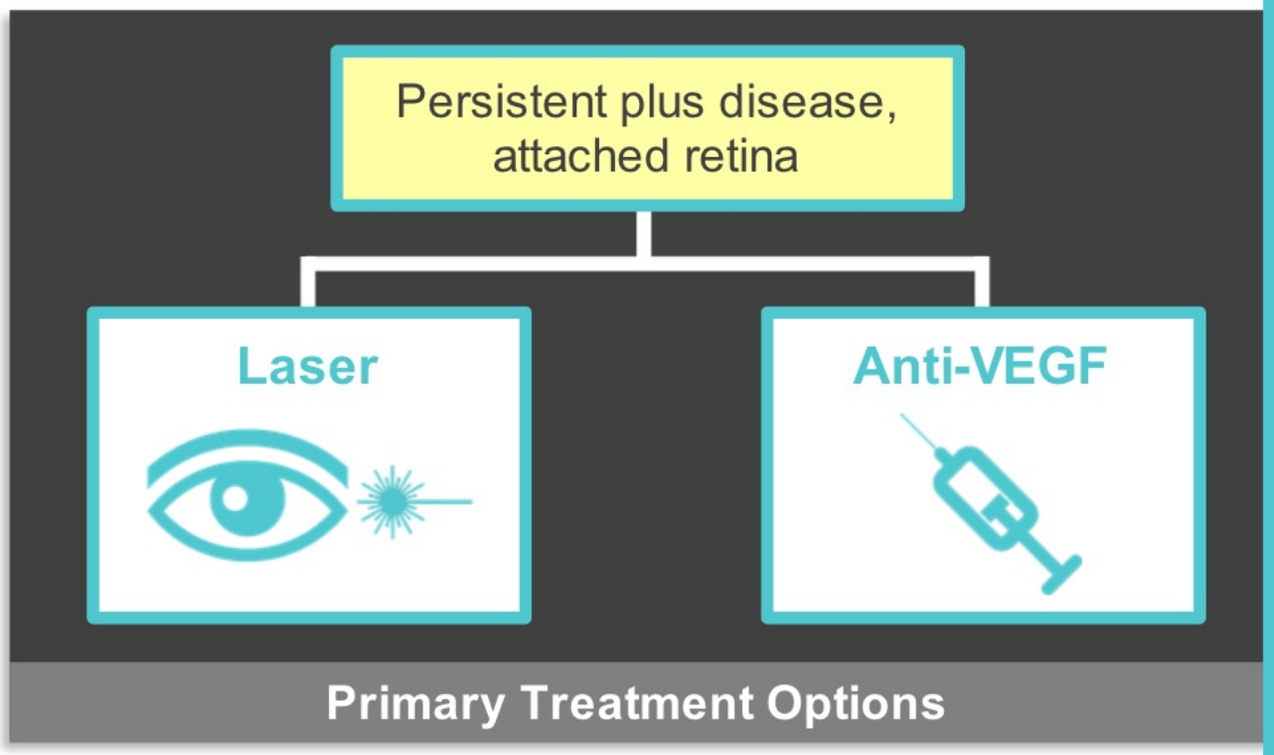
Click 'Next' to continue

Management of Progressive ROP After Primary Treatment

In the management of progressive ROP when there is persistent plus disease and the retina is attached, the **two primary treatment options** are:

- **Laser**
- **Anti-VEGF**

Click the 'Next' button to learn about important factors to consider following each of these primary treatments.



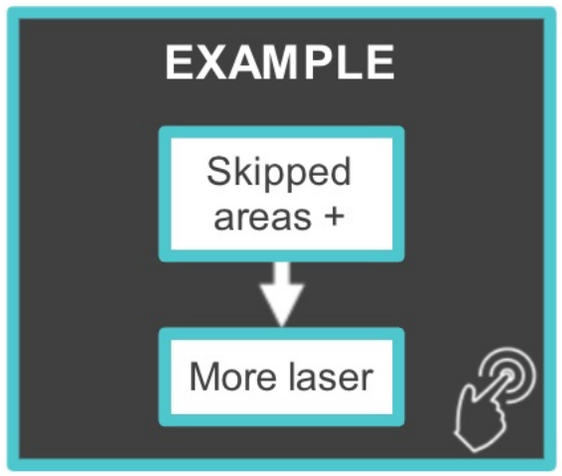
Primary Treatment Options

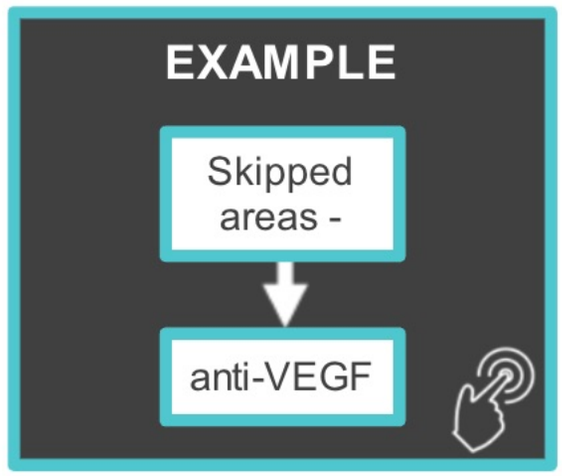
After Primary Laser Treatment

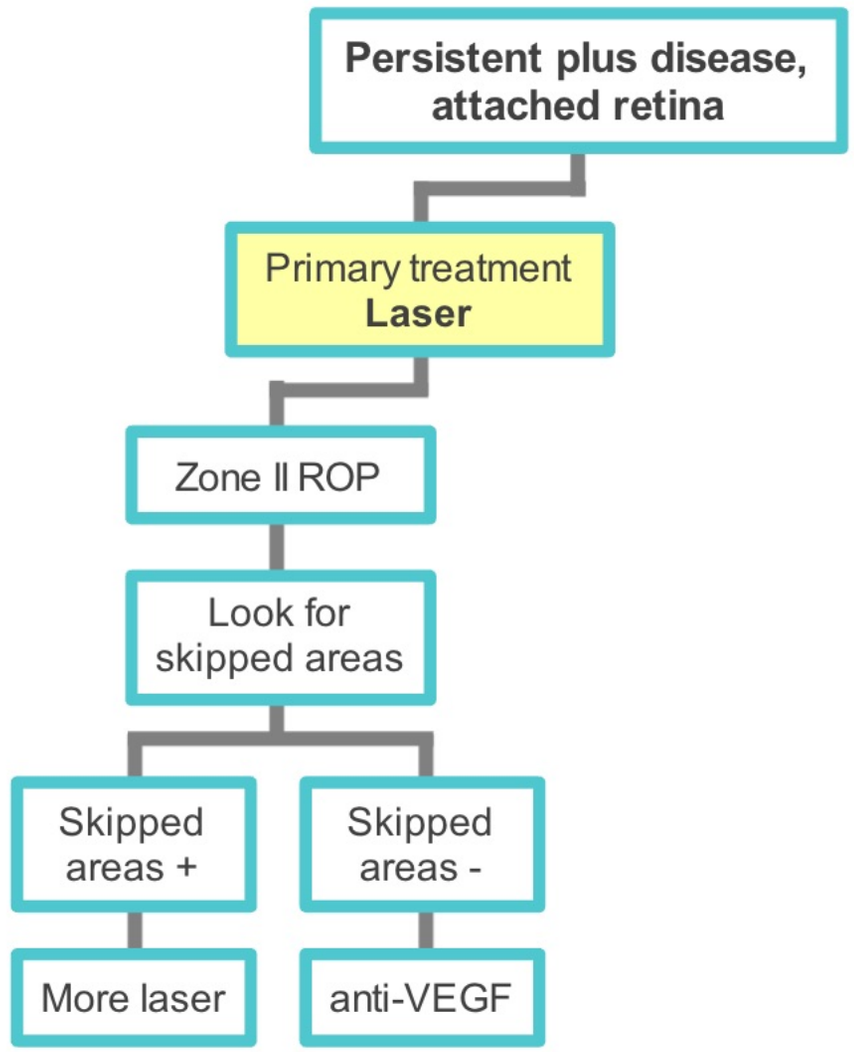
Checking for **skipped areas** is essential, following **primary laser treatment for zone II ROP**.

- With laser treatment, areas can sometimes be skipped which allows progression of the ROP to continue. In these cases, it is necessary to go back and look for skipped areas; **re-laser if skipped areas are found**, and typically these babies will do well.

- On the other hand, even if adequate laser treatment is given (i.e. all the avascular zone is successfully lasered) and no skipped areas are found, the disease can still continue progressing. In these cases use intravitreal **anti-VEGF treatment**.

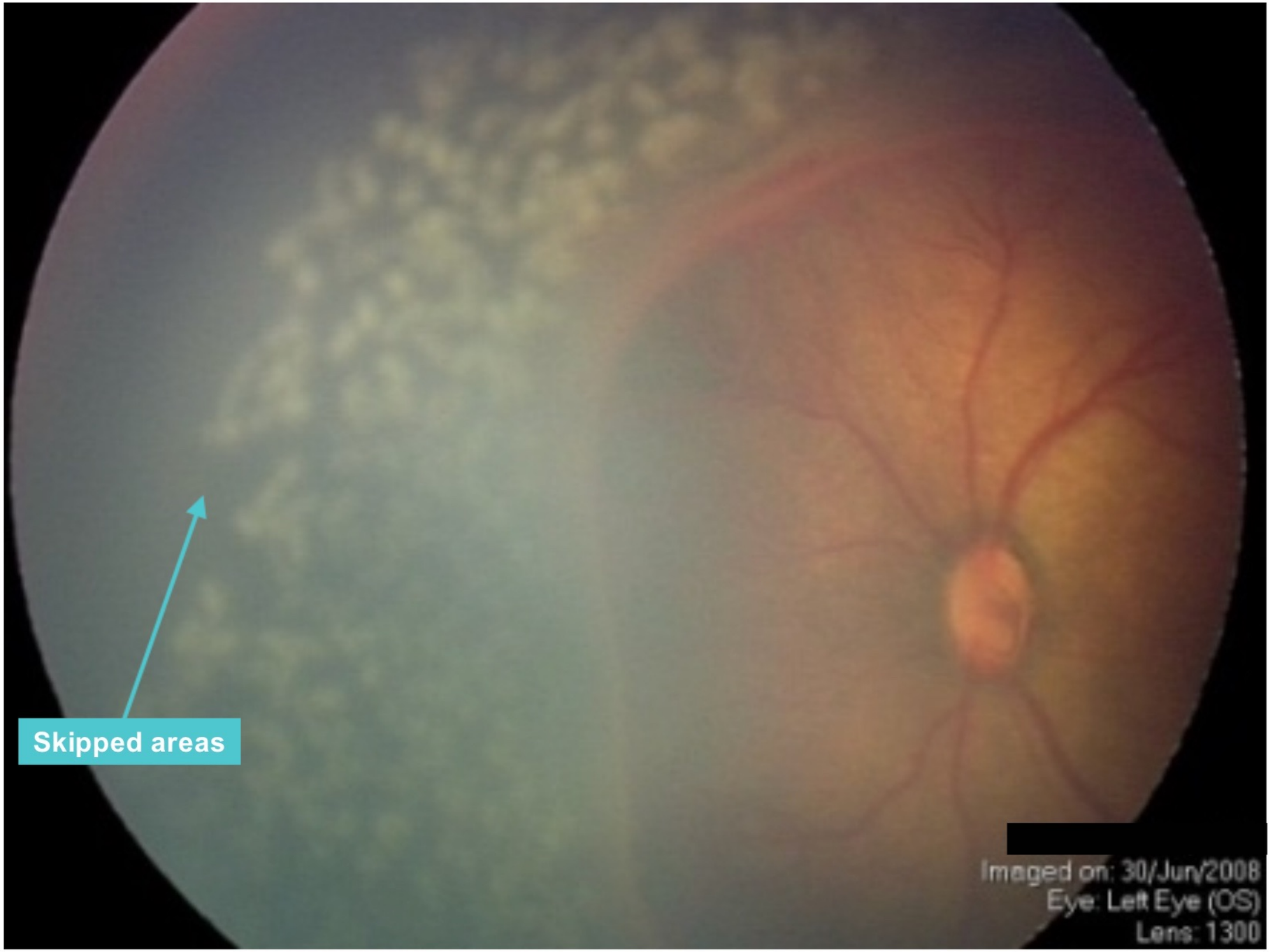






Prevention
Adequate laser = near confluent spots in all the avascular area

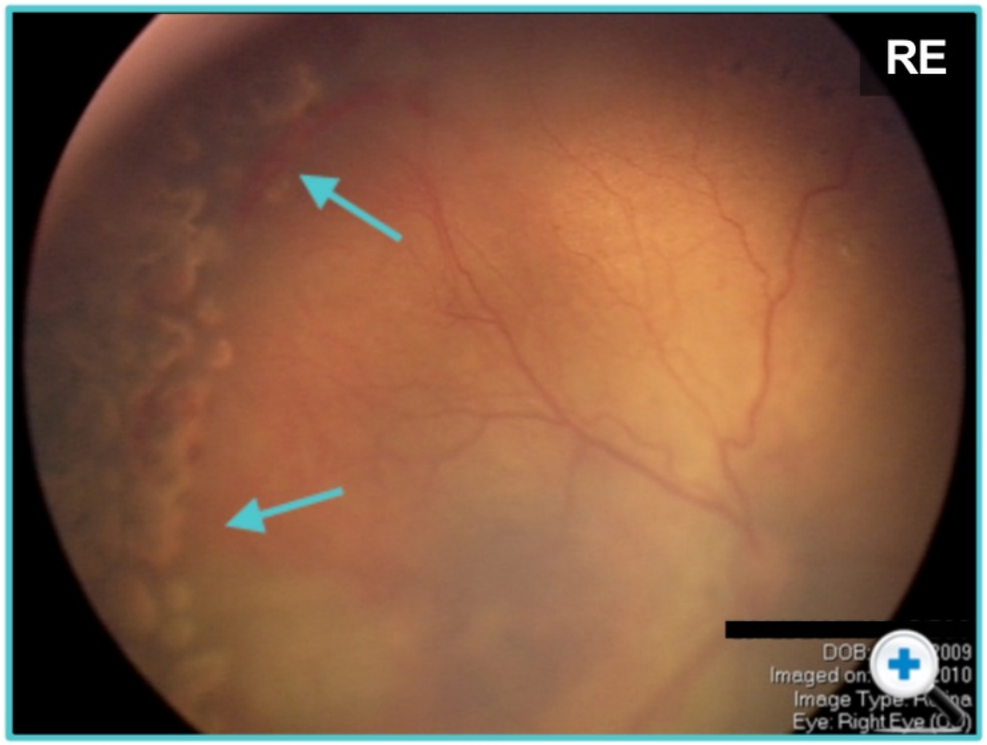
Skipped areas present, need to re-laser



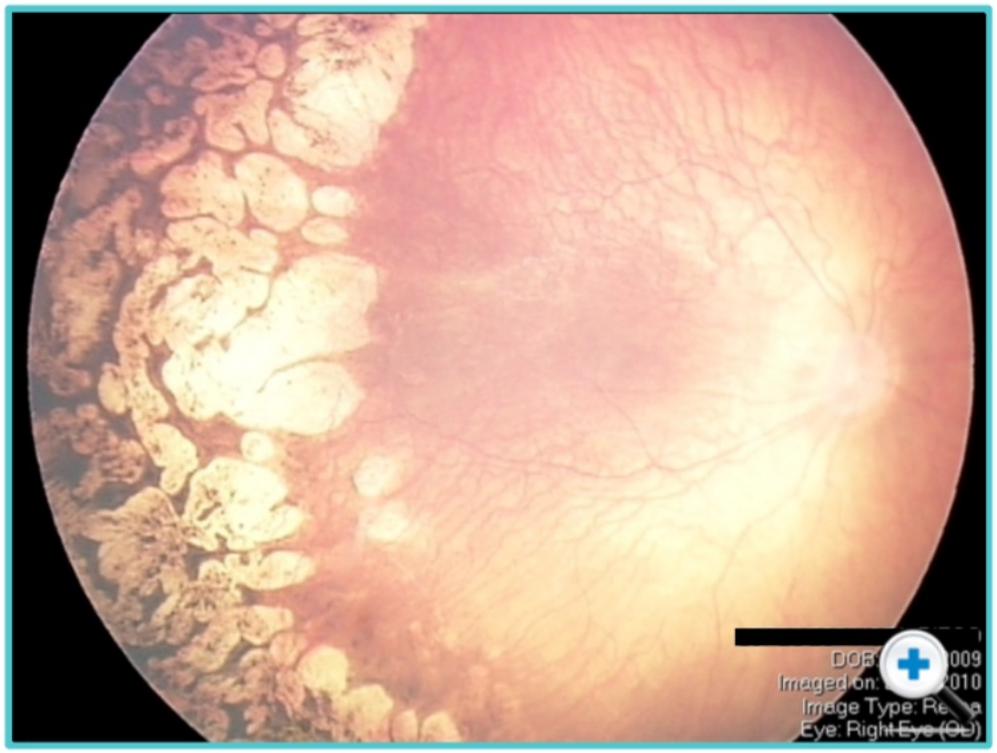
No Skipped areas present, use anti-VEGF

In this example, the infant has stage 5 ROP in the other eye.

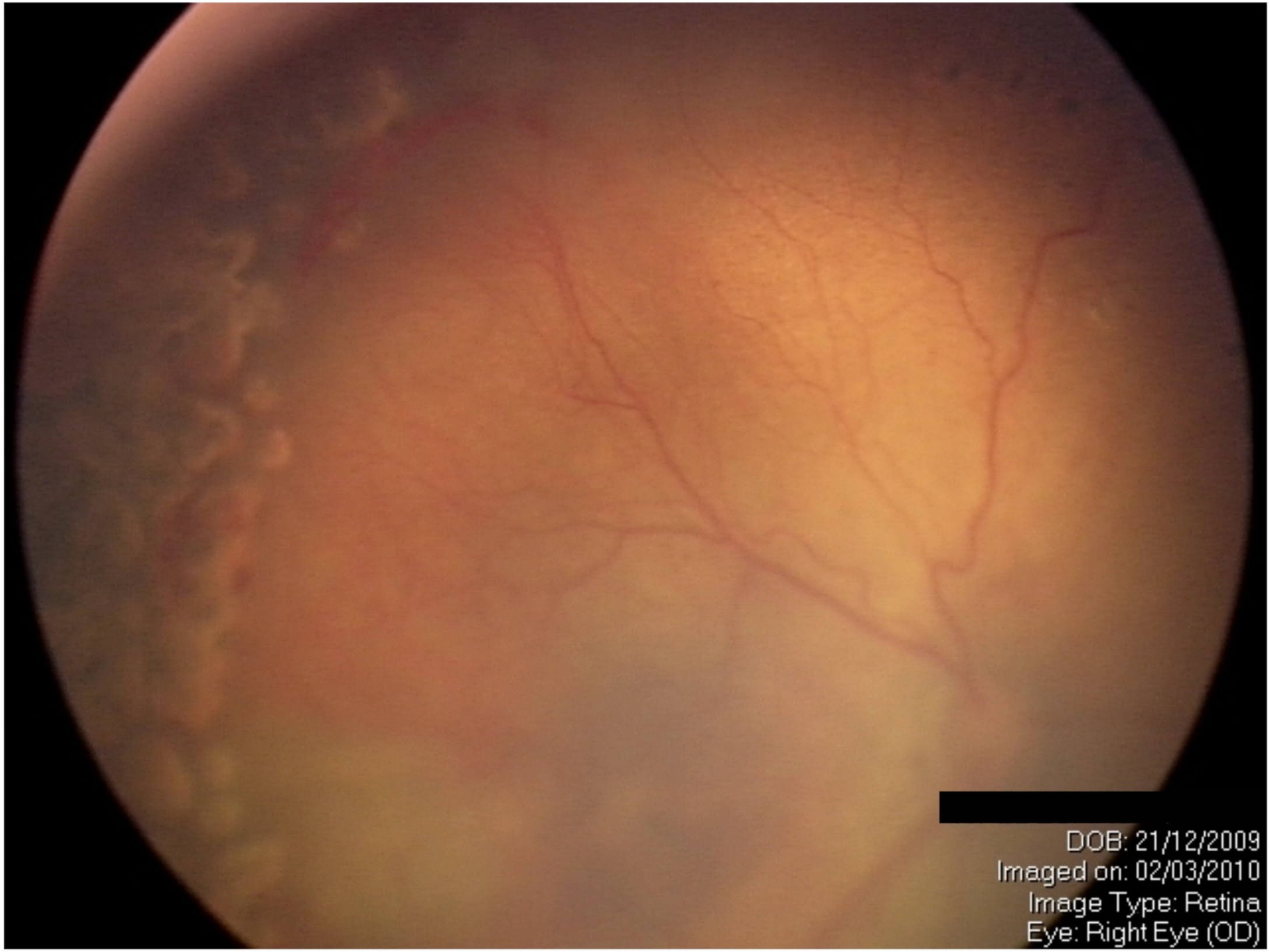
An Avastin injection is given and the ROP regresses.



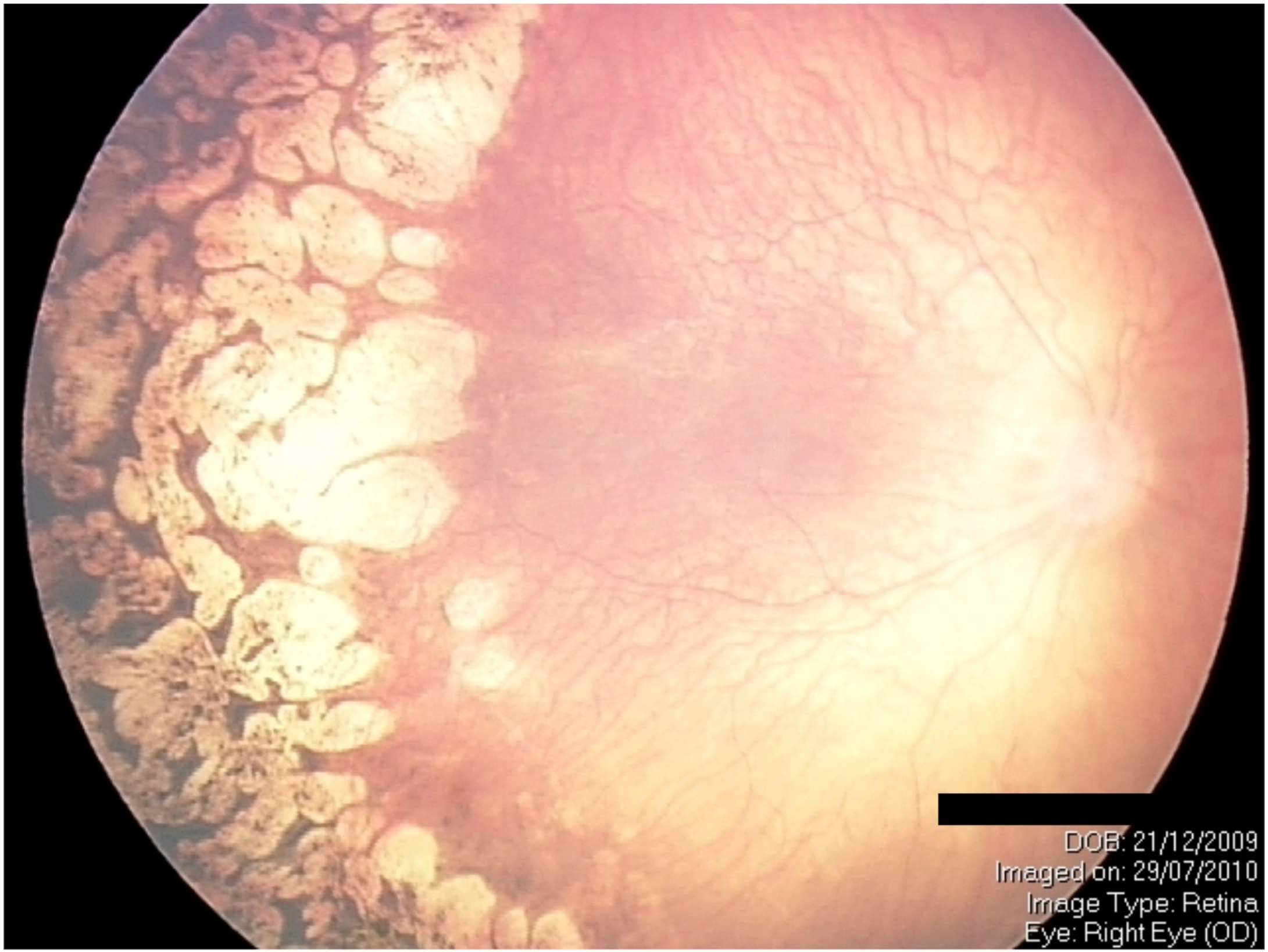
One Avastin injection



Persistent vascular activity and no skipped areas. Use intravitreal anti-VEGF treatment.



After one Avastin injection



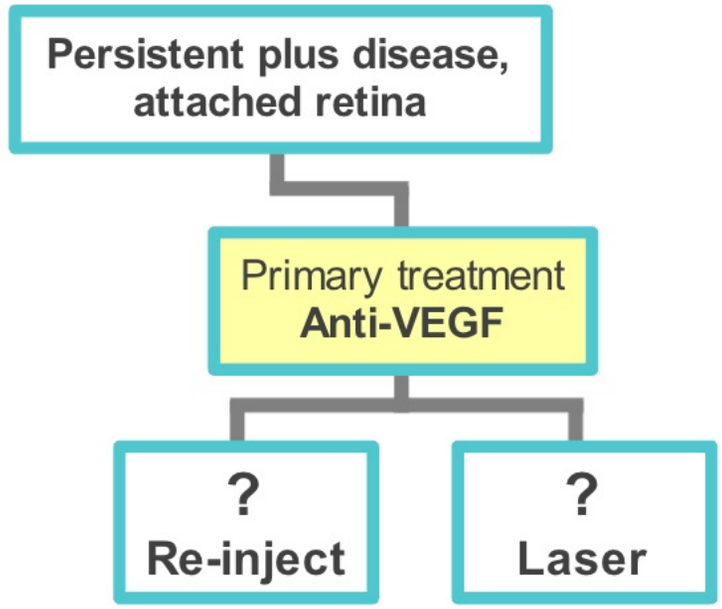
After Primary Anti-VEGF Treatment

Primary treatment using intravitreal anti-VEGF drugs is a different situation (than using laser) in the management of progressive ROP.

If persistent activity continues following the primary anti-VEGF treatment, what secondary treatment should be used – laser or more anti-VEGF? Several factors must be taken into consideration when making the decision.

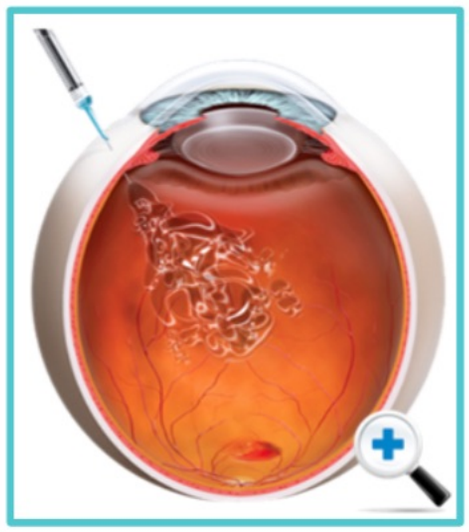
When using anti-VEGF treatment, the **balance between anatomic success versus potential side effects is not always easy to determine**. Factors to consider include:

- Zone
- Functional issues



Laser?

or



Anti-VEGF?

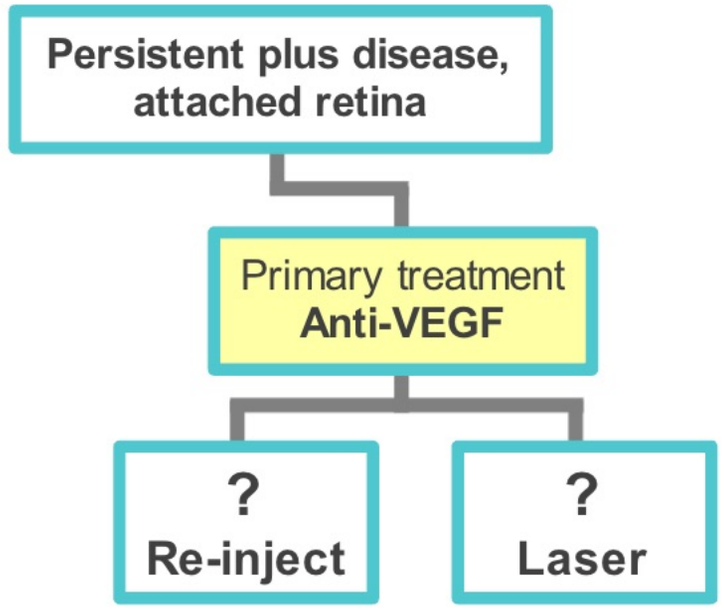
After Primary Anti-VEGF Treatment

Primary treatment using intravitreal anti-VEGF drugs is a different situation (than using laser) in the management of progressive ROP.

If persistent activity continues following the primary anti-VEGF treatment, what secondary treatment should be used – laser or more anti-VEGF? Several factors must be taken into consideration when making the decision.

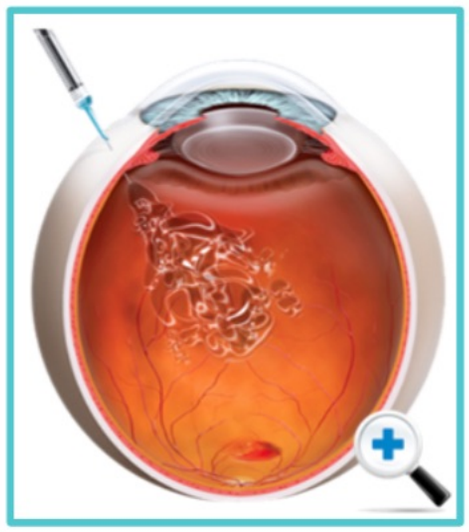
When using anti-VEGF treatment, the **balance between anatomic success versus potential side effects is not always easy to determine**. Factors to consider include:

- Zone
- Functional issues
- Local issues
- Systemic issues



Laser?

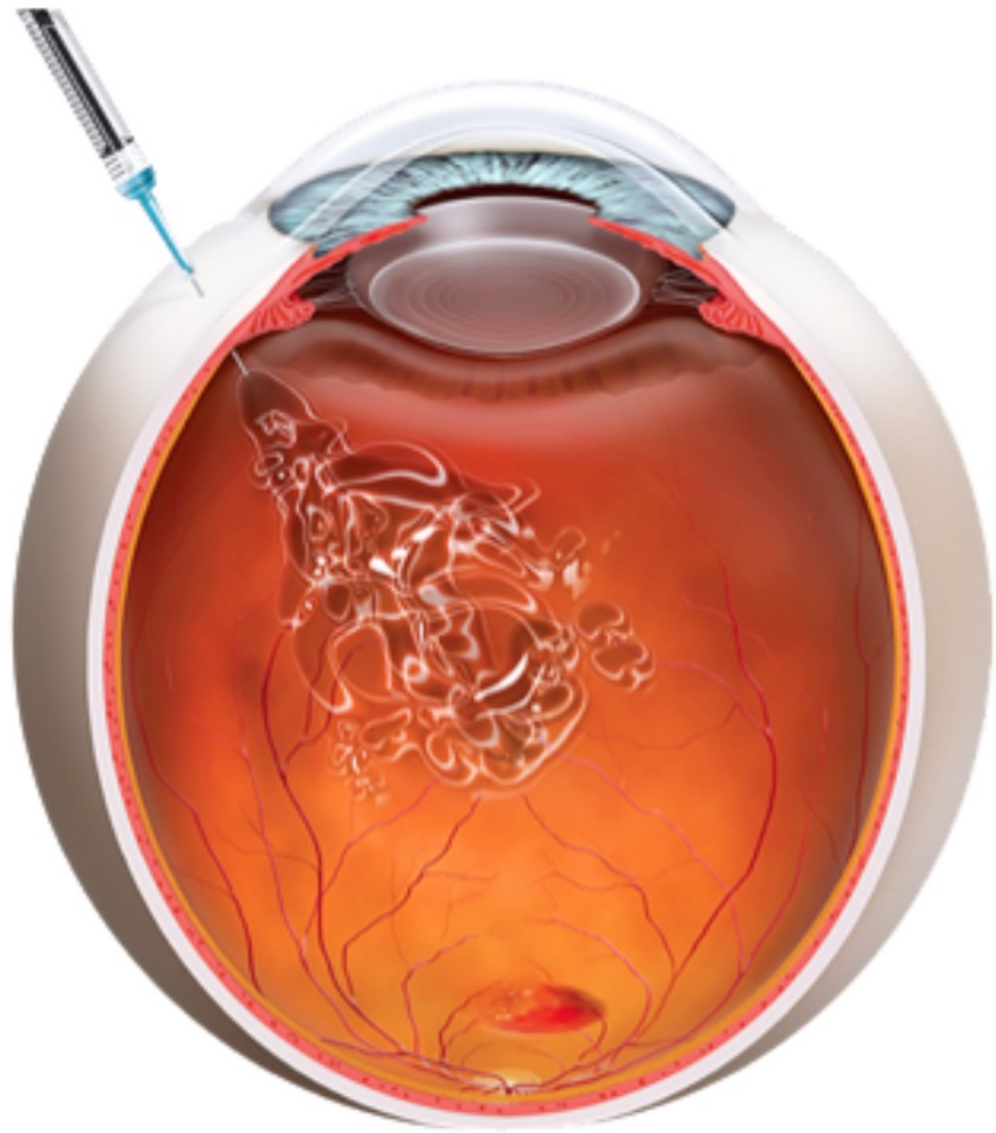
or



Anti-VEGF?

Laser

Anti-VEGF



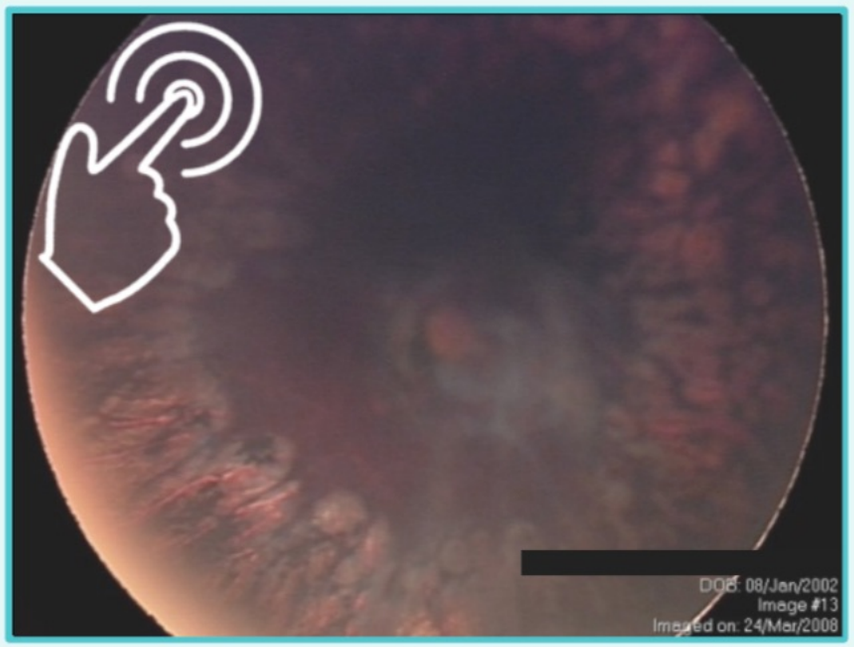
Laser vs Anti-VEGF

When deciding whether to use laser or anti-VEGF treatment it is necessary to **consider certain anatomical and functional factors**. The examples below highlight some of the characteristics of each of these treatment options.

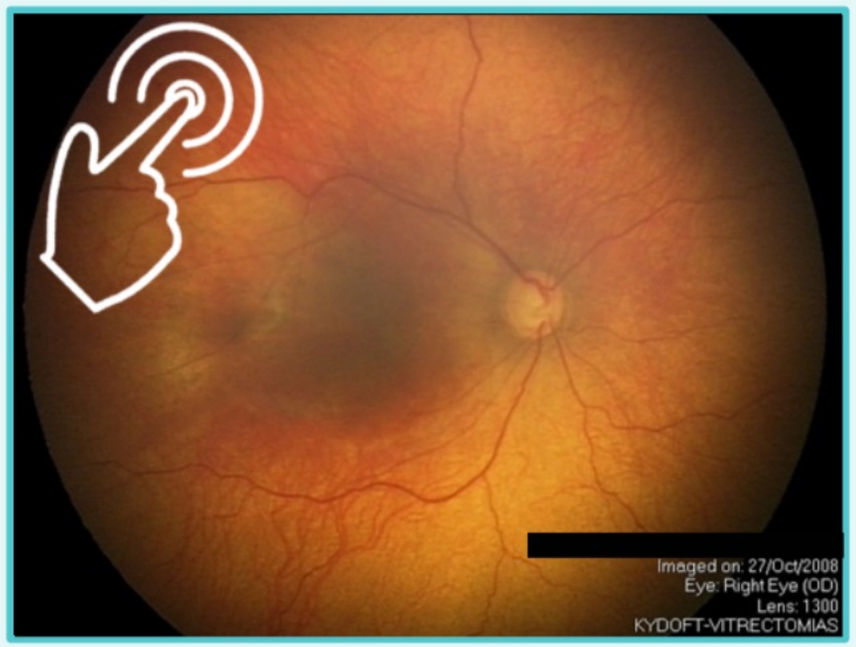
COMPARISON EXAMPLE

The examples below show two patients treated for a posterior zone I ROP - one patient is treated with laser and other patient with an anti-VEGF. Laser photocoagulation is a destructive procedure. This is especially important in cases with posterior zone I ROP where favourable anatomic results can be sometimes obtained, but where functional outcomes can be poor.

LASER



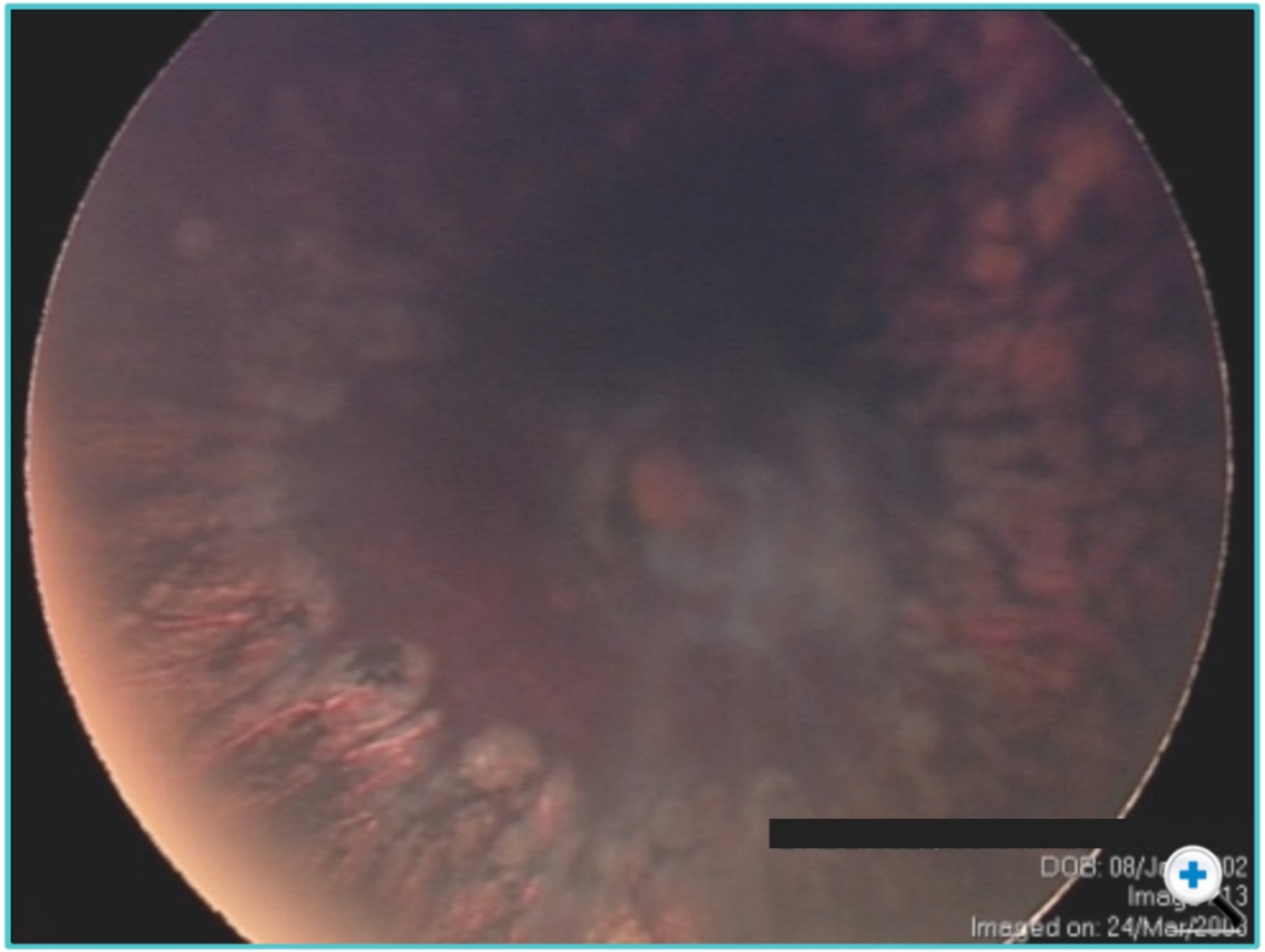
Anti-VEGF



Laser

Several factors need to be considered when using laser:

- Destroys a large area of the peripheral retina
- Incomplete vascularisation
- High myopia
- Decreased visual field
- High incidence of strabismus
- Poor development of foveal depression in some cases



Laser destroys a large area of the peripheral retina. As a result, the infant can end up with high myopia and be left with a very small functional retina.

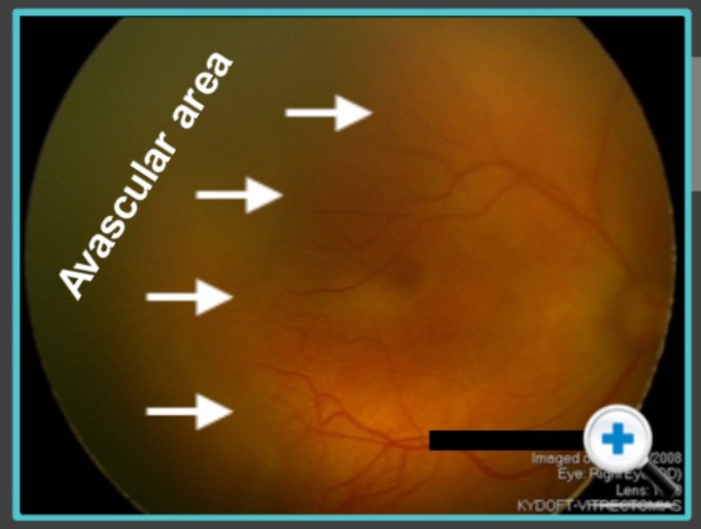
Laser

Anti-VEGF

Anti-VEGF has a number of advantages over laser, including:

- Can produce good anatomical and visual results with less retinal destruction
- Less myopia
- It takes considerably less time
- Less systemically distressful

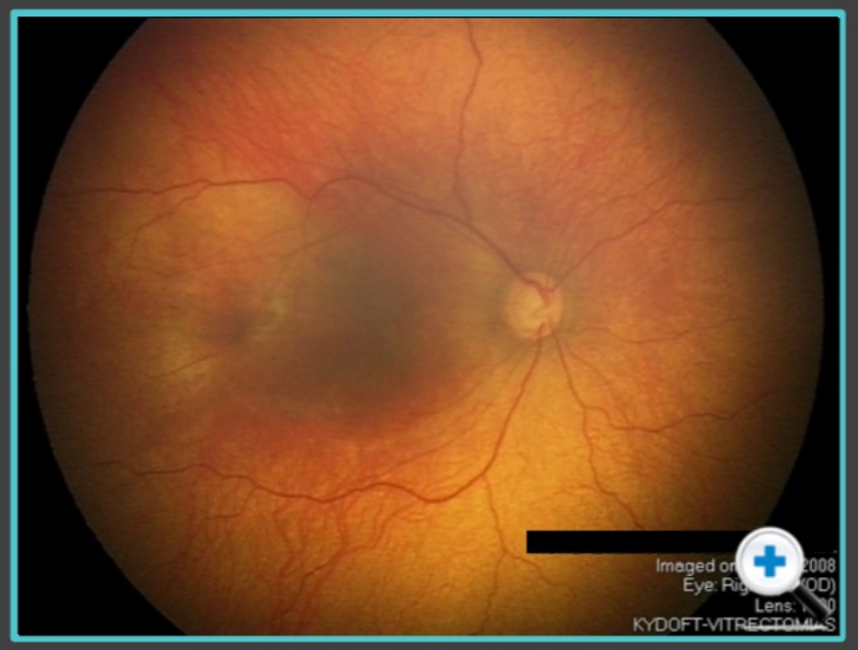
EXAMPLE: Treatment using an anti-VEGF, even with a very large avascular area as in this case, can produce very good anatomical results and visual results. In addition, a normal macular configuration can develop in many of these eyes.

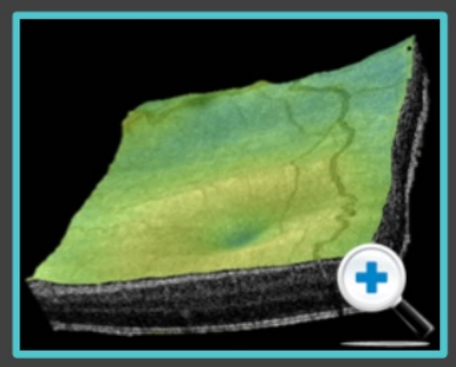


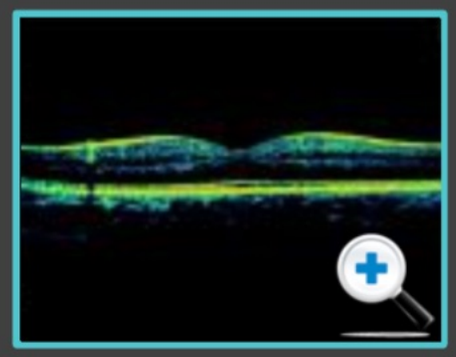
Posterior zone I ROP

GE 23w, 760gr

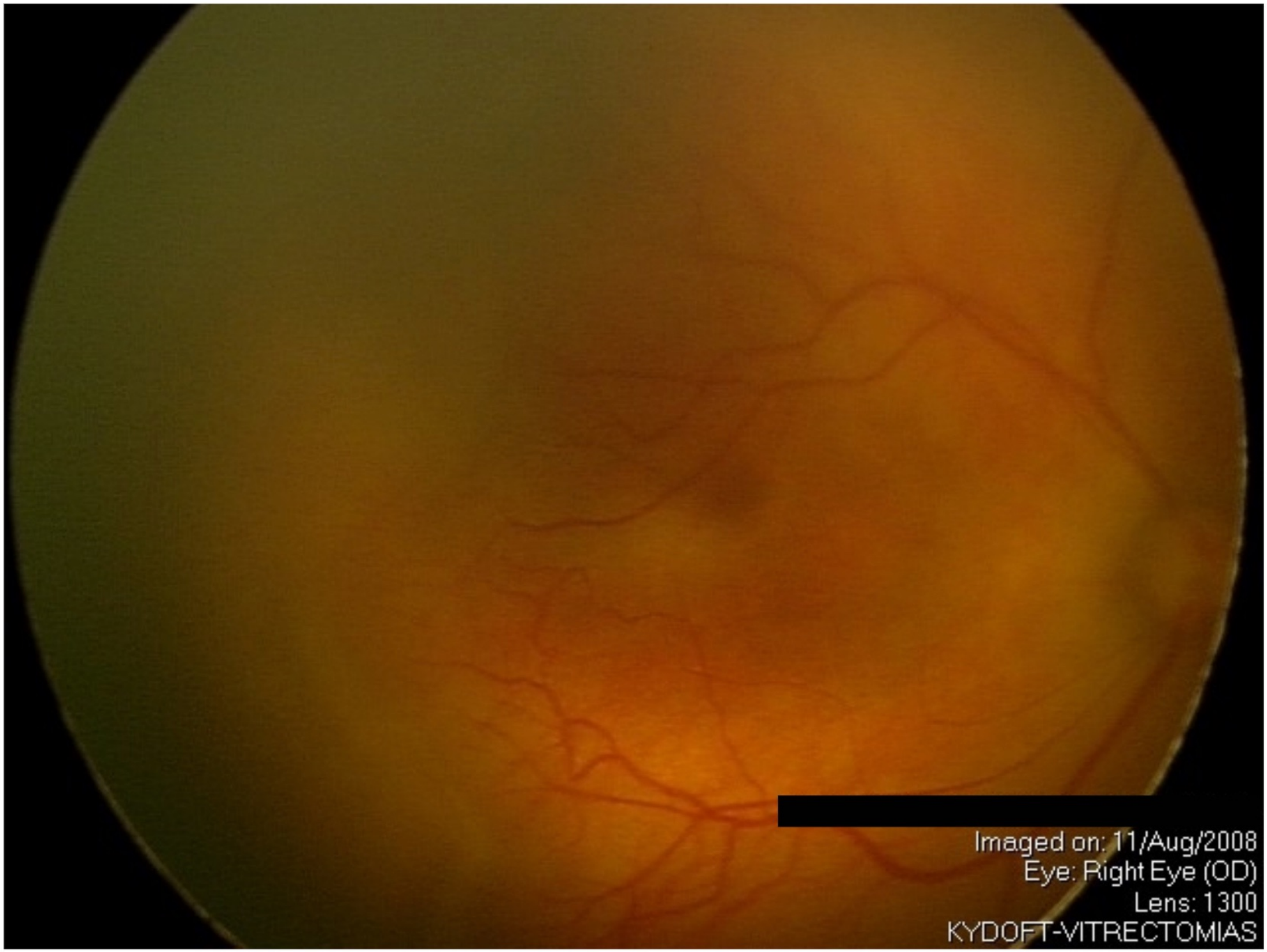
Anti-VEGF treatment



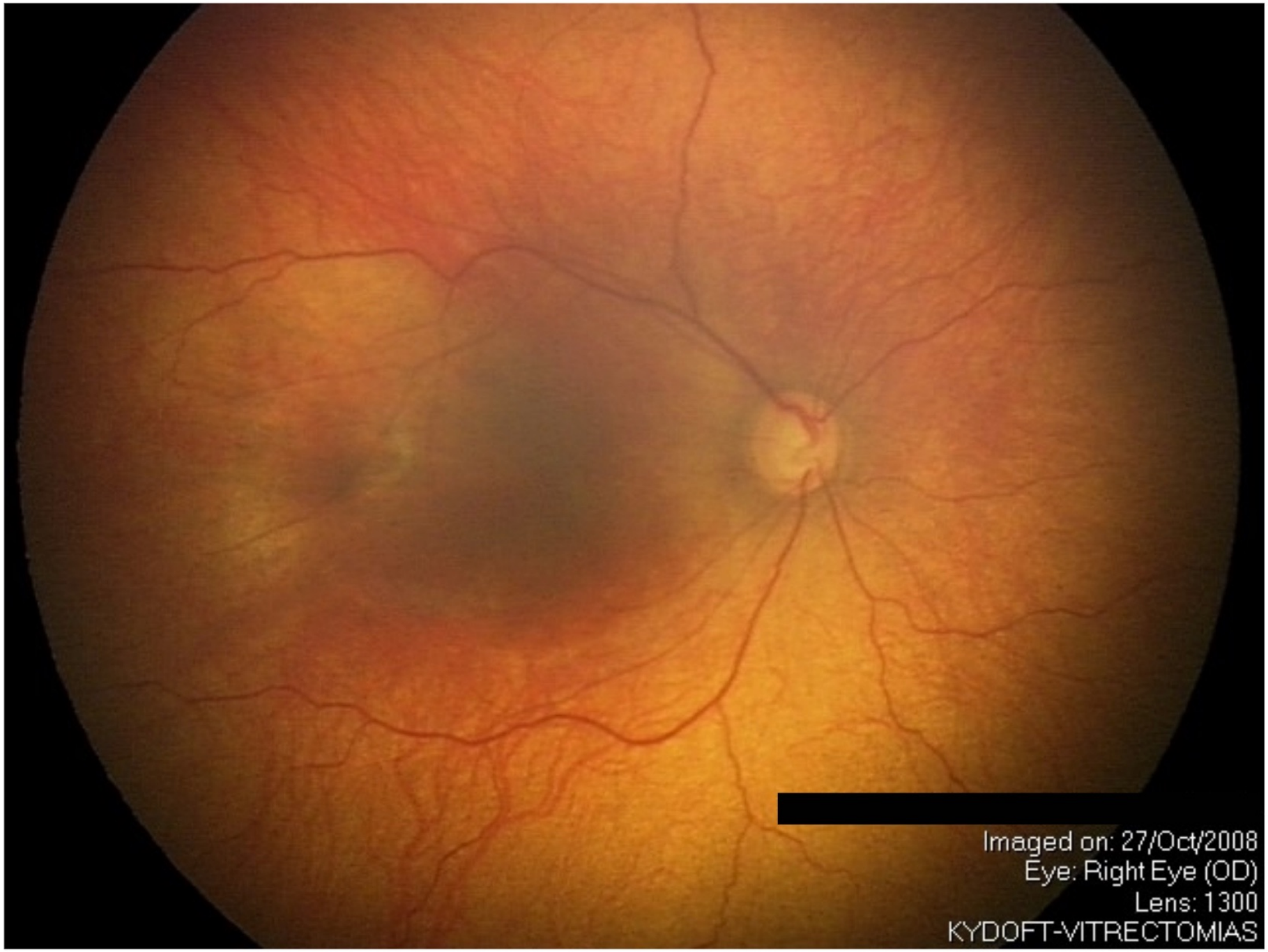




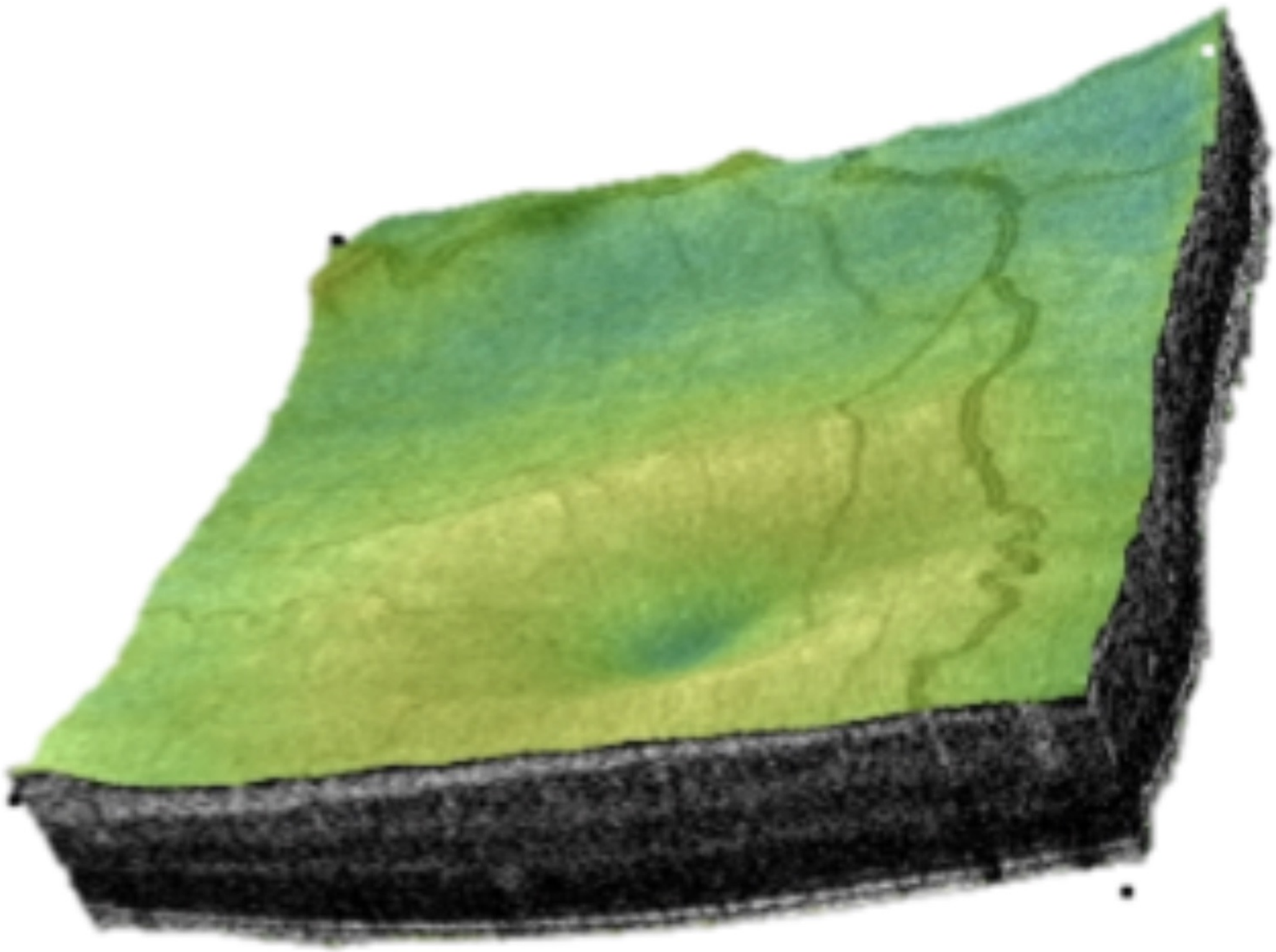
Posterior zone I ROP



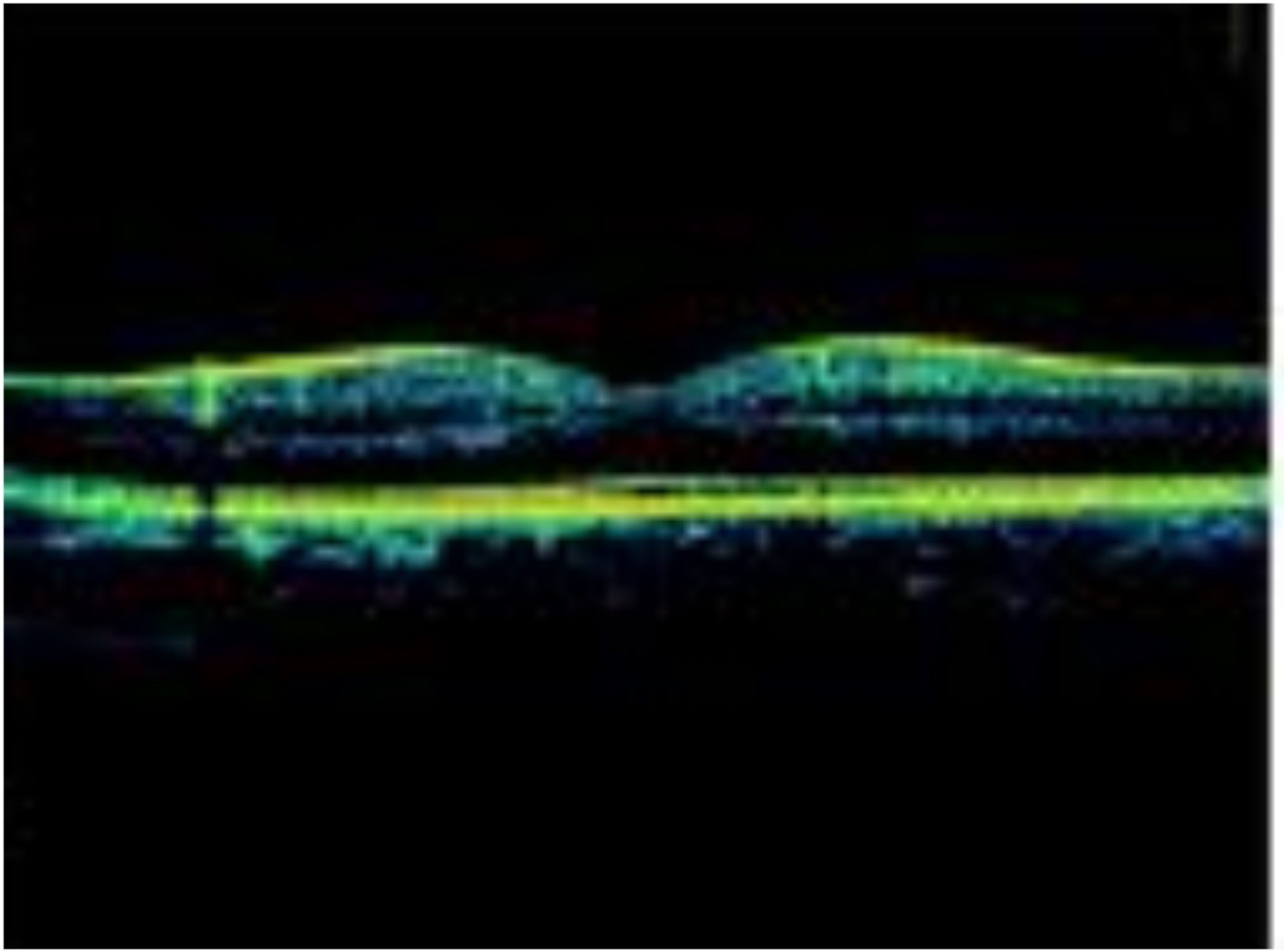
After anti-VEGF treatment



After anti-VEGF treatment



After anti-VEGF treatment



After Primary Anti-VEGF Treatment: Systemic Considerations

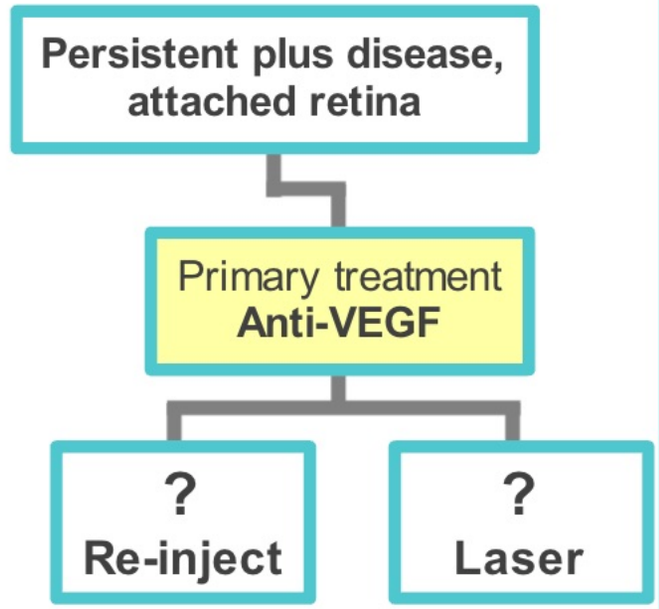
Further investigation is required into **whether the use of anti-VEGF produces systemic problems in preterm infants** – many questions still remain unanswered.

Systemic Considerations

Higher levels of systemic anti-VEGF:

- Preterm infants have more **immature avascular retina in zone I** through which **higher levels of systemic anti-VEGF can enter the circulation** of patients with zone I ROP, and can remain in the systemic circulation for weeks after intravitreal injection (VEGF expression can be inhibited during this period).
- Considered alongside this must be the **potential damage to the blood-retina barrier** after laser treatment.

Therefore, treating patients with either a re-injection of intravitreal anti-VEGF or laser, after the infant has had primary treatment with anti-VEGF, may increase the potential systemic risks / effects.



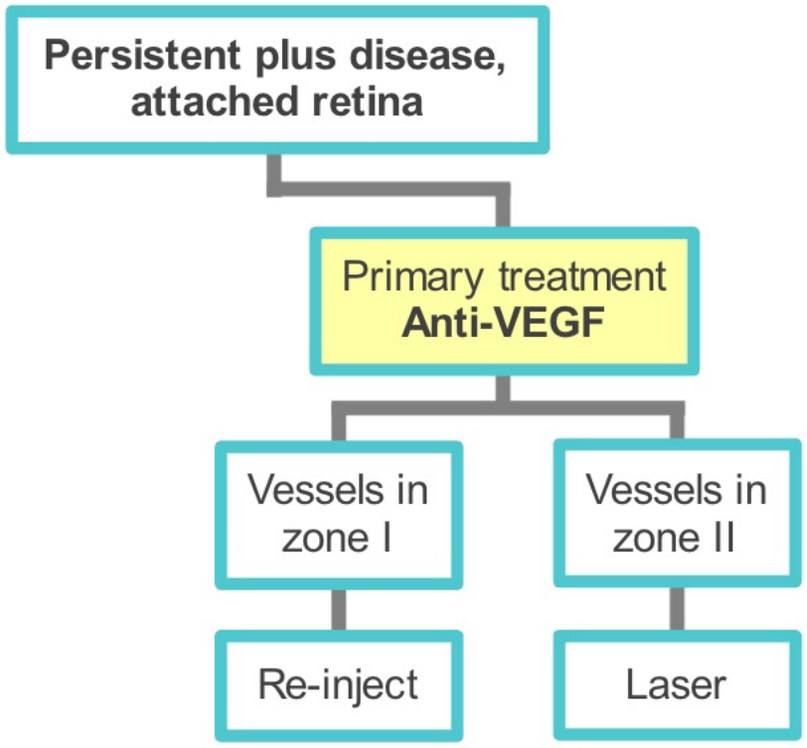
References

After Primary Anti-VEGF Treatment: Secondary Treatment

If progression continues after the primary anti-VEGF treatment, a **secondary treatment approach needs to be decided on**.

Secondary Treatment Approach

- If the **vessels are still in zone I** then **re-injection with an anti-VEGF** is recommended because the risk of an unfavourable outcome (that is the anatomic considerations) takes priority.
- However, if the **vessels have already reached zone II**, then **laser treatment** is recommended. Laser may be a better alternative in these cases due to the increase risk of potential side effects of an anti-VEGF re-treatment.



The location of the vessels can help inform the most suitable secondary treatment.

Click to learn about which brand and dose of anti-VEGF to use.

Secondary Anti-VEGF Treatment - Which Drug? What Dose?

Relative unknowns: when using anti-VEGF as either a primary or secondary treatment, the following details are still relatively unknown:

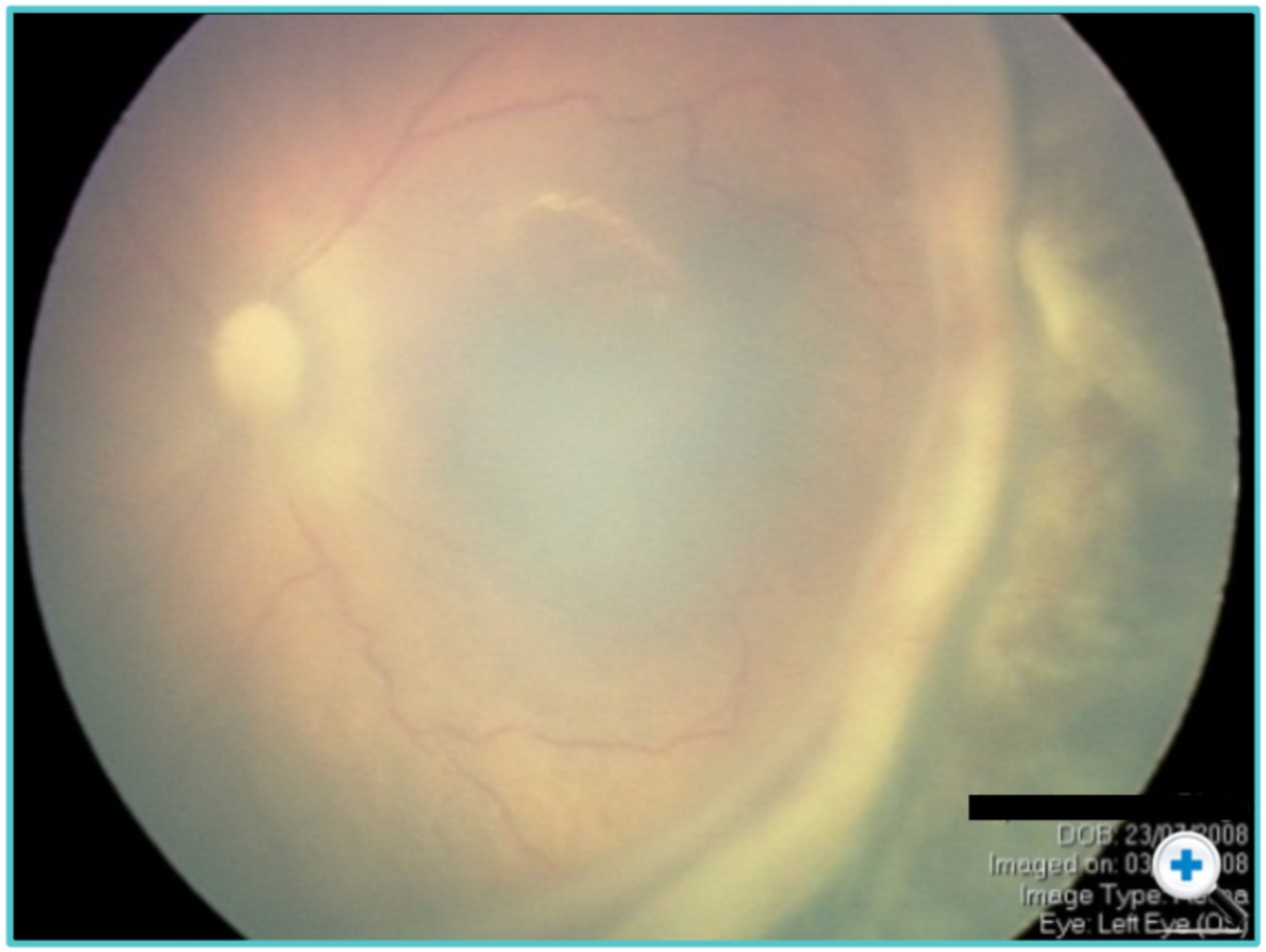
- **What type/brand of anti-VEGF drug is best to use?**
  - *The answer is still unknown*
- **What is the optimal dosage of anti-VEGF with which to treat patients?**
  - *The answer is still unknown*

Preventing RD After Using Anti-VEGF Drugs to Treat ROP

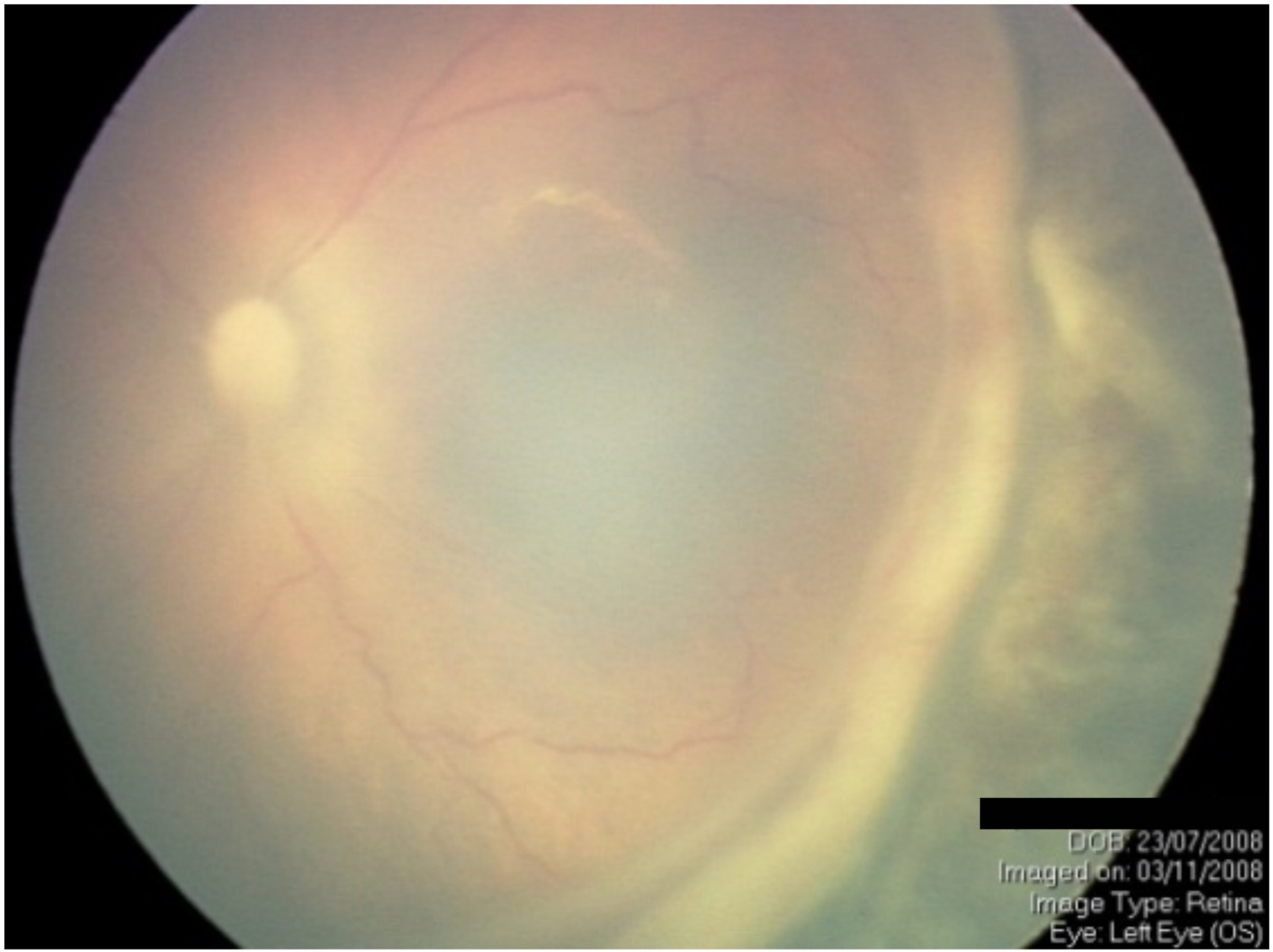
When anti-VEGF treatment is used, another issue to be aware of is **delayed-onset retinal detachment (RD) despite early regression**, which has even been reported after 60 weeks of postmenstrual age (PMA).

Patterns of regression and recurrence are not yet well known in patients treated with anti-VEGF. Therefore, in order to avoid missing the diagnosis of delayed-onset retinal detachment despite early regression, **extended follow-up** is essential and **must be performed** after the use of anti-VEGF injections.

If for any reason follow-up is not possible, lasering of the peripheral retina (zone II or III) is recommended in order to give a stabilised eye.



Delayed-onset retinal detachment (RD) despite early regression



Re-Treatments After Anti-VEGF

Although anti-VEGF is a valuable treatment option in the management of progressive ROP many **studies report a high number of re-treatments required following the use of anti-VEGF**.

Why is there such a high number of re-treatments in some reports?

Factors that may explain this high number of re-treatments include:

- Different Patient Types
- Injection Issues
- Unnecessary Re-Treatments

Click the tabs to learn more about the factors that may increase re-treatments

Re-Treatments After Anti-VEGF

Although anti-VEGF is a valuable treatment option in the management of progressive ROP many **studies report a high number of re-treatments required following the use of anti-VEGF**.

Why is there such a high number of re-treatments in some reports?

Factors that may explain this high number of re-treatments include:

- Different Patient Types
- Injection Issues
- Unnecessary Re-Treatments

Click the tabs to learn more about the factors that may increase re-treatments

Different Patient Types

Different types of patients/populations with different gestational age (GA), birth weight (BW) and genotypes. More immature with different evolution *vs* more mature and sicker?

	GA	BW	PMA at IVB
BEAT ROP	24,2	615g	34,5
Chilean series	25,6	846g	34

Close this window

Re-Treatments After Anti-VEGF

Although anti-VEGF is a valuable treatment option in the management of progressive ROP many **studies report a high number of re-treatments required following the use of anti-VEGF**.

Why is there such a high number of re-treatments in some reports?

Factors that may explain this high number of re-treatments include:

- Different Patient Types
- Injection Issues
- Unnecessary Re-Treatments

Click the tabs to learn more about the factors that may increase re-treatments

Injection problems:

Simple issues with the injection such as:

- Time of injection
- Syringe and volume issues (ensure to correctly inject the anti-VEGF into the eye otherwise it will result in poor results)

Close this window

Re-Treatments After Anti-VEGF

Although anti-VEGF is a valuable treatment option in the management of progressive ROP many **studies report a high number of re-treatments required following the use of anti-VEGF**.

Why is there such a high number of re-treatments in some reports?

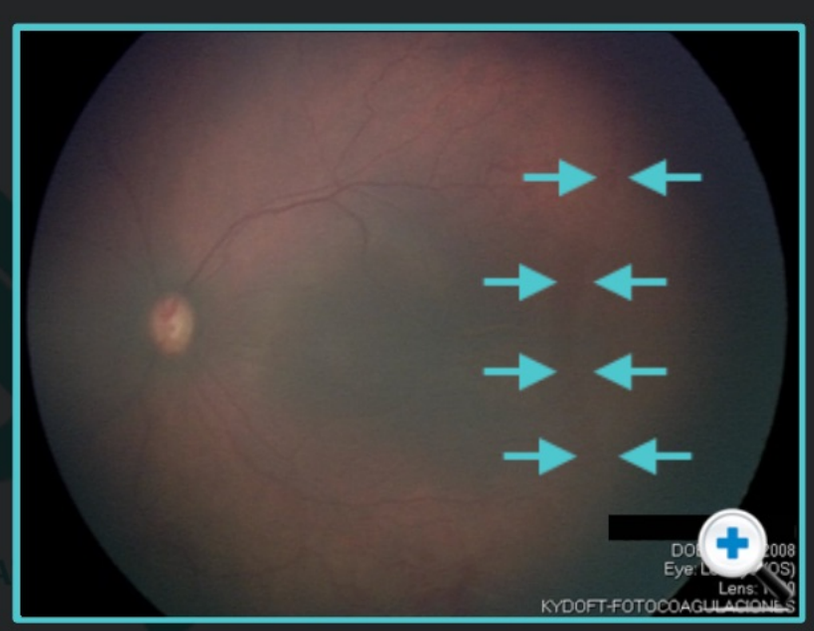
Factors that may explain this high number of re-treatments include:

- Different Patient Types
- Injection Issues
- Unnecessary Re-Treatments

Click the tabs to learn more about the factors that may increase re-treatments

Unnecessary re-treatments?

Unnecessary re-treatments due to the fact that patterns of regression and recurrence are not yet well known in patients treated with anti-VEGF. For example, doctors are tempted to re-treat without waiting long enough to see the effects of the anti-VEGF.



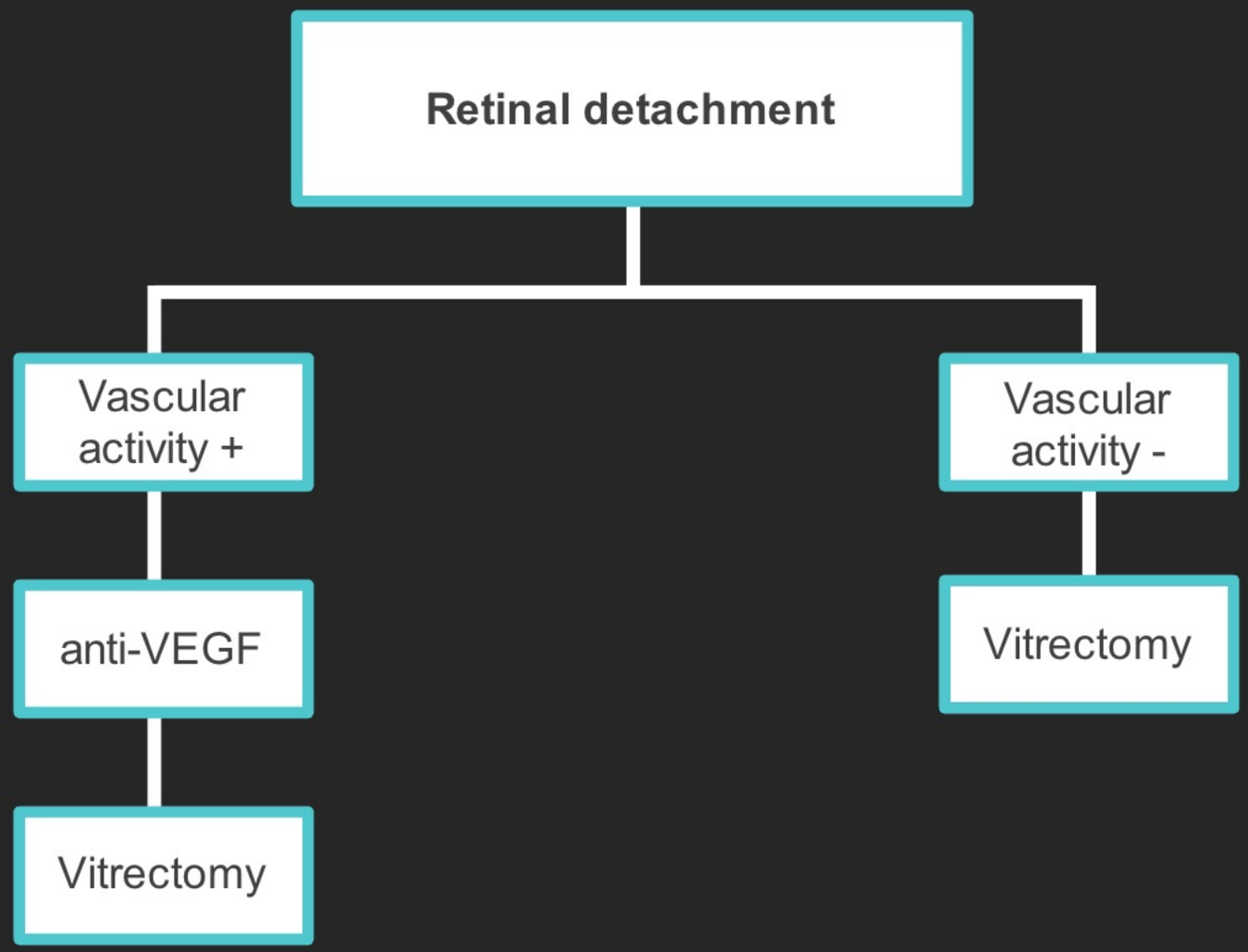
Close this window

Module Progress:

Retinal Detachment

Management of Progressive ROP

Detached Retina

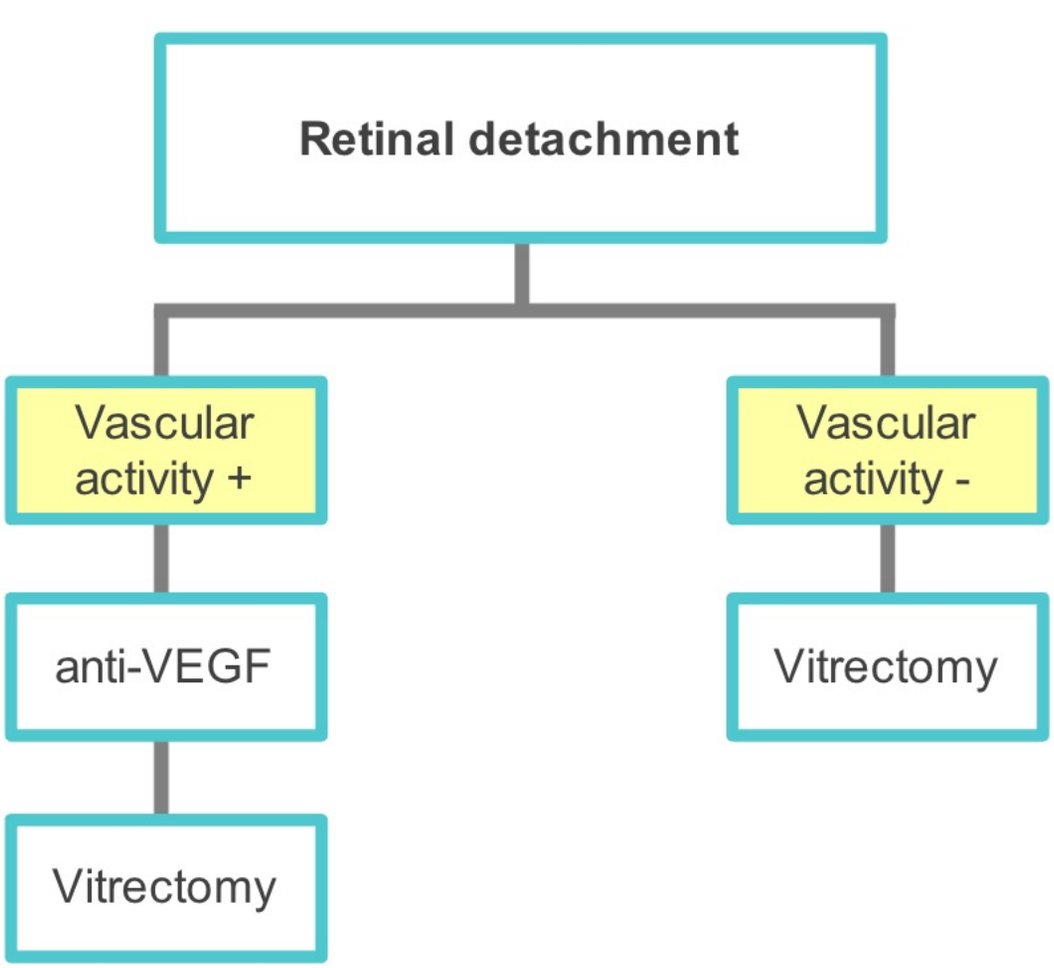


Click 'Next' to continue

Management of Progressive ROP: Retinal Detachment

This topic examines **progressive ROP where a retinal detachment is present**, which is a completely different situation in the management of progressive ROP.

The **vascular activity** must be checked in a patient with progressive ROP with retinal detachment - the presence or absence of vascular activity will inform the subsequent steps (i.e. whether adjunct anti-VEGF is required prior to vitrectomy).

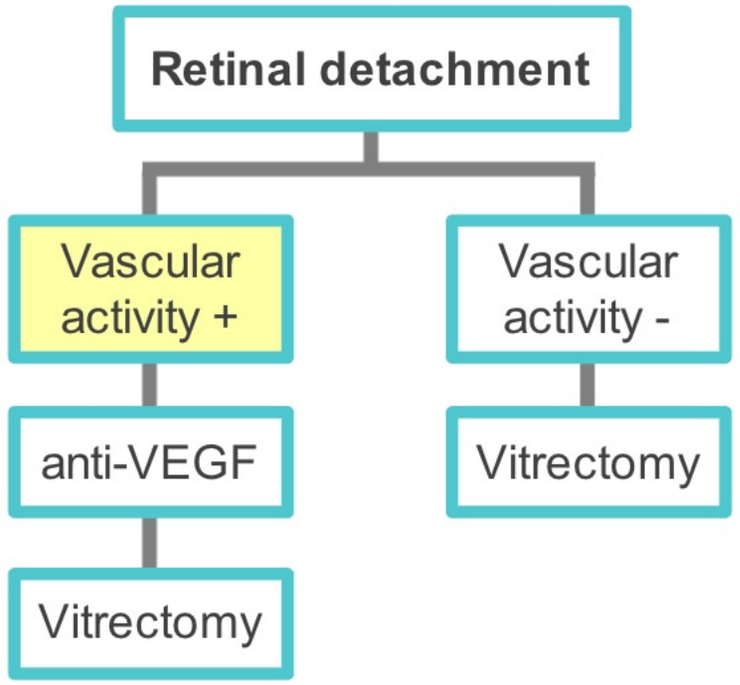


Anti-VEGF as an Adjunct in ROP Retinal Surgery (Vascular Activity)

Vascular activity is a major problem when operating ROP retinal detachments; operating on active ROP typically gives very poor results.

On the other hand, delaying surgery in the hope that the eye will become spontaneously "quiet" can lead to progression of the detachment.

The **solution in these situations is the use of preoperative anti-VEGF drugs** to make the eye "quiet", which then allows surgery to proceed.



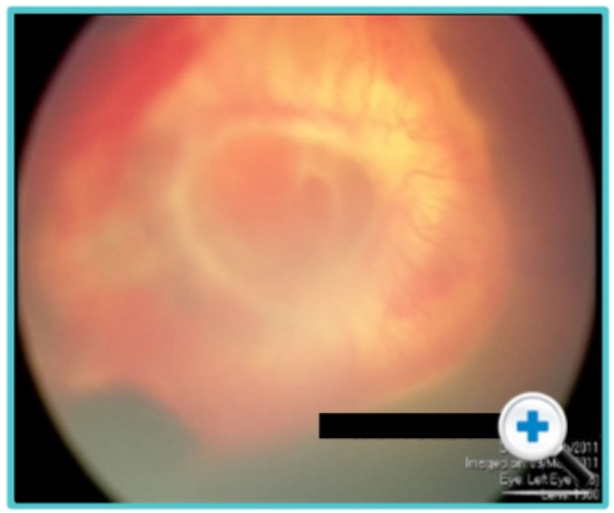
Anti-VEGF as an adjunct prior to vitrectomy

Using anti-VEGF as an adjunct should significantly **reduce vascular activity**. This reduction then allows for a straightforward vitrectomy in a quiet eye which in turn can lead to good anatomical results.

ADJUNCT

Adjunct Anti-VEGF Example

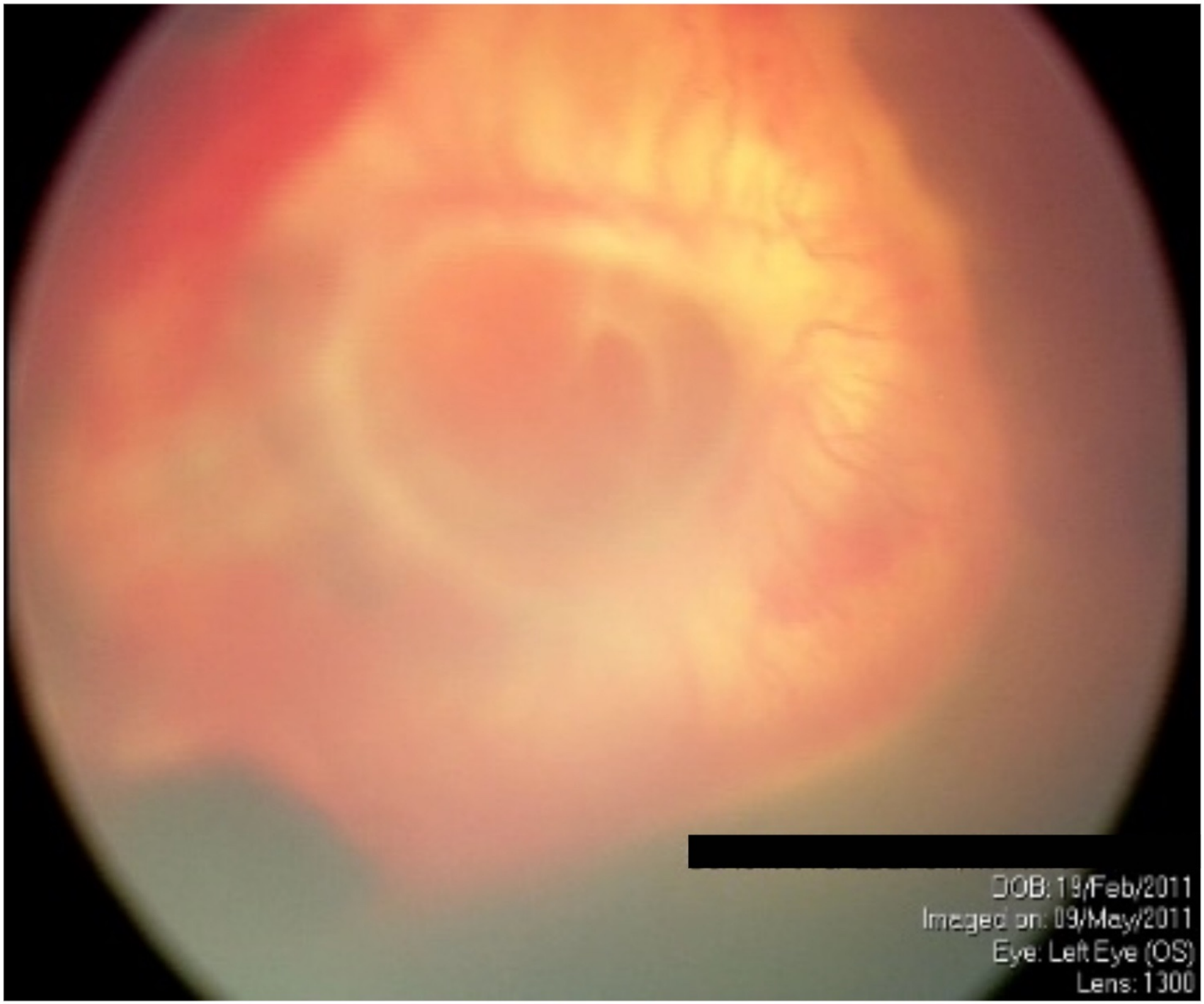
Earlier Intervention?



Vascular Activity

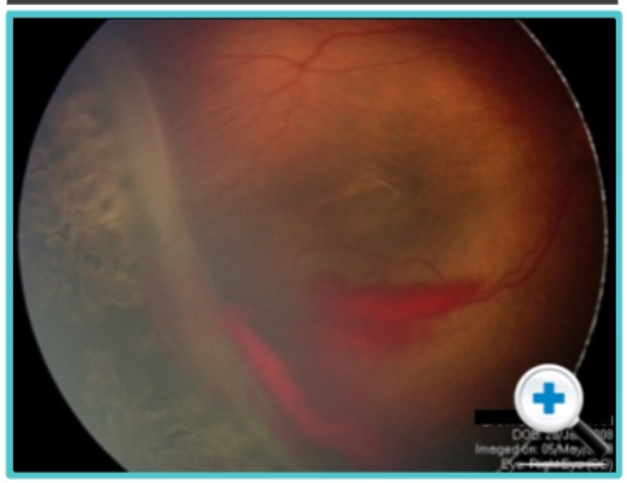
Click each tab to learn more about using anti-VEGF as an adjunct

Vascular Activity



Example of anti-VEGF as an adjunct

Avastin
(IV 0,625mg)

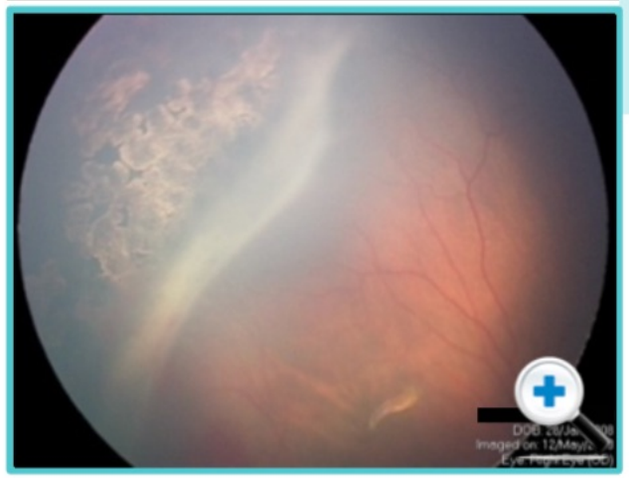


38 weeks

1 week later

- This example shows a **vascular active stage 4A detachment that is injected with Avastin at 38 weeks**.
- A week later (39 weeks) a vitrectomy is performed in a **vascularly inactive eye**.

Vitrectomy
25g LS Vity

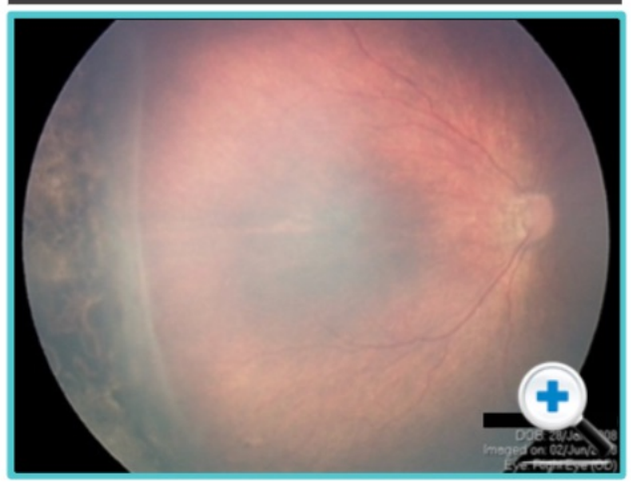


39 weeks

A very significant reduction in the vascular activity is observed one week later when the vitreo-retinal surgery is performed.

3 weeks later

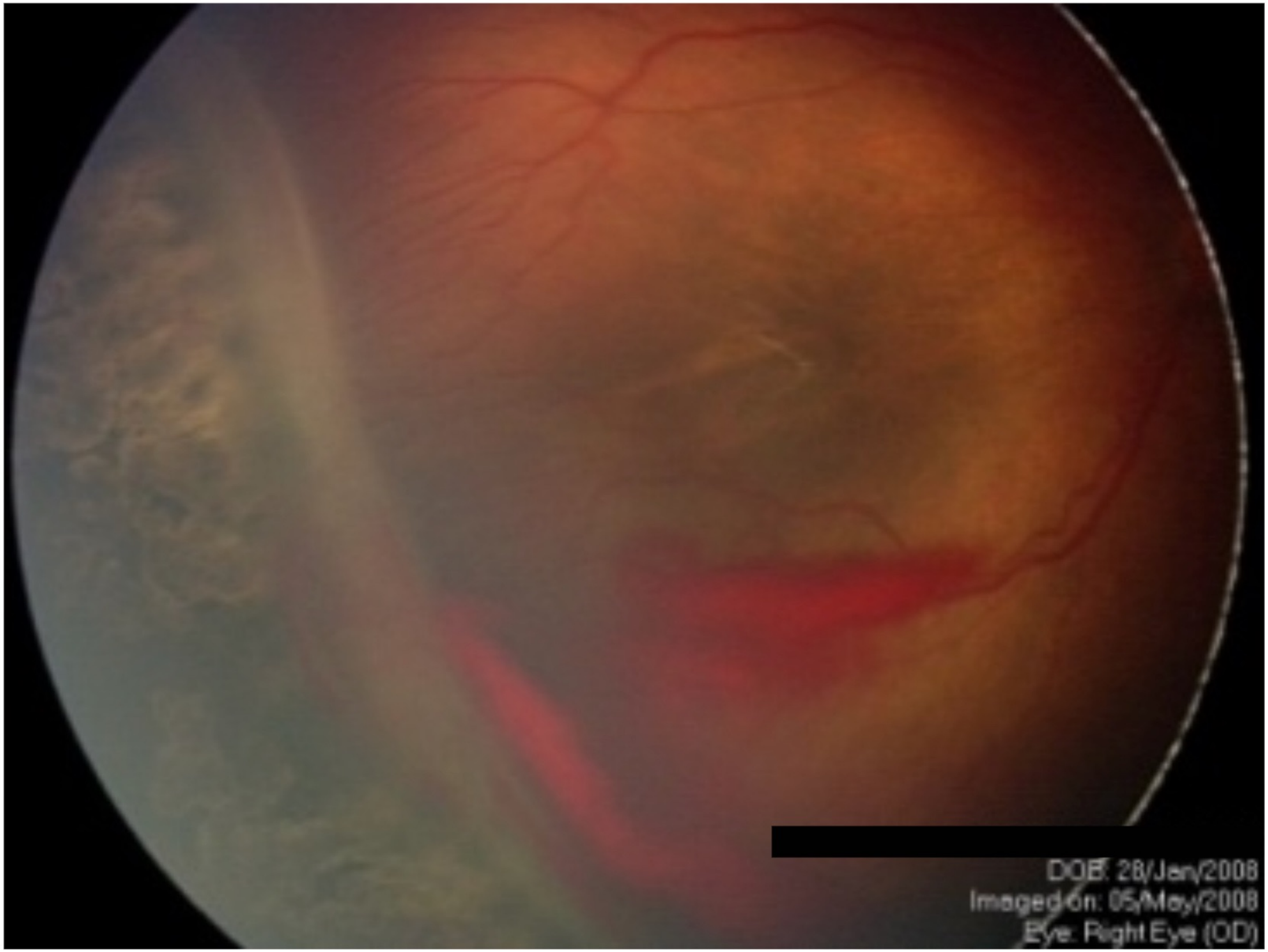
3 weeks post Vitrectomy,
4 weeks post Avastin



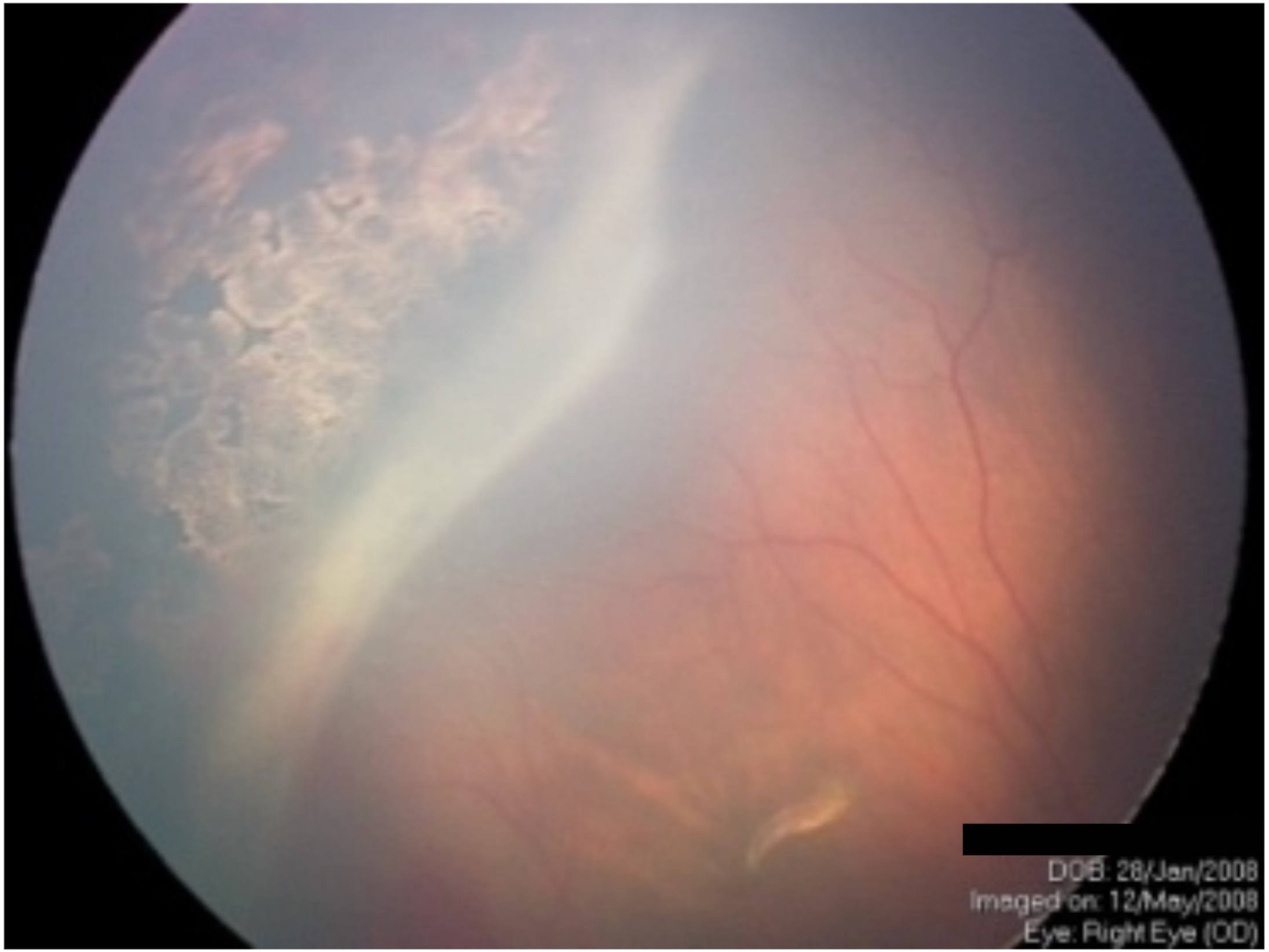
42 weeks

RESULTS:
11 eyes (8 patients), 100% favourable results

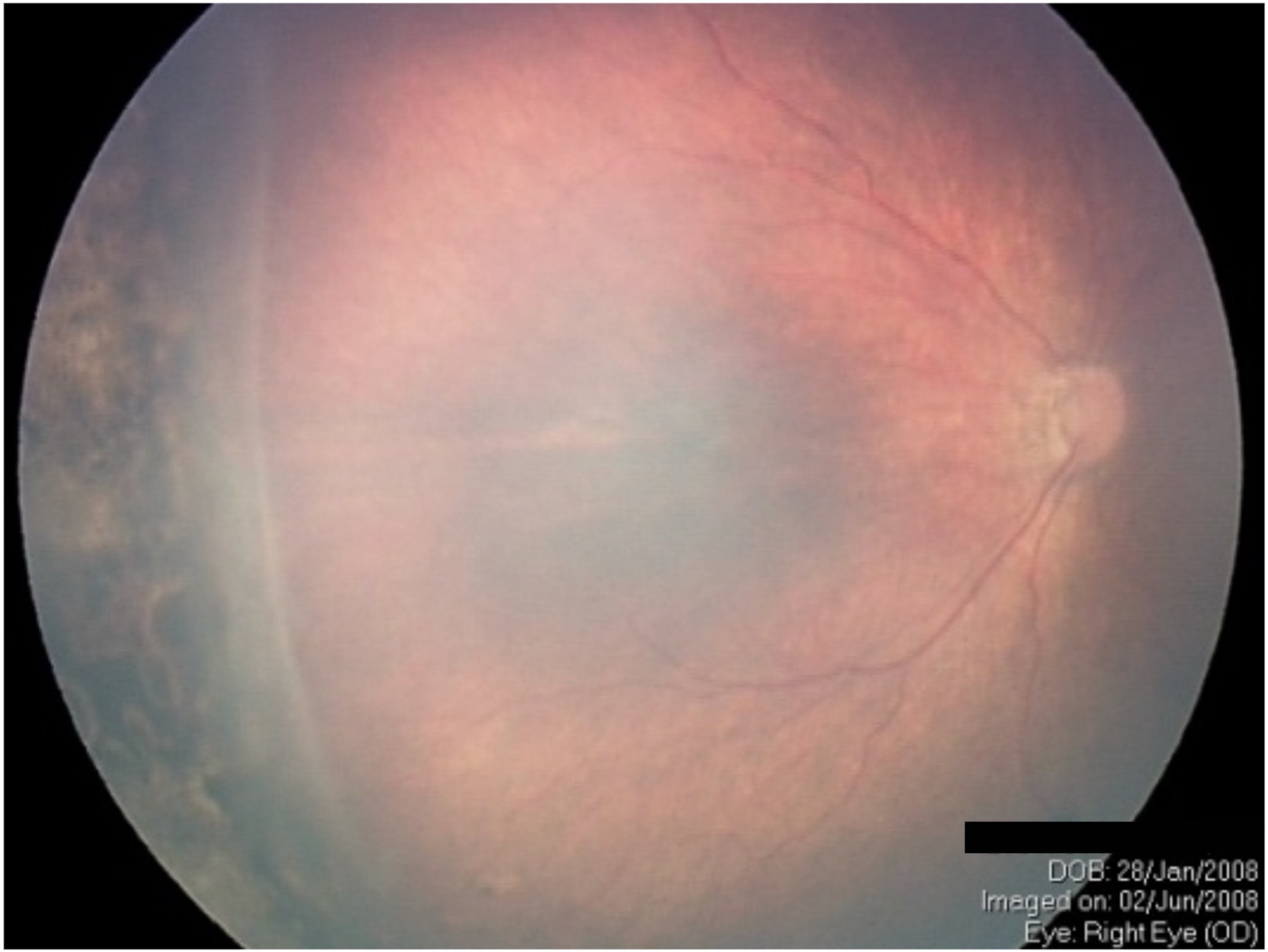
38 weeks



39 weeks



42 weeks



Does combining anti-VEGF and LSV in stage 4A ROP result in earlier intervention?

The typical **average time for surgical intervention** (vitrectomy) for stage 4A ROP is close to **40 weeks**.

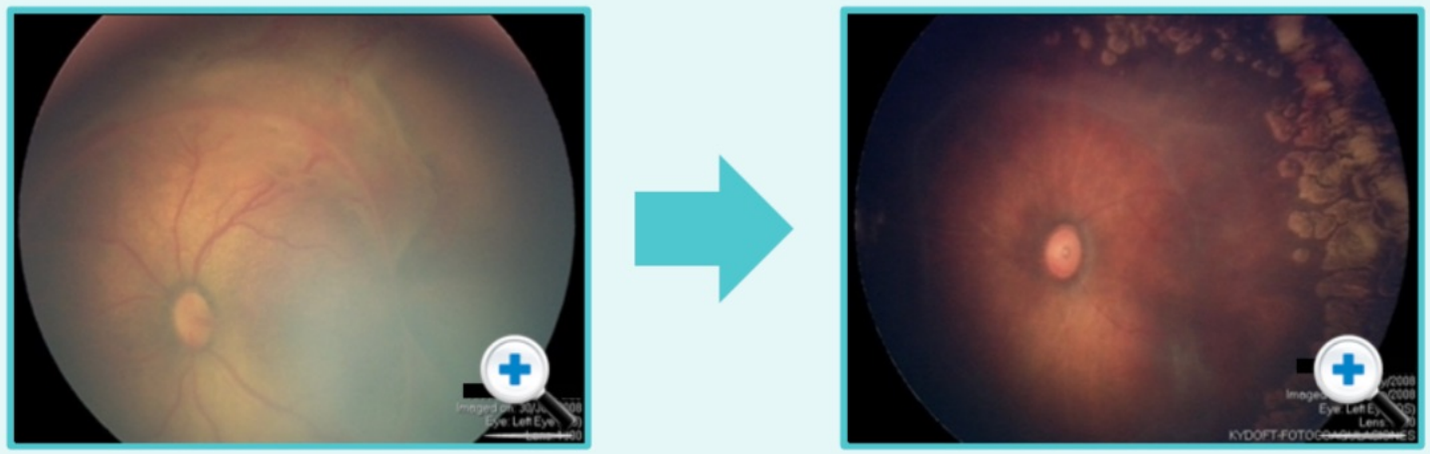
Two-step approach

Combining adjunct anti-VEGF and lens-sparing vitrectomy (LSV) may support **earlier surgery** (than was previously possible due to the presence of vascular activity), hence **potentially increasing functional results**. This is like any other detachment in the sense that **the sooner you operate the better**.

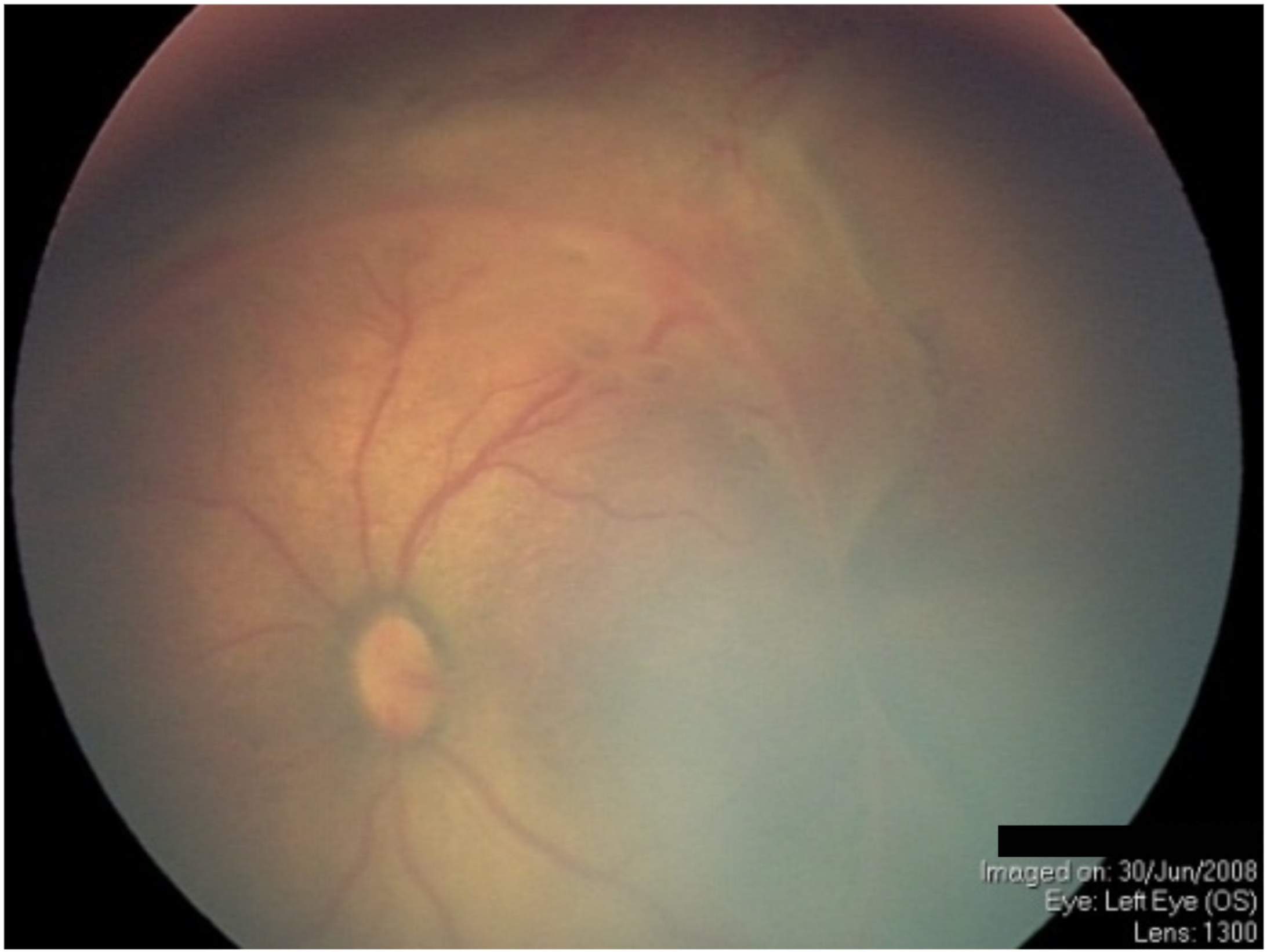
Example: Combining the use of an anti-VEGF injection (Avastin) with a lens-sparing vitrectomy in stage 4A cases proved to be very effective in a study by Dr Kychenthal (module editor) et al. who were able to perform the vitrectomies at an earlier stage – closer to **38 weeks.**

	BW	GE	ROP ZONE	LASER TREATMENT	ROP AT PRESENTATION	AVASTIN	STAGE AT SURGERY	SURGERY
RE+LE	1740	31	II	yes	4A	39	4A	25G Vpp lensparing @40 wks
P6 (RE+LE)	866	24	II	INCOMPLETE	4A	36	4A	25G Vpp lensparing @37 wks
P7 (RE+LE)	760	24	I	37 wks	4A	37	4A	25G Vpp lensparing @38 wks
P8 (RE)	810	25	II	INCOMPLETE	4A	38	4A	25G Vpp lensparing @39 wks
Average	**1044**	**26**				**37,5**		**38,5**

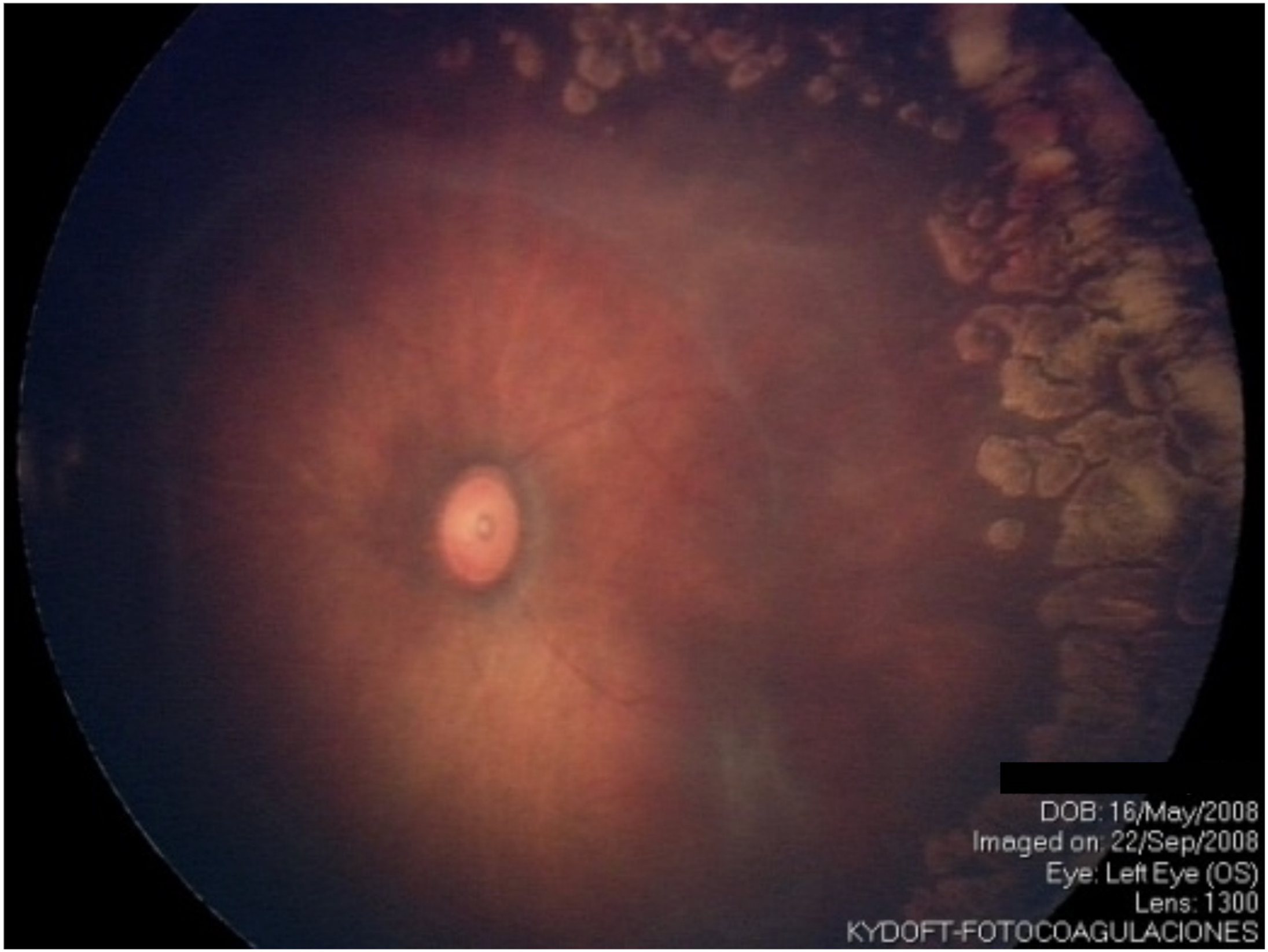
RESULTS:
7 eyes (4 children) with stage 4A, 100% with favourable outcome



Combining Anti-VEGF and LSV in Stage 4A ROP



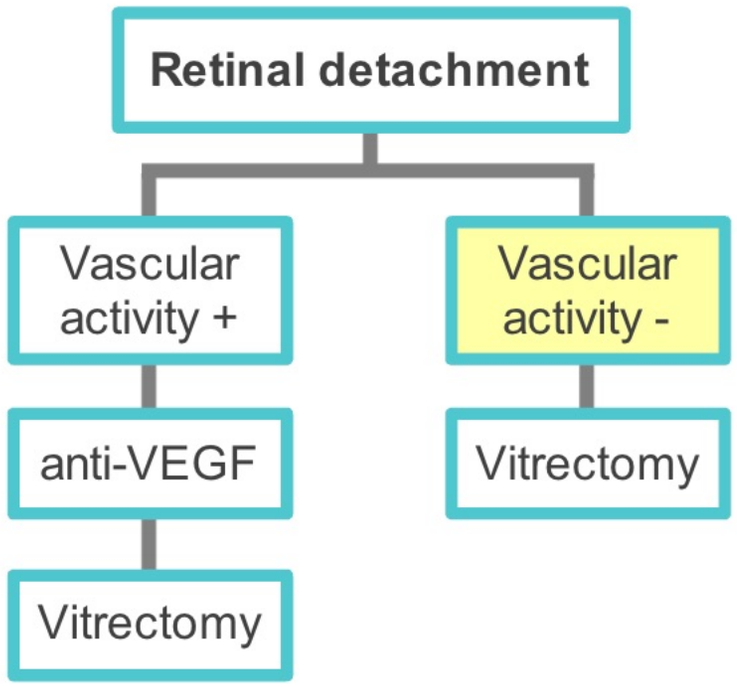
Combining Anti-VEGF and LSV in Stage 4A ROP



Retinal Detachment (No Vascular Activity)

The other situation in progressive ROP with a retinal detachment is where there is **no vascular activity**, and this is typically seen in patients with:

- Untreated ROP (stage 5)
- Longstanding primary treatment failures
- Referrals for re-operations



In these cases, **no adjuvant treatment (anti-VEGF) should to be used** prior to vitrectomy.

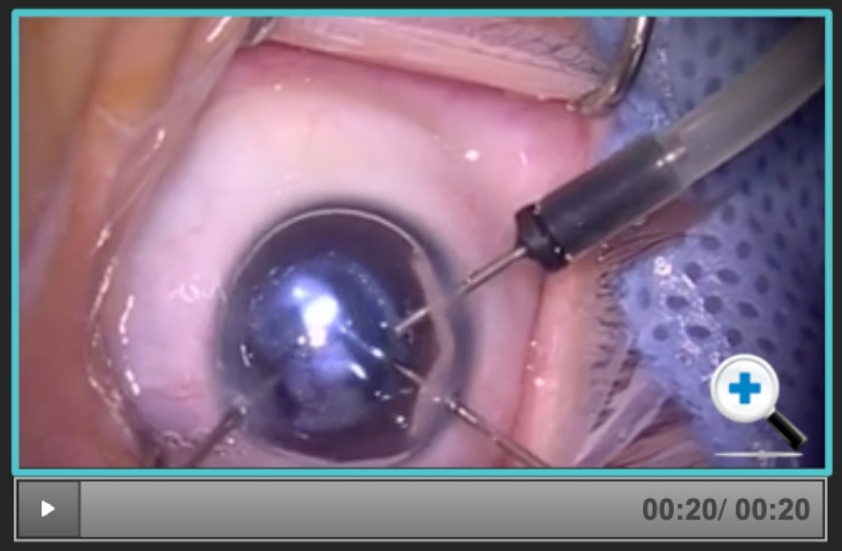
Managing RD: Immediate Sequential Bilateral Vitrectomy

In cases where patients receive **no primary treatment and develop stage 5 ROP** (and in many other paediatric conditions also), **immediate sequential bilateral vitrectomy** is recommended because:

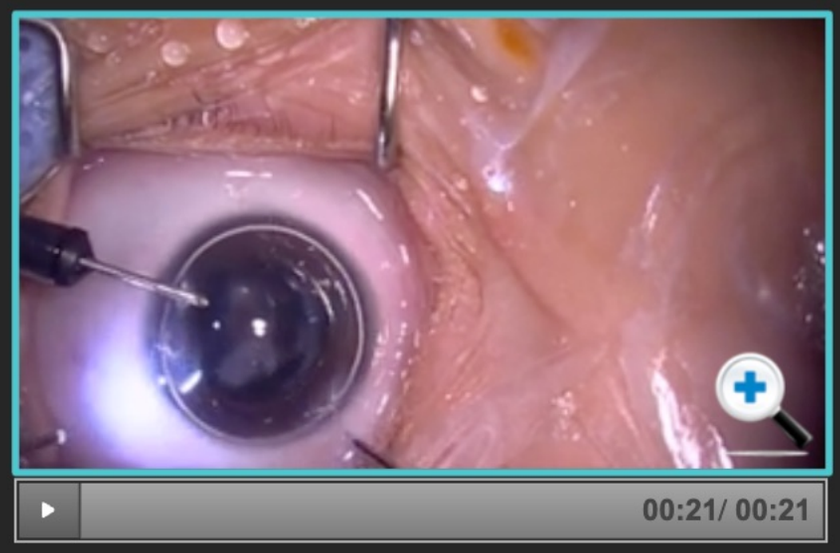
- There is **less risk of general anaesthesia**
- It is **more cost effective**

Example: Immediate sequential bilateral vitrectomy for untreated stage 5 ROP (no primary treatment)

RE



Re-drape



LE

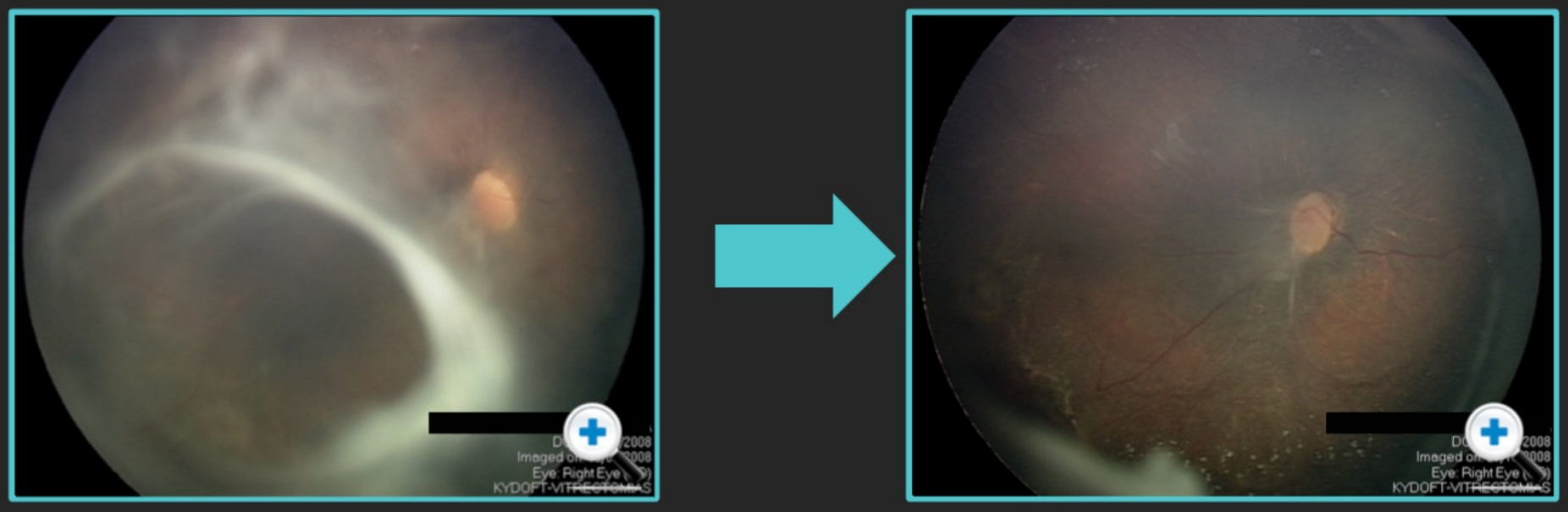
Stage 5 ROP, 28 weeks, 1200 gr, zone I, no primary treatment,
age at vitrectomy = 1 year old

Re-operations in ROP

ROP is a **progressive disease** in a growing eye which can induce unfavourable results, even after a primary vitrectomy (i.e. a primary vitrectomy failure).

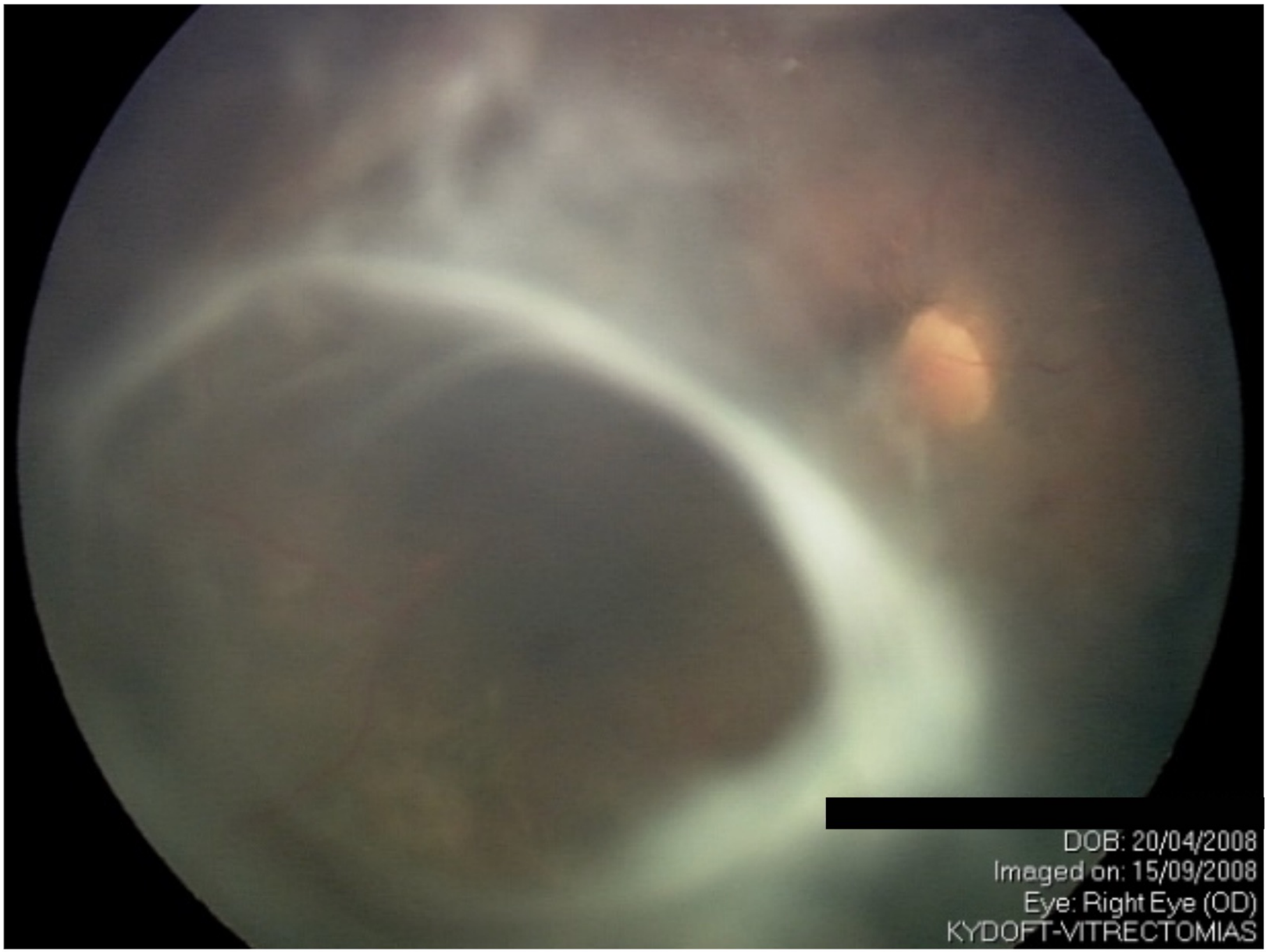
Re-operations should be considered in these cases. Although these types of cases may not look very promising, they can have good anatomical outcomes and potentially good functional prognosis with further surgery.

Example: A lot of residual traction is seen in this patient who was referred **after a primary vitrectomy for ROP**. Re-attachment of the retina can be achieved in some of these cases by performing another vitrectomy.



Case referral after vitrectomy failure in a ROP. Case born at 25 weeks with BW 750 grams.

Re-operations in ROP



Re-operations in ROP

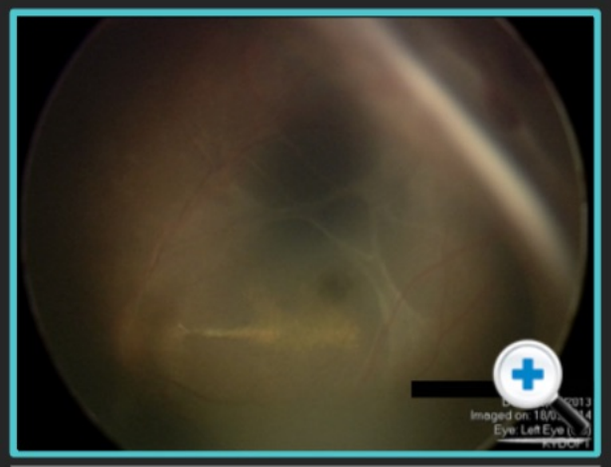
Scleral Buckling in Re-Operations

A **scleral buckling band** may be more suitable in other cases of progressive ROP where a patient is referred after vitrectomy failure, and where there is a retinal detachment with a lot of residual traction.

SCLERAL BUCKLING EXAMPLE

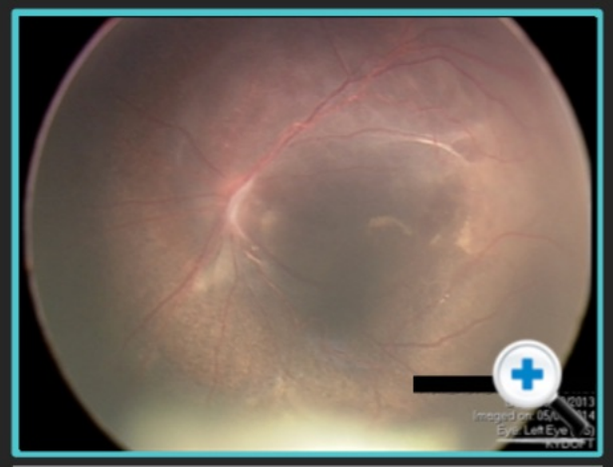
A 360° band is used in this case where the patient had previous vitrectomy, and where there is a lot of residual traction. The retina settled over several weeks.

Important to remember when using bands in such cases: The patient is not an adult so the retina will not flatten in 24 hours. After surgery, it may take **several weeks** for the retina to re-attach.



Total RD after vitrectomy

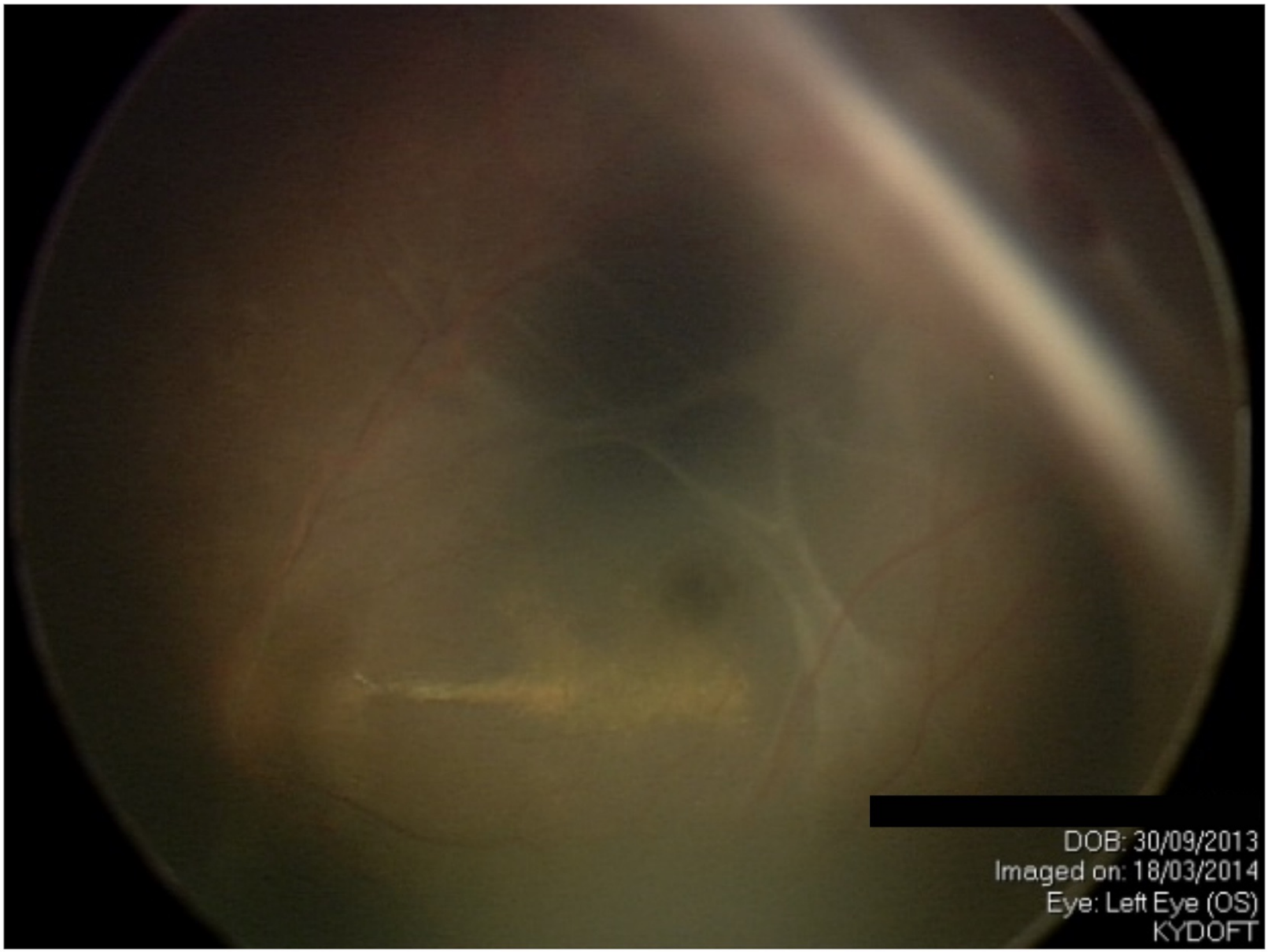
360° band



Retina attached after surgery over a period of **several weeks**

Case referral after vitrectomy failure in a ROP. Case born at 26 weeks with BW 1000 grams.

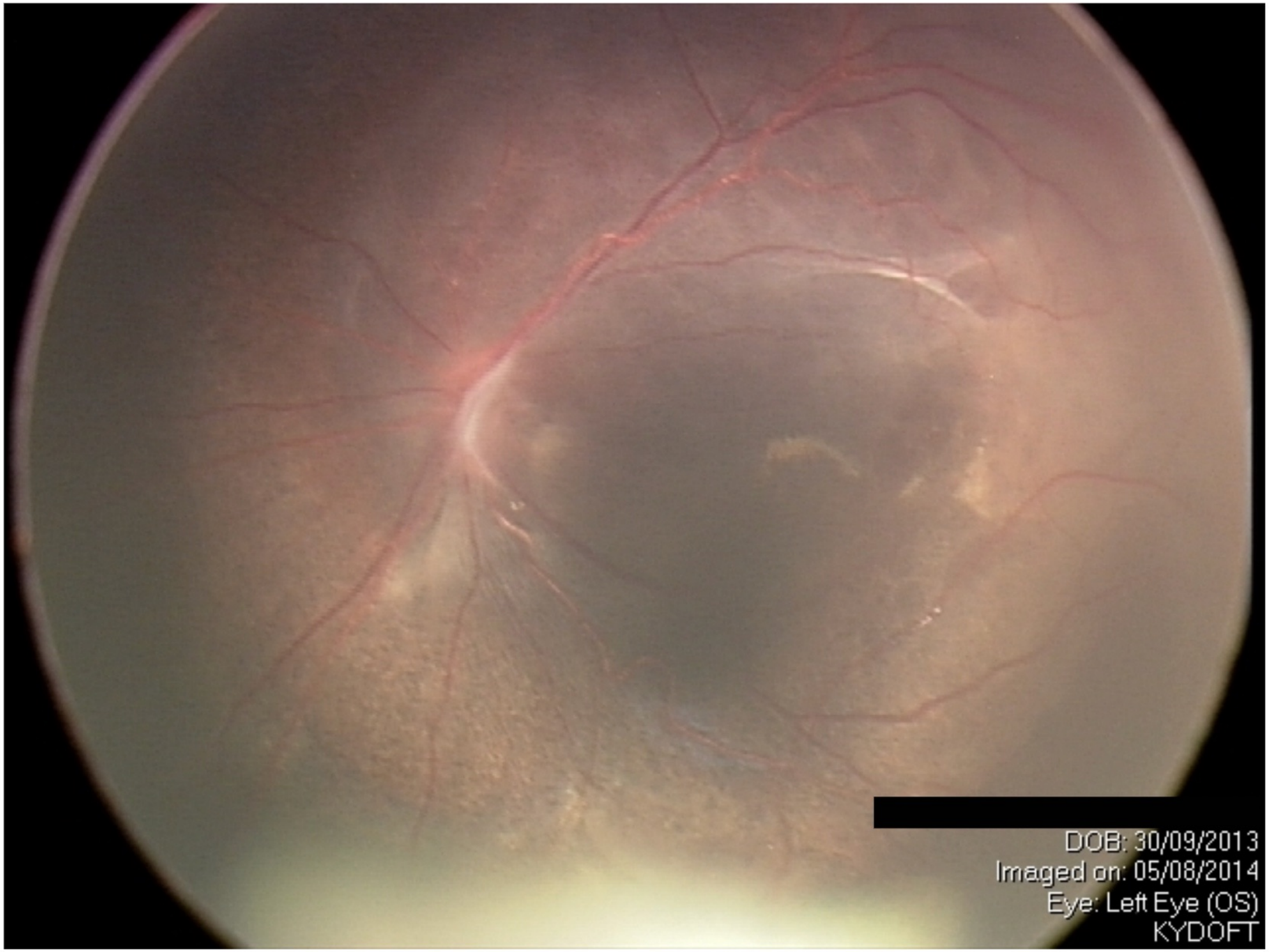
Total RD after primary vitrectomy



360º band

SCLERAL BUCKLING EXAMPLE

Retina attached after surgery over a period of several weeks



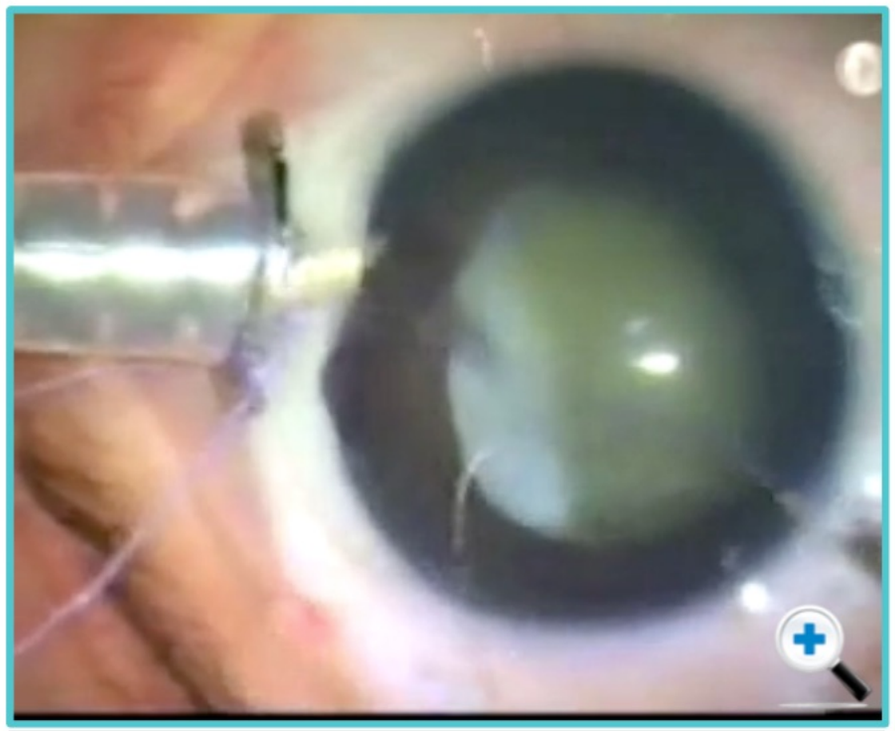
Instrumentation & Surgical Technique for ROP Retinal Detachments

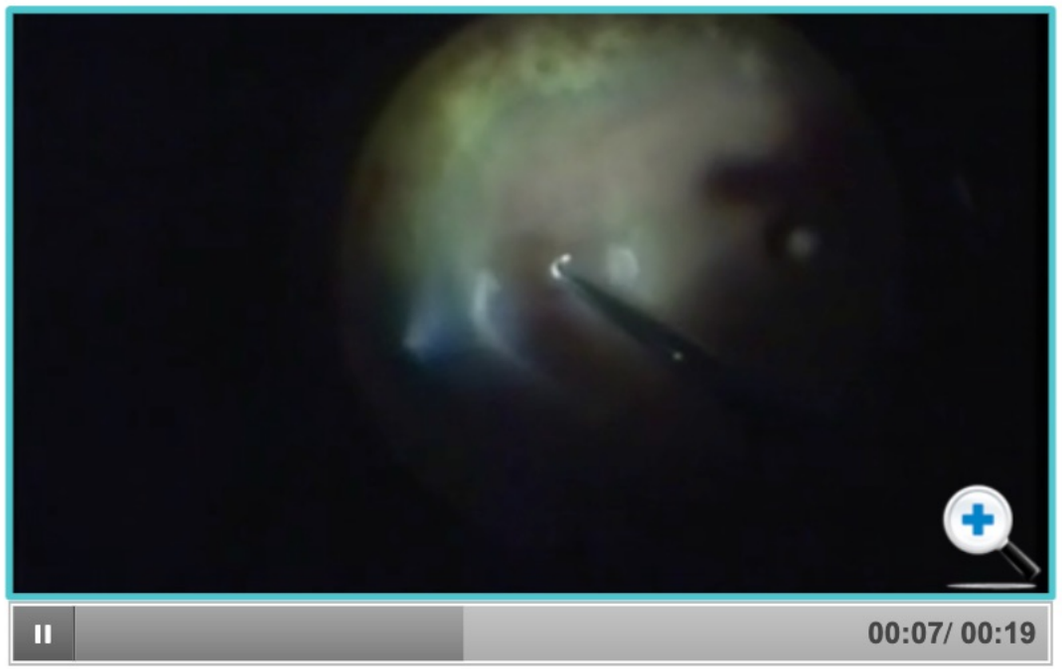
Different techniques/approaches are used for performing vitrectomies in ROP and in paediatrics, with options including:

- Two or three ports
- Standard 20 gauge or small-gauge vitrectomy (micro-incision vitrectomy surgery (MIVS), 23 - 25 - 27g).

} **These choices are surgeon dependent**

Each surgeon, or group, has to decide which techniques give them the best results.





MIVS in ROP

Dr Kychenthal (module editor) and his team have used small-gauge vitrectomy as their preference in ROP cases for over 10 years, and have obtained very good anatomical results using this approach. Compared to 20g vitrectomy, Dr Kychenthal believes that micro-incision vitreous surgery (MIVS) is better for a baby's eye.

25-gauge lens-sparing vitrectomy, in the early stages of the detachment, gives the best chance of achieving:

- Total retinal reattachment
- Undistorted posterior pole
- Preservation of the lens
- Central fixation

RESERACH STUDY RESULTS

Kychenthal & Dorta (2008) researched whether surgical intervention with a three port 25-gauge transconjunctival sutureless vitrectomy is an effective technique to attach the retina in patients with stage 4A retinal detachment in ROP.

Click to learn more about this research study and its findings

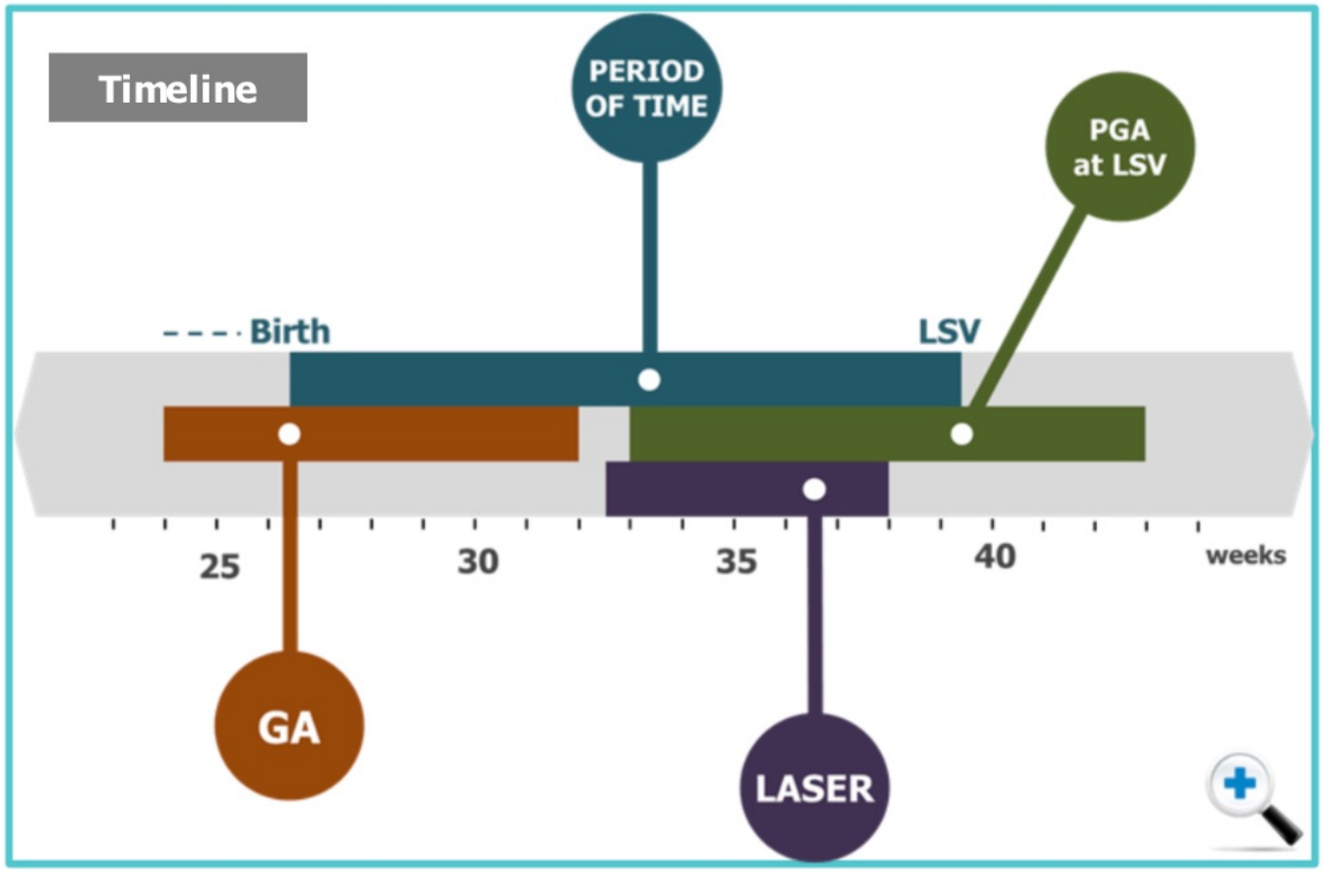
RESEARCH

Kychenthal A, Dorta P. 25-gauge lens-sparing vitrectomy for stage 4A retinopathy of prematurity. *Retina.* 2008; 28(3 Suppl): S65-8.

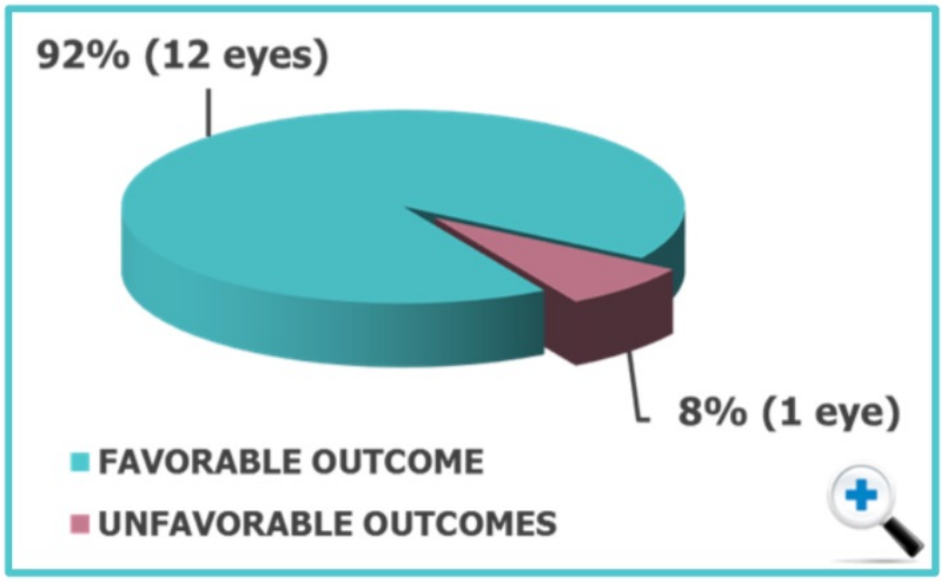
Study Background and Results

- 13 eyes of 10 preterm infants with stage 4A retinal detachments in ROP
- 8 females and 2 males
- **Average birth weight was 1,133grams**
- **Average gestational age was 26.4 weeks**
- All eyes were previously treated with indirect laser for stage 3 ROP before retinal detachment developed
- **Mean post-gestational age at time of surgery was 39.3 weeks** (range, 33-44 weeks)
- With an average follow-up of 17 months (range, 4-36 months) **12 (92%) of the 13 eyes achieved successful retinal reattachment**

Kychenthal A, Dorta P. 25-gauge lens-sparing vitrectomy for stage 4A retinopathy of prematurity. *Retina.* 2008; 28(3 Suppl): S65-8.

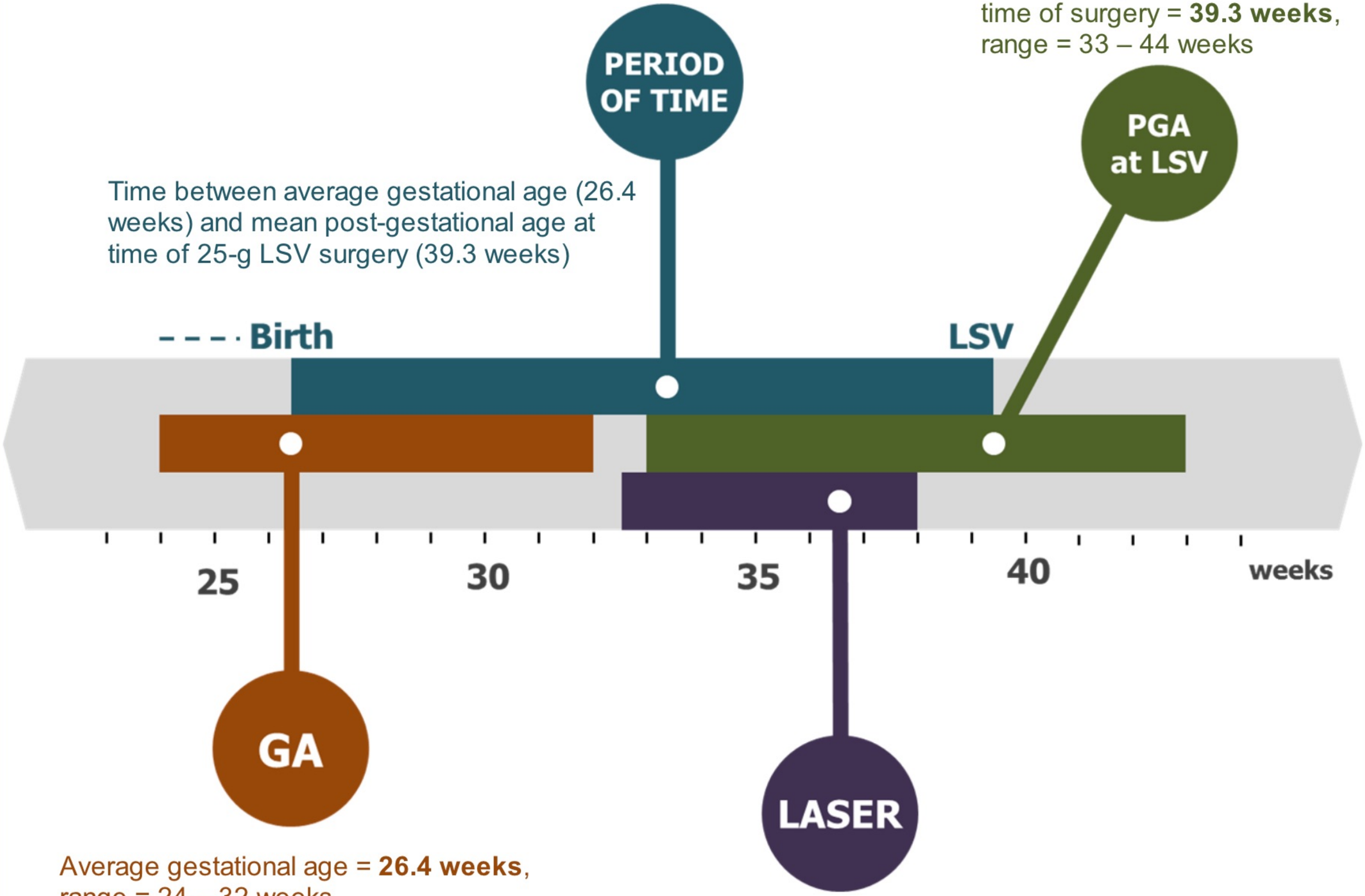


Total Reattachment of the Retina

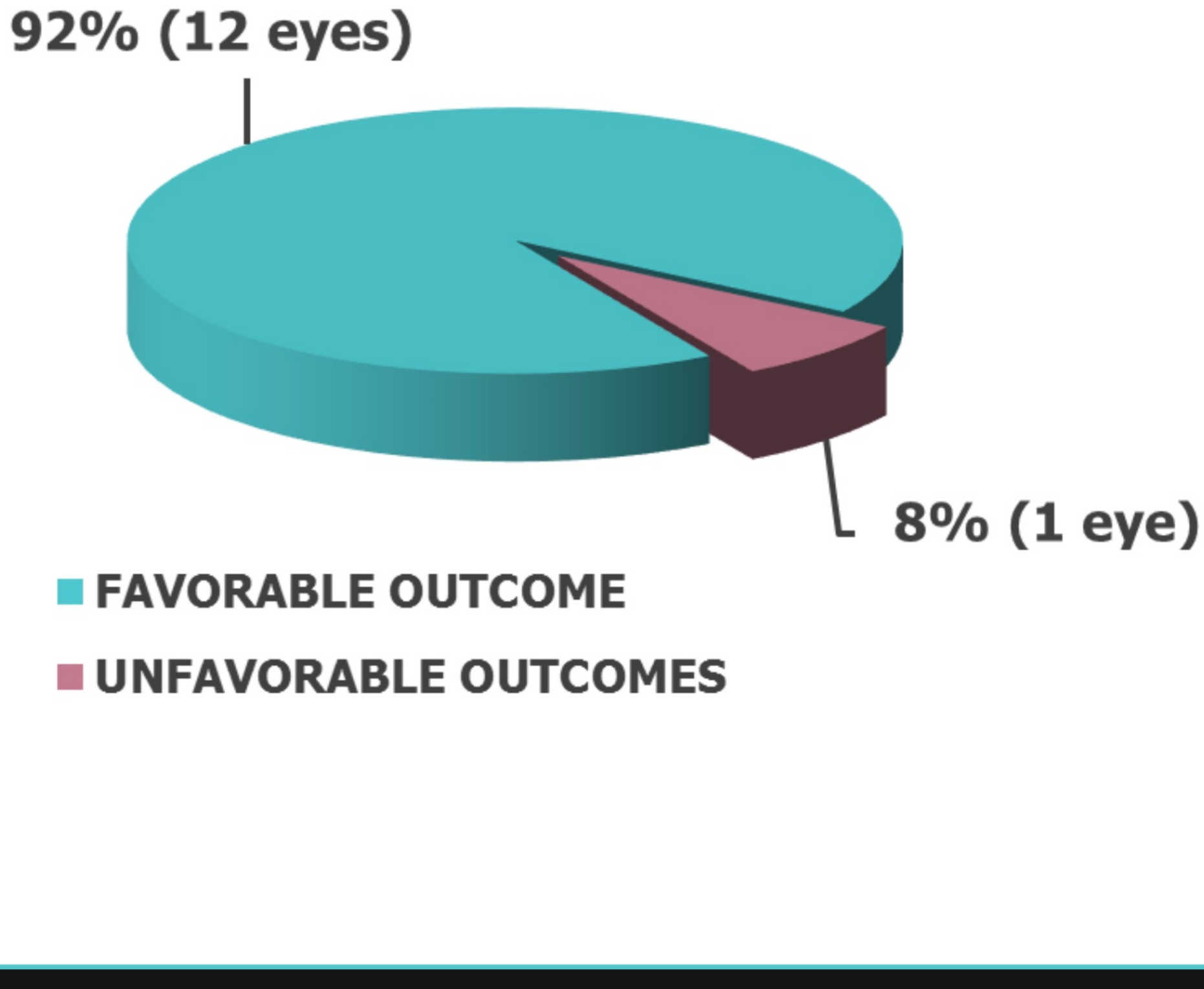


Conclusion:
Surgical intervention with a three port 25-gauge transconjunctival sutureless vitrectomy is an **effective technique** to attach the retina in patients with stage 4A retinal detachment in ROP.

Timeline


Mean post-gestational age at time of surgery = **39.3 weeks**, range = 33 – 44 weeks
PERIOD OF TIME
PGA at LSV
Time between average gestational age (26.4 weeks) and mean post-gestational age at time of 25-g LSV surgery (39.3 weeks)
Birth
LSV
25
30
35
40
weeks
GA
LASER
Average gestational age = **26.4 weeks**, range = 24 – 32 weeks

Total Reattachment of the Retina



Surgery for Stage 5 ROP

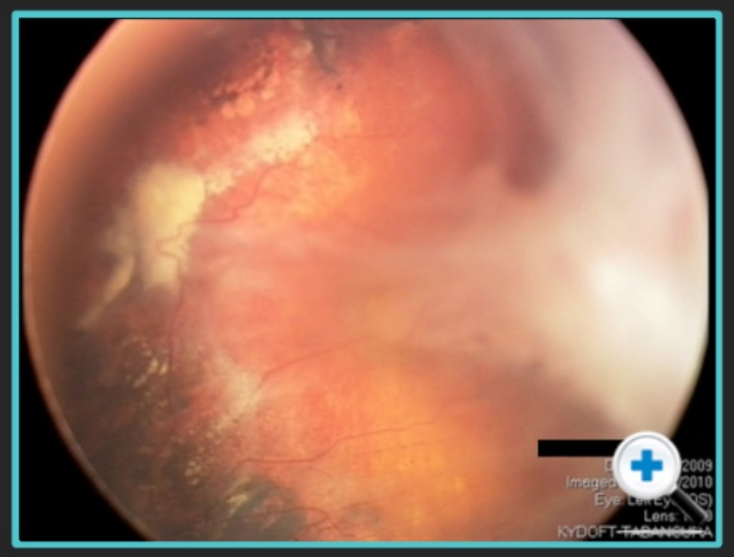
Uncertainty still remains around whether or not to operate on stage 5 ROP. So, what should you do in these cases?

STAGE 5 ROP

It is very **important to operate on stage 5 ROP as patients do better than the natural history**.

If even only a small proportion of the retina can be preserved, **keeping that area of the retina viable opens the door for future therapies to improve vision**.

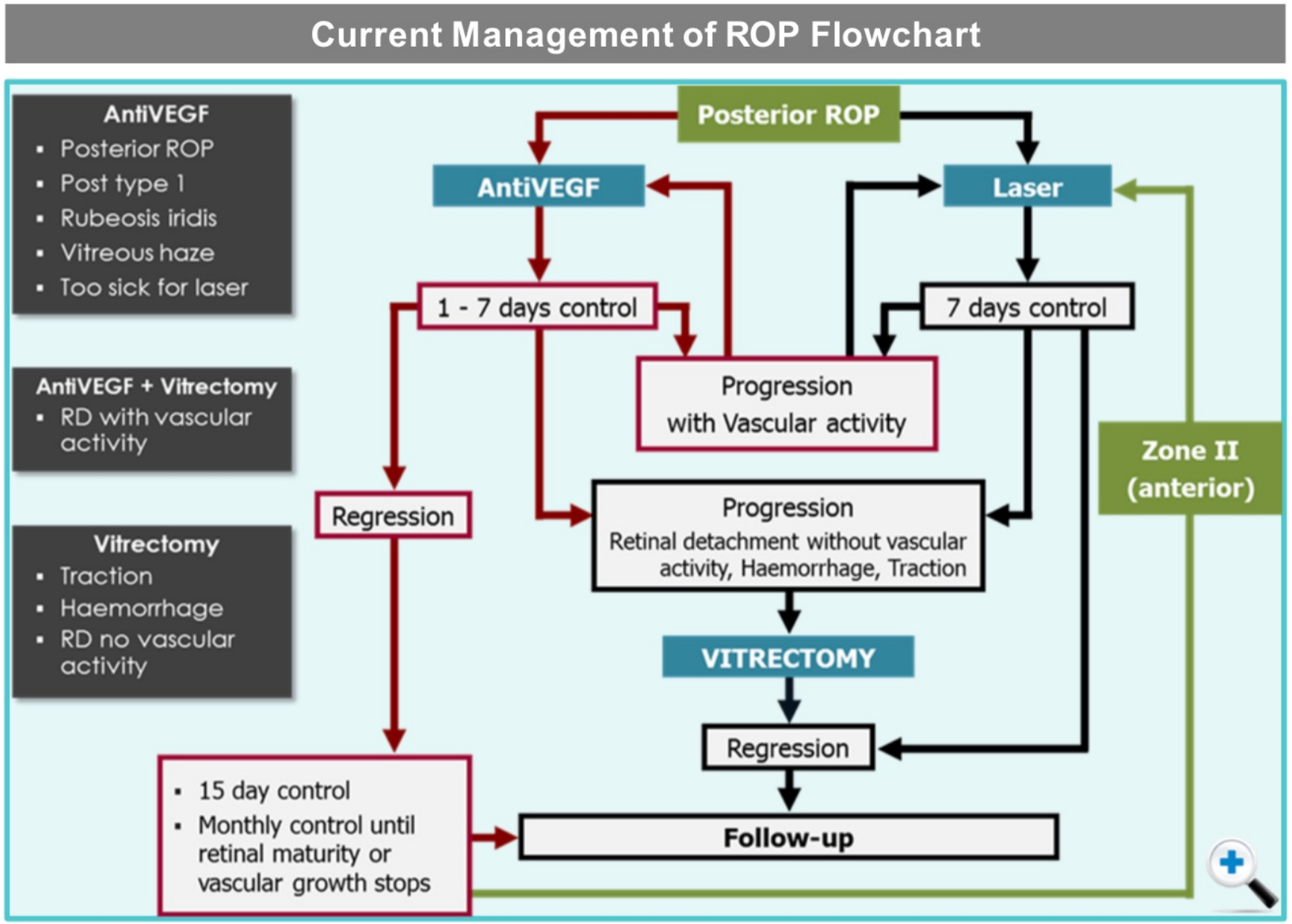
Dr Kychenthal (module editor) strongly believes that stage 5 ROP deserves a surgical chance.



The development of better instrumentation has made the use of MIVS Dr Kychenthal's preferred surgical technique.

Current Management of ROP Flowchart

This flowchart shows the management and treatment of ROP. It presents the different initial treatment (depending on the zone where the disease is located) and what to do if the disease progresses.

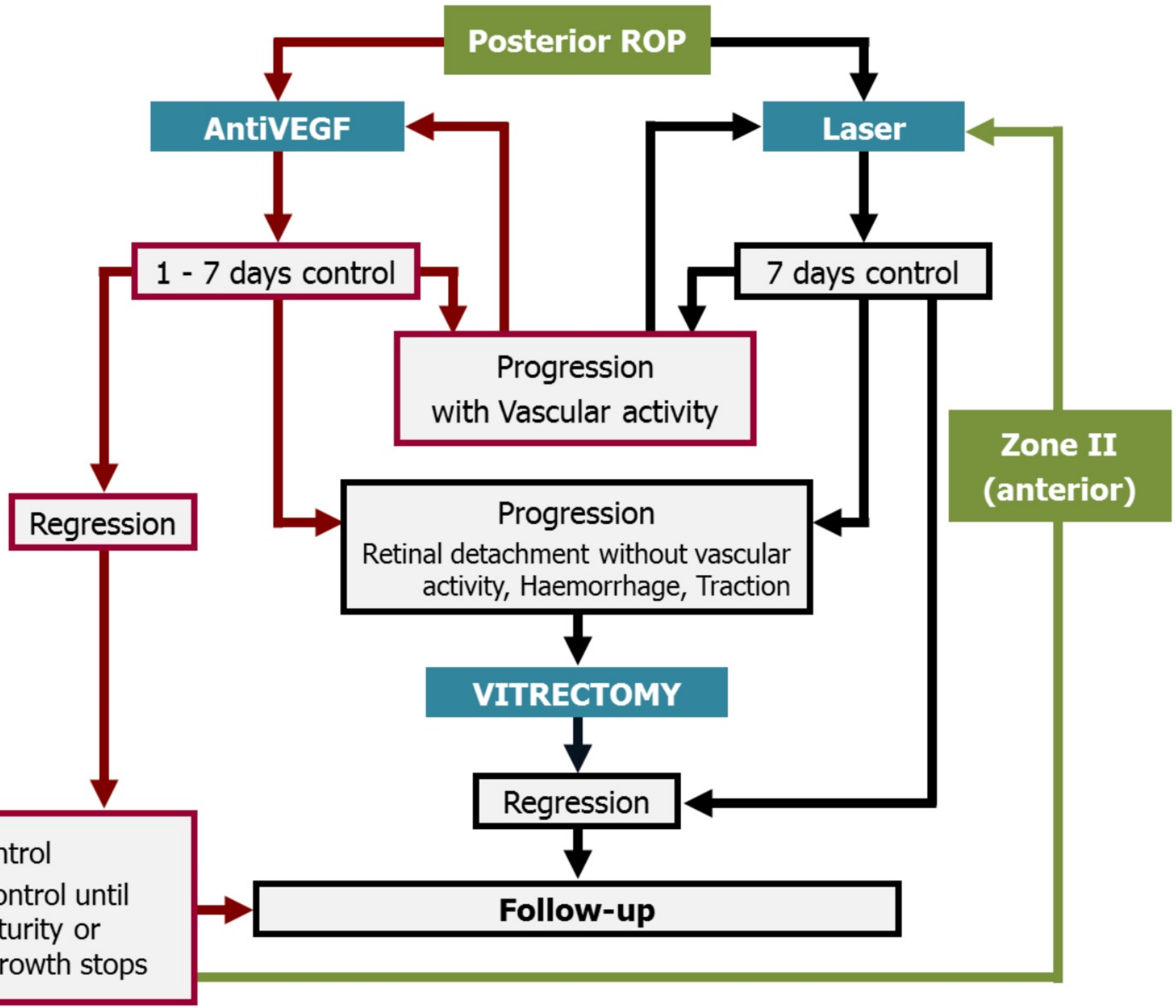


Current Management of ROP Flowchart

AntiVEGF
- Posterior ROP
- Post type 1
- Rubeosis iridis
- Vitreous haze
- Too sick for laser

AntiVEGF + Vitrectomy
- RD with vascular activity

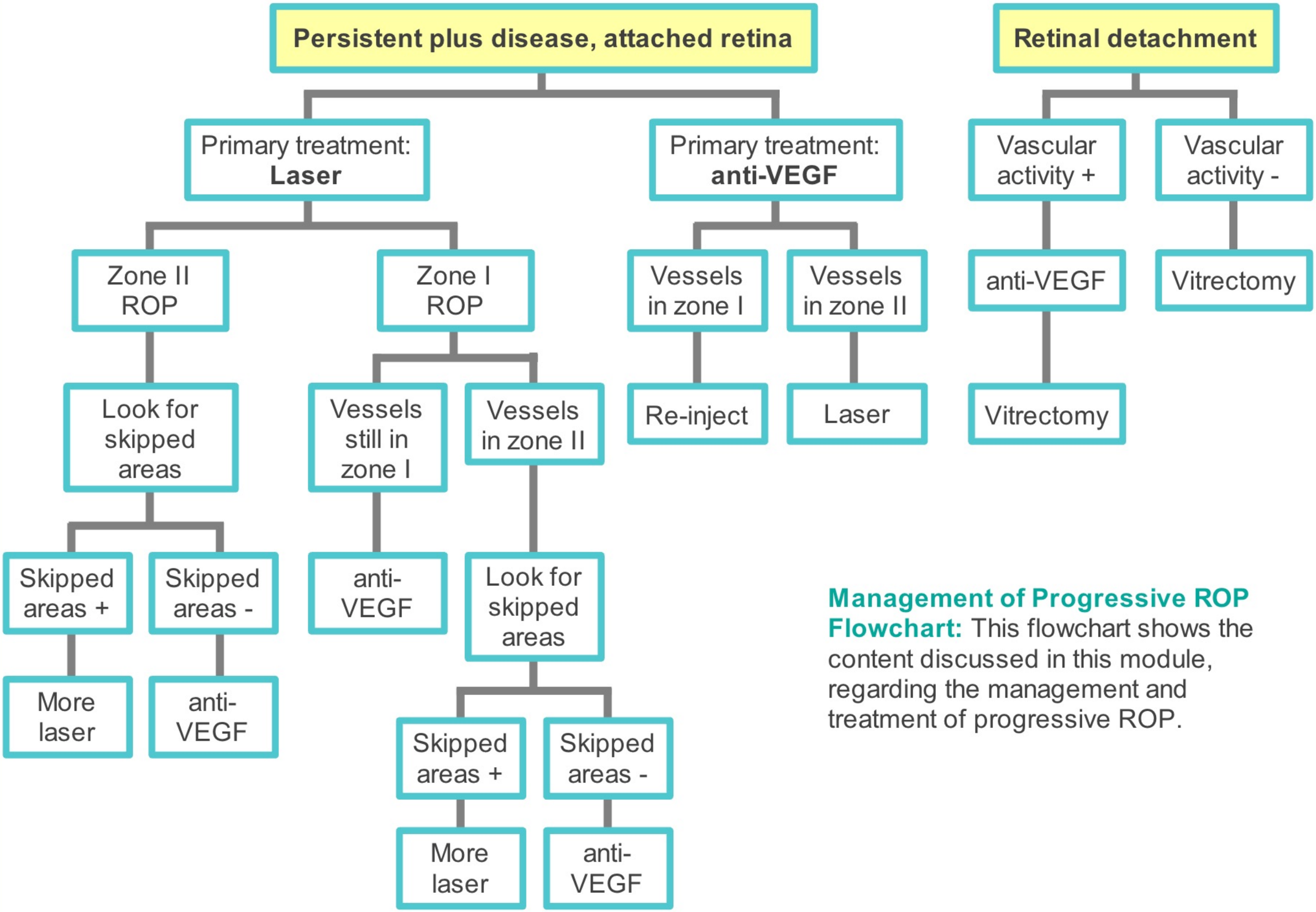
Vitrectomy
- Traction
- Haemorrhage
- RD no vascular activity



Conclusions

- The use of anti-VEGF drugs has modified ROP management
- If there is progression of ROP after primary treatment, even in the most advanced cases, therapeutic options are available to help obtain good anatomical and functional results
- Nevertheless, significant doubts remain regarding which alternatives will demonstrate to be better in the long term

Click for the complete management of progressive ROP flowchart



Management of Progressive ROP Flowchart: This flowchart shows the content discussed in this module, regarding the management and treatment of progressive ROP.