How to plan treatment for RETINAL VEIN OCCLUSION?? evidence based approach

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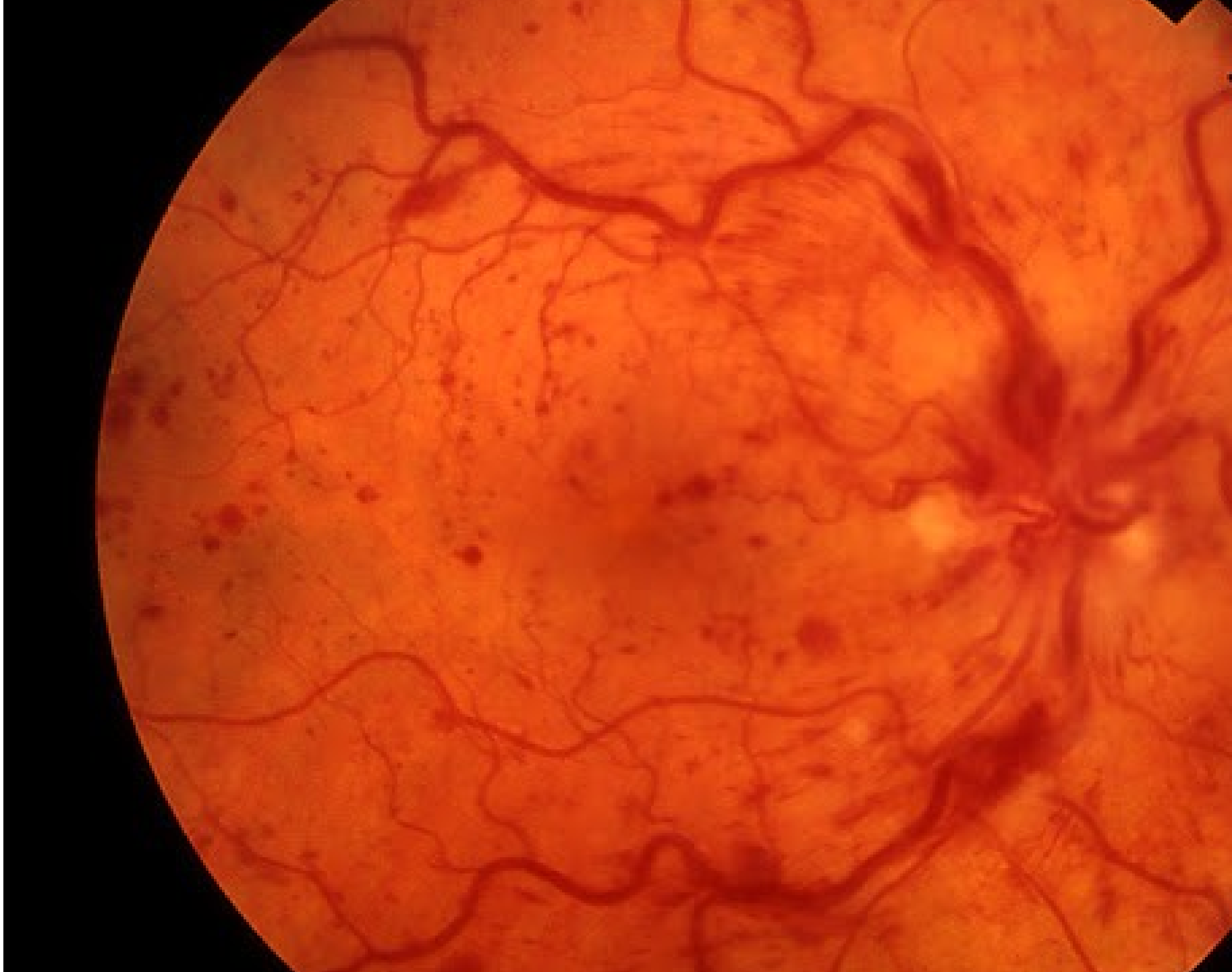
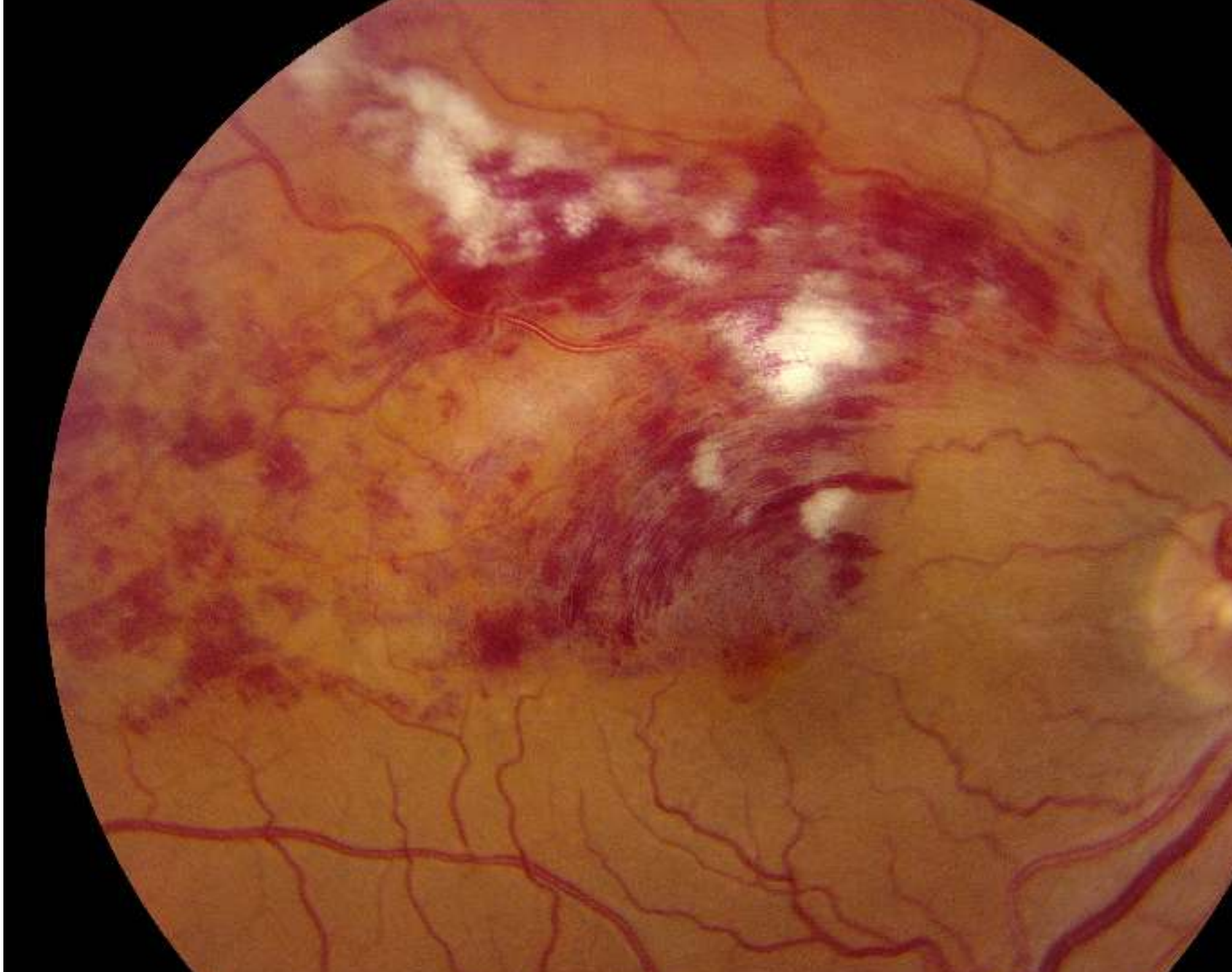
- ***Retinal vein occlusion (RVO) is among the leading causes of visual impairment and is often due to an underlying systemic disease.***

CRVO



BRVO




Hemiretinal vein occlusions
display similar signs on half of
the retina only.

First line therapy?

Anti-VEGF LASER Steroid?

Anti-VEGF Agents

Intraretinal and intraocular VEGF levels are increased in most patients with RVO .

VEGF upregulation increases vessel permeability leading to macular edema and neovascularization

Anti-VEGF Therapy in RVO

Anti-VEGF therapy has led to better treatment of RVO compared with laser, demonstrating significant reductions of ME, improved visual acuity (VA), and decreased neovascular complications.

Given the efficacy and favorable side effect profile compared to steroids , it is now first-line therapy worldwide.

Ranibizumab: BRAVO and CRUISE Studies

The BRAVO and CRUISE randomized, controlled trials led to FDA approval of monthly intravitreal ranibizumab 0.5 mg for the treatment of ME secondary to BRVO and CRVO, respectively.

This was because of significant visual gains with monthly therapy of 0.5-mg ranibizumab vs sham therapy.

COPERNICUS, GALILEO, and VIBRANT Studies

The COPERNICUS and GALILEO studies demonstrated rapid and durable improvement of VA in patients receiving monthly aflibercept 2 mg for the treatment of ME secondary to CRVO.

The VIBRANT study, which randomly assigned patients to monthly aflibercept 2 mg through 6 months vs macular laser photocoagulation, resulted in FDA approval of aflibercept for the treatment of ME secondary to BRVO.

BALATON and COMINO studies

- BALATON and COMINO studies demonstrated that ***faricimab*** provided early and sustained improvement in vision in people with branch and central RVO, meeting the primary endpoint of non-inferior visual acuity gains at 24 weeks compared to aflibercept.

Is it necessary to inject monthly?

HORIZON study

- Patients in the BRAVO and CRUISE studies were followed for an additional year in an open-label extension study.
- Contrary to the ***monthly therapy***, these patients were followed every ***3 months*** and treated on an as-needed basis.
- The authors reported reduced follow-up and fewer intravitreal injections of ranibizumab in the second year, ***however, there was a decline in vision in patients with CRVO (–4.1 letters) but stability in those with BRVO (–0.7 letters).***

Conclusion

- ***Patients with RVO likely benefit from an individual follow-up and management paradigm that involves more frequent follow-up and extended treatment.***

Conclusion

- *No extension without monthly follow up,*

Immediate VS Delay in Treatment

Immediate VS Delay in Treatment

In all the ranibizumab and aflibercept trials, delayed patients uniformly demonstrated inferior VA results at 52 weeks relative to patients who were initiated on anti-VEGF therapy at the onset.

So, it is imperative to begin immediate therapy for patients with ME secondary to RVO.

WHICH DRUG AND HOW FREQUENT?

SCORE2 Study

evaluating the efficacy of bevacizumab vs aflibercept for the management of ME secondary to CRVO and HRVO.

The study concluded that intravitreal monthly bevacizumab was noninferior to aflibercept with respect to the primary outcome of VA at 6 months.

LEAVO study

the LEAVO study was a multicenter, phase 3, double-masked, randomized, controlled noninferiority trial comparing the clinical efficacy and cost-effectiveness of intravitreal therapy with ranibizumab, aflibercept, and bevacizumab for ME due to CRVO.

The primary outcome was change in best-corrected VA from baseline to 100 weeks.

Results

- In all arms, there was substantial and sustained improvement in VA at weeks 52 and 100.
- Bevacizumab was inferior to ranibizumab at 100 weeks.
- Bevacizumab was inferior to aflibercept at weeks 52 and 100.
- Aflibercept was noninferior to ranibizumab but not superior.

- ***The authors concluded that bevacizumab may not be interchangeable with aflibercept or ranibizumab.***

BALATON and COMINO studies

- BALATON and COMINO studies demonstrated that ***faricimab*** provided early and sustained improvement in vision in people with branch and central RVO, meeting the primary endpoint of non-inferior visual acuity gains at 24 weeks compared to aflibercept.

Conclusion

- ***No firm results to support superiority of specific anti-VEGF over the other types , so use any of them to start with.***

WHICH DRUG AND HOW FREQUENT?

Treatment Schedules

- ***Monthly injections according to The FDA registration trials .***
- ***As-needed***
- ***Treat-and-extend.***

The SHORE study

- The SHORE study evaluated patients originally enrolled in BRAVO and CRUISE. ***After 7 monthly*** ranibizumab treatments, patients were randomly assigned to as-needed injections vs continued monthly treatment.

- ***At month 15, there were no differences in VA between patients receiving as-needed treatments vs continued monthly therapy.***

- In SCORE2, 293 participants who responded well to bevacizumab or aflibercept during the first 6 months of the clinical trial were subsequently randomly assigned to either continued monthly treatment or a treat-and-extend schedule.

- ***the treat-and-extend arms provided similar visual outcomes compared with monthly treatment during the 6-month extension period of the trial.***

- ***Collectively, these studies support the diversity of treatment paradigms used by clinicians.***

- ***However, an initial momthly injection period was mandatory***

For how long??

Long-Term Anti-VEGF Outcomes

The data evaluating long-term outcomes in patients with RVO are limited.

The RETAIN study, however, evaluated patients out to 5 years and found that 50% of 34 patients with BRVO and 56% of 32 patients with CRVO required ranibizumab injections 4 years after therapeutic onset.

Therapeutic Strategies

Investigations

Good quality FFA is mandatory to detect numerically the delayed venous filling.

Good quality OCT to evaluate the macular edema.

Aim of treatment?

Aim of treatment?

- ***Treat macular edema and possible neovascularization waiting for recanalization of the obstructed vein***

- Start with monthly injection and follow up with monthly OCT.
- ***Continue injection till*** complete resolution of edema.

OR

- Minimal Residual edema with stable VA for three consequtive injections.

What is next ??

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- Start with monthly injection and follow up with monthly OCT.
- ***Continue injection till*** complete resolution of edema.

OR

- Minimal Residual edema with stable VA for three consequtive injections.

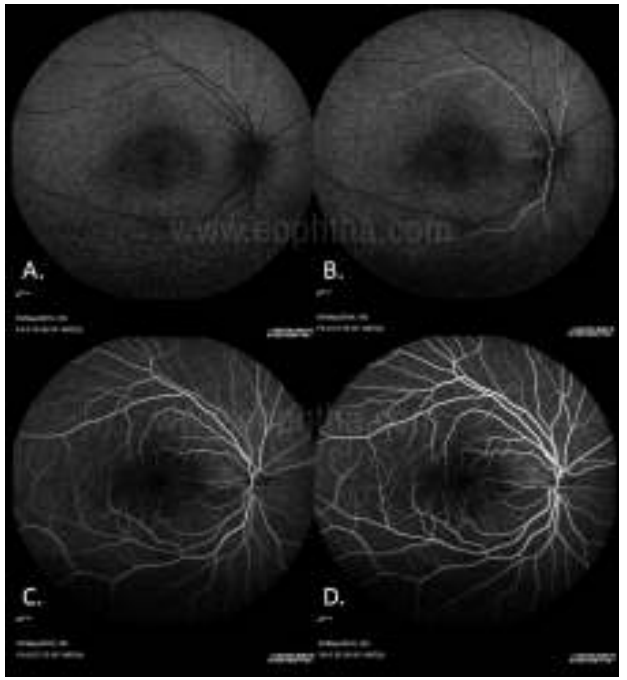
What is next ??

- FFA is done to assess normalization of venous filling (recanalization) and the presence or absence of neovascularization.

FFA findings in absence of ME on OCT

If venous filling is normalized

Stop injection .



FFA findings in absence of ME on OCT

If venous filling is normalized with no NV

Stop injection .

If venous filling is delayed

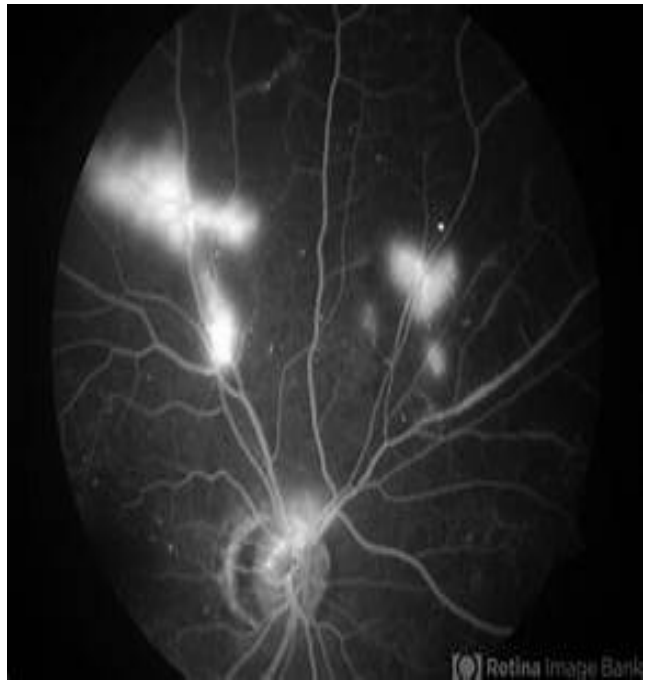
Continue with PRN or T&E But with monthly OCT.

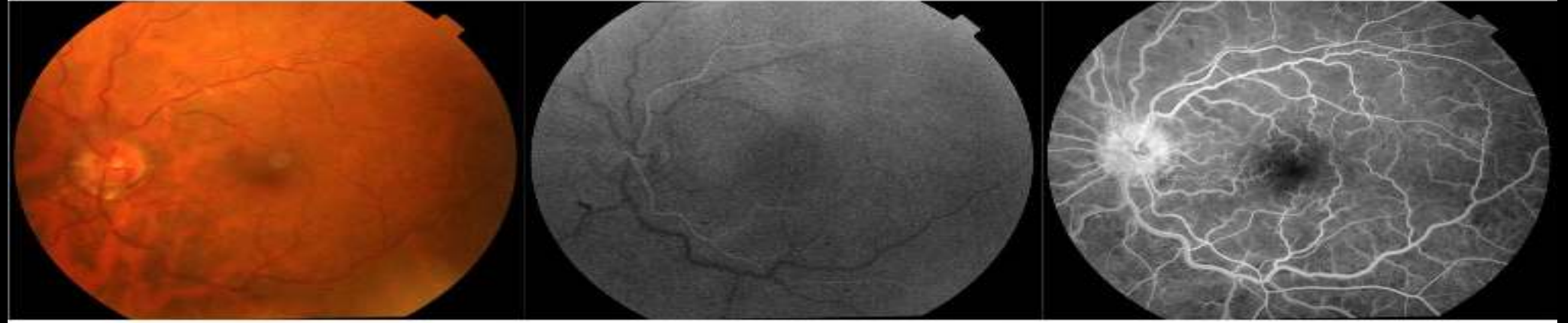
Repeat FFA every three months till normalization of venous filling.

FFA findings in absence of ME on OCT

If NV at any time

PRP.

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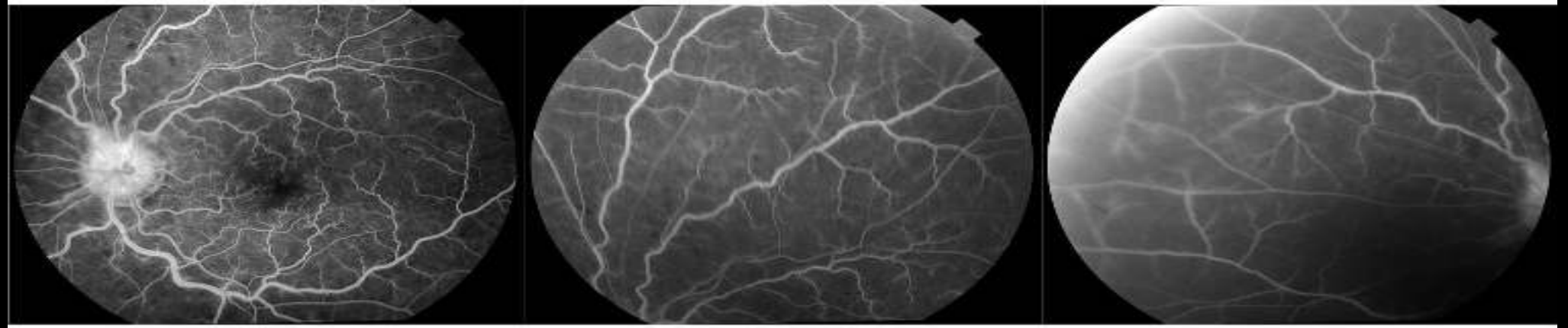
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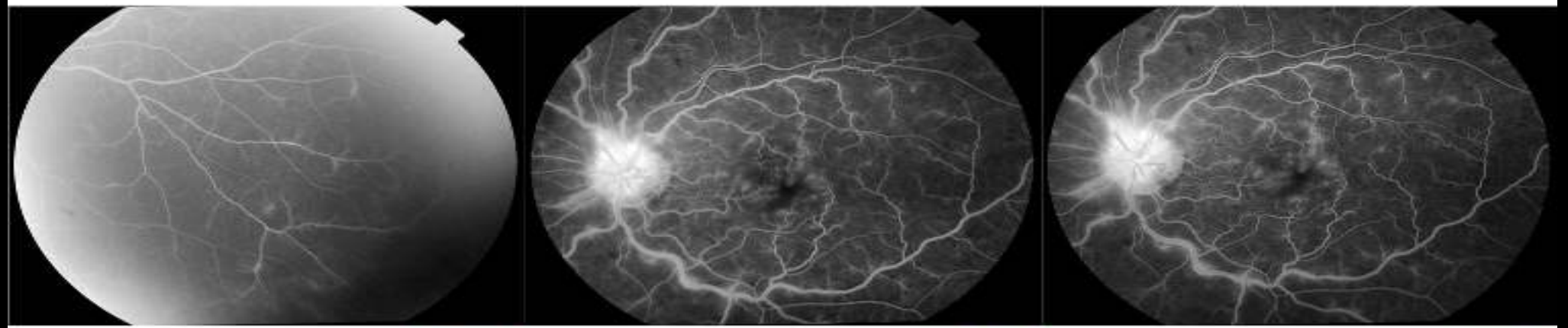

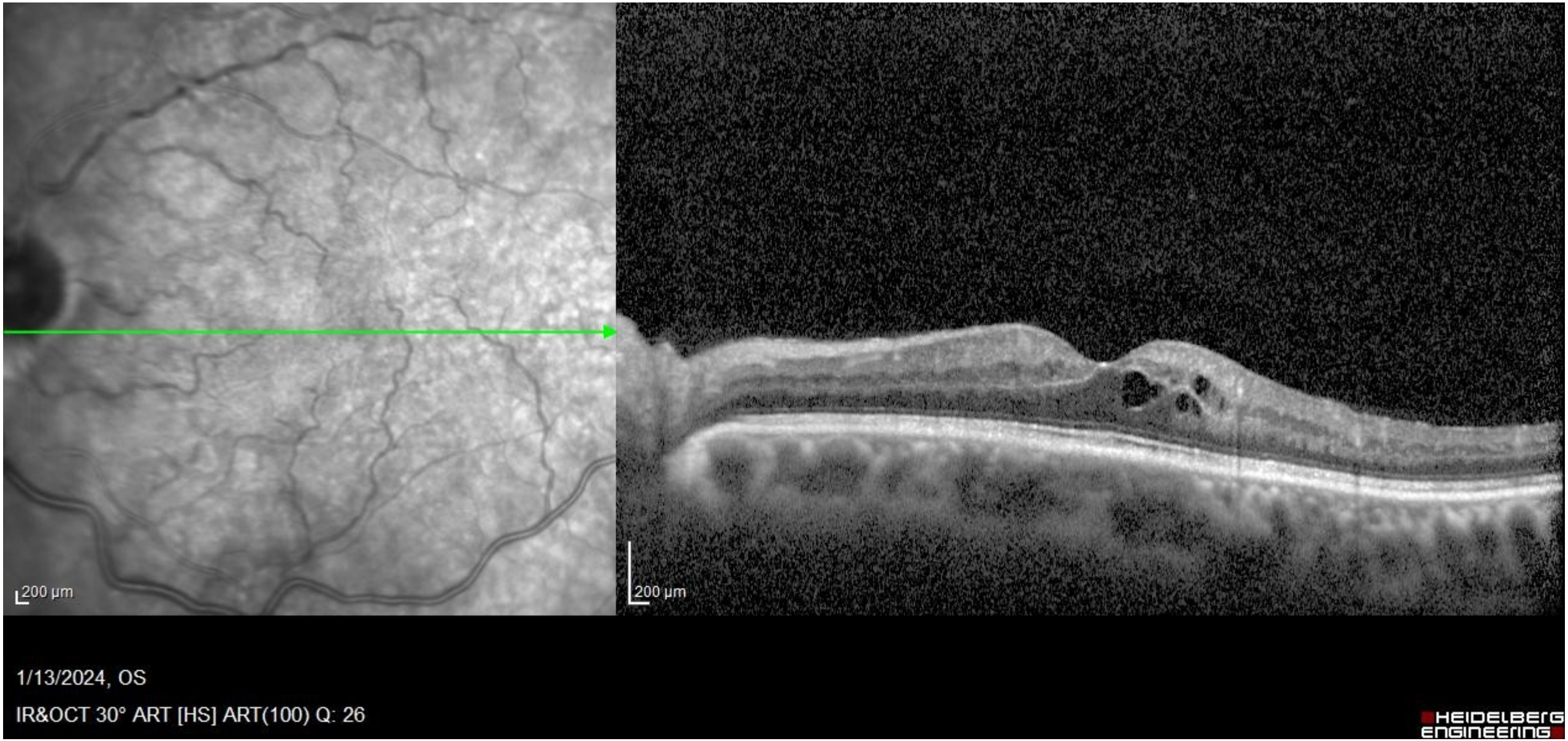
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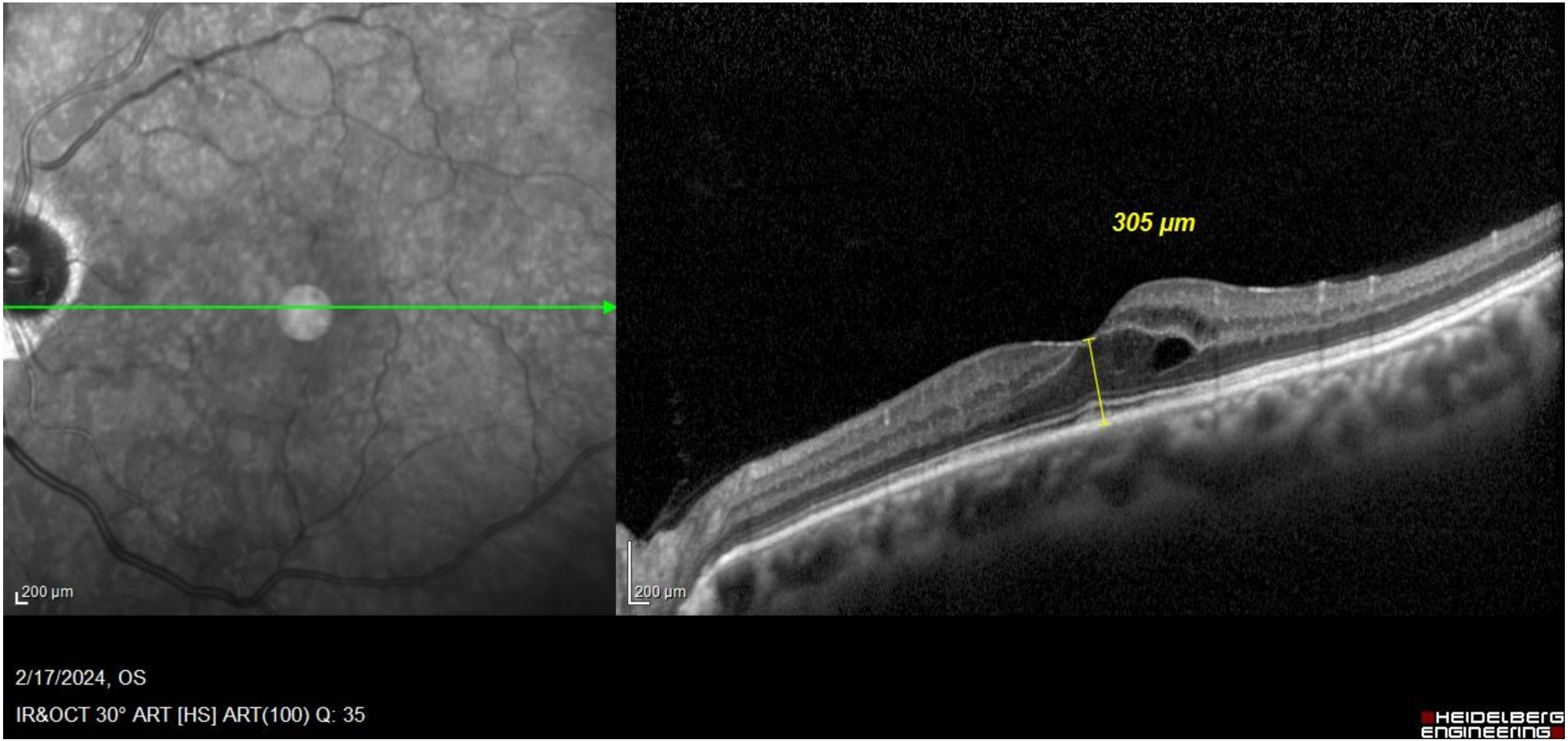
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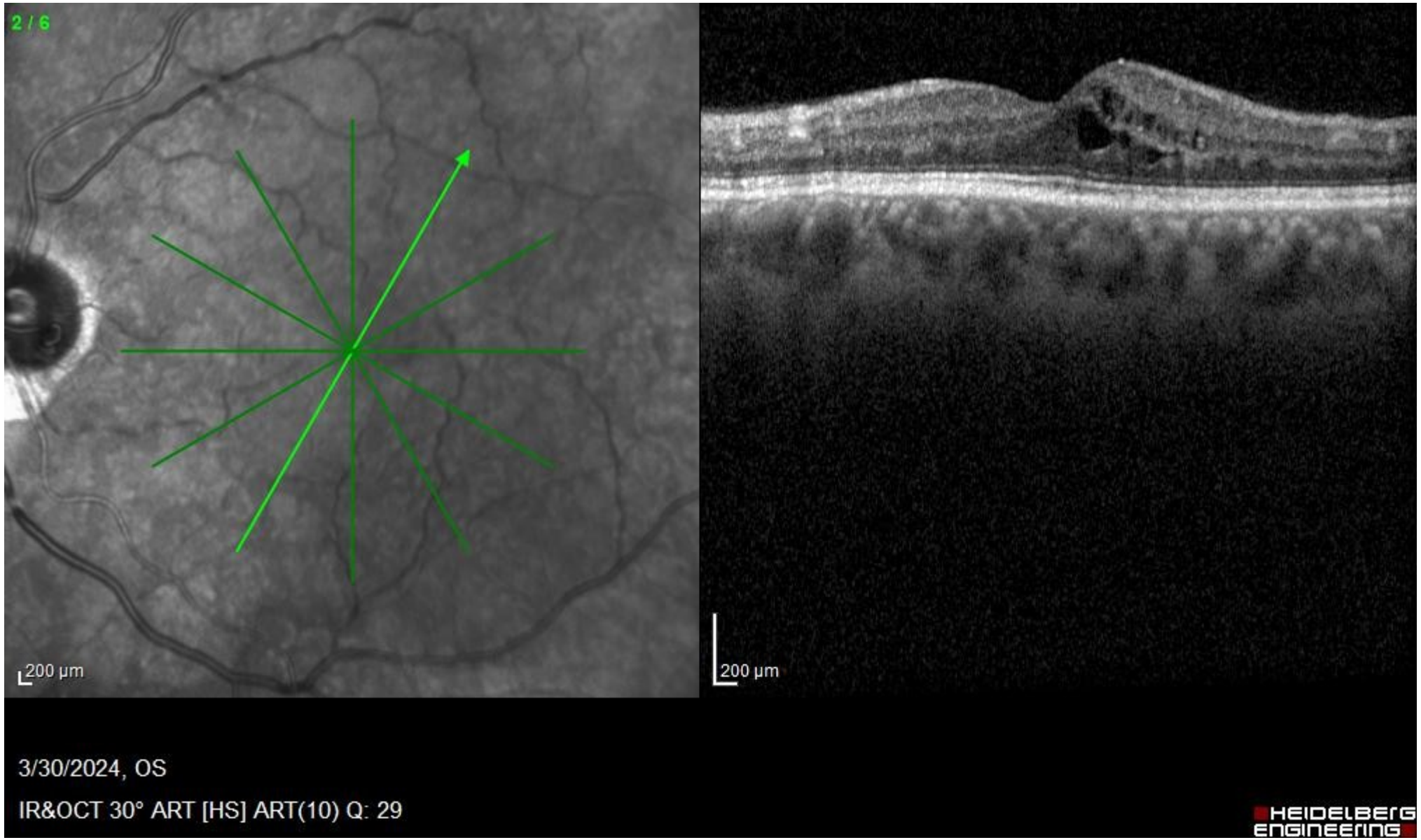
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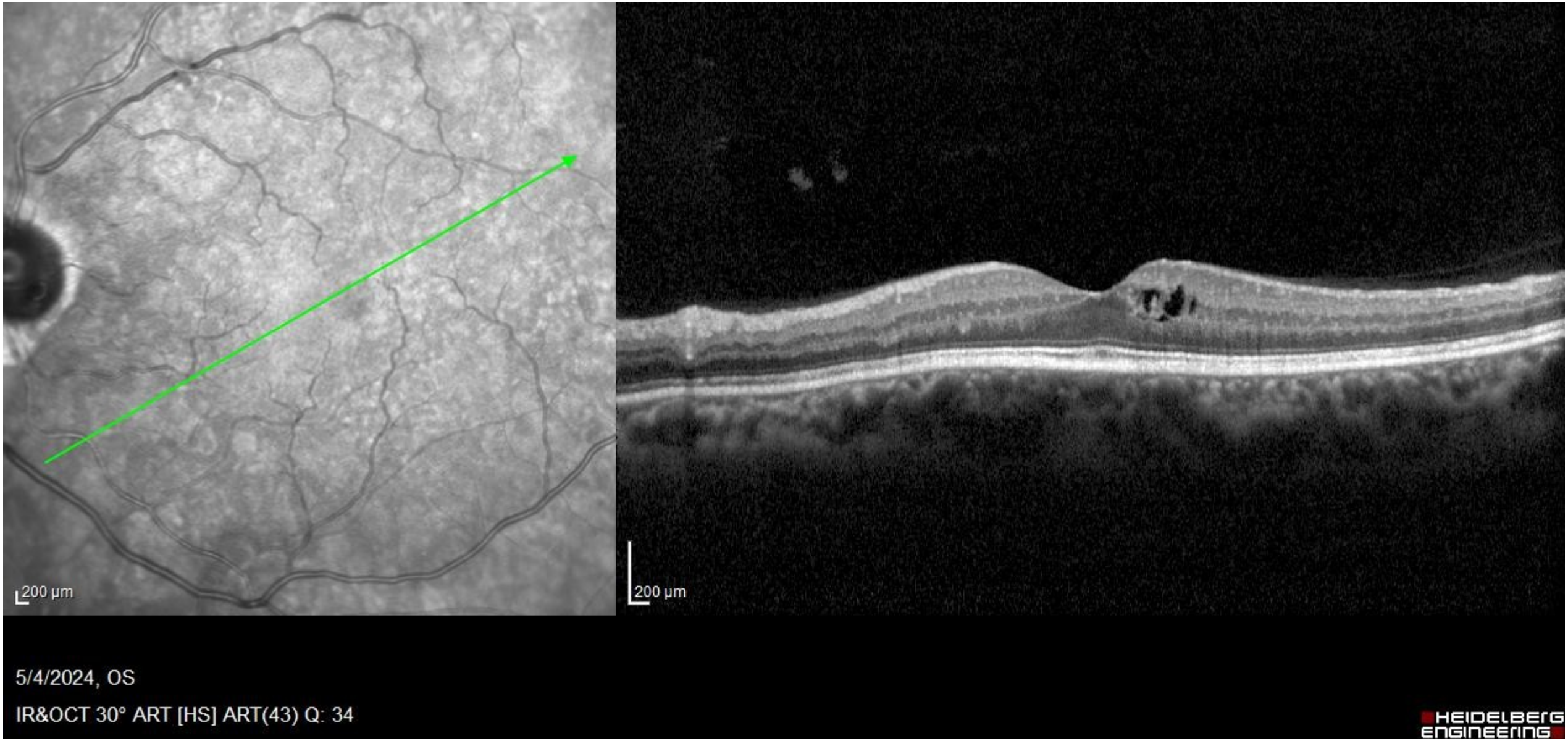
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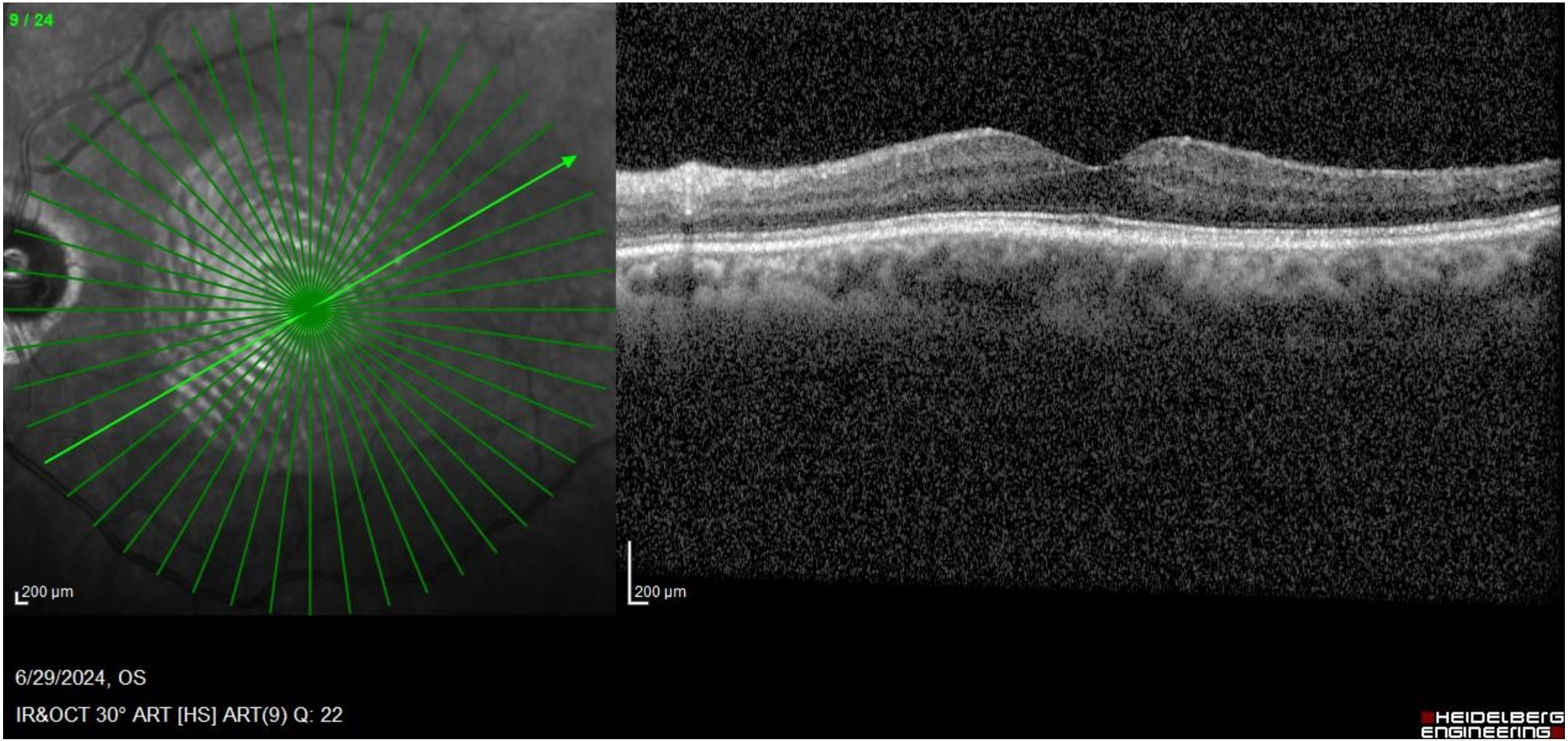
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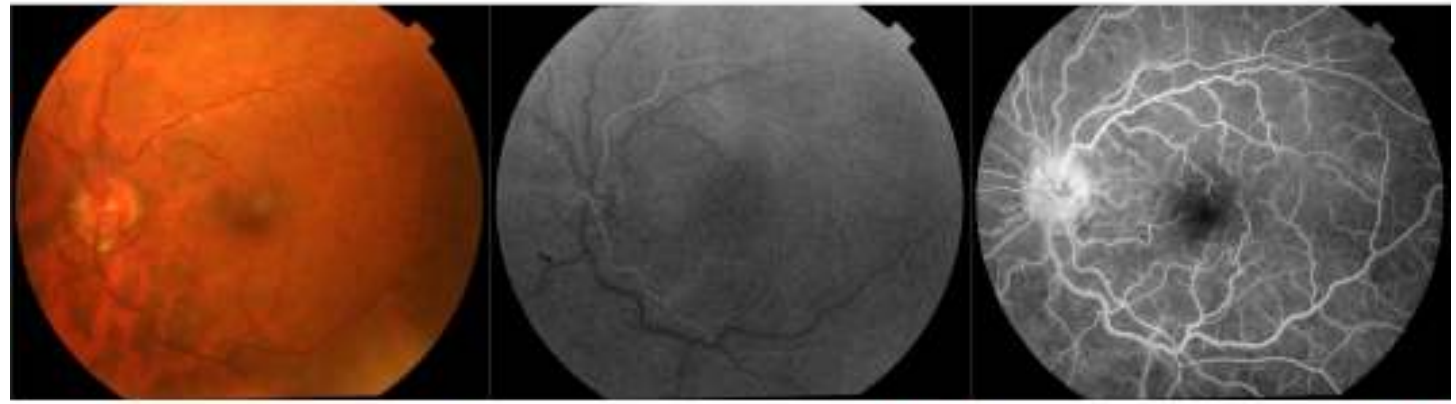

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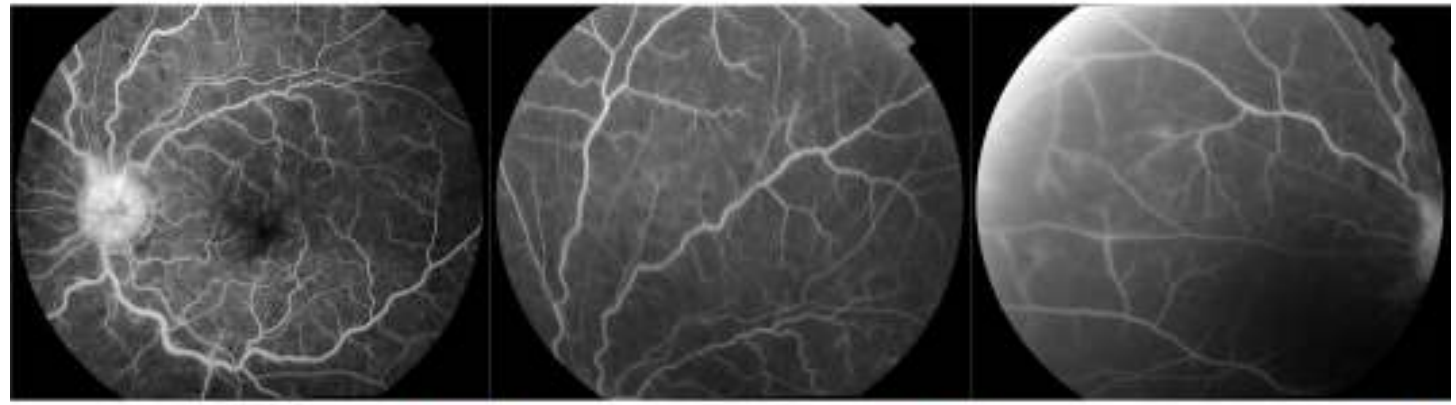

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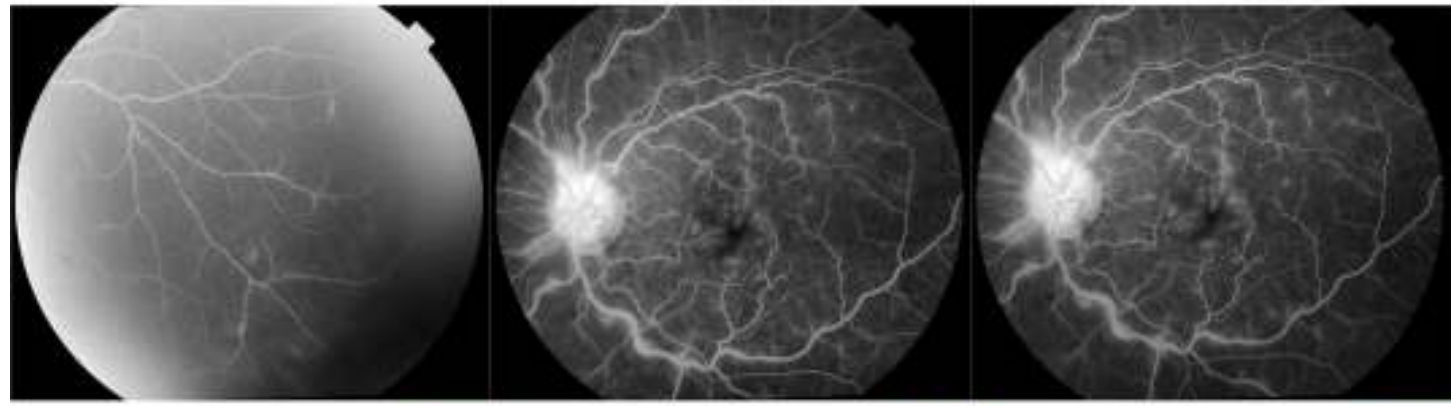

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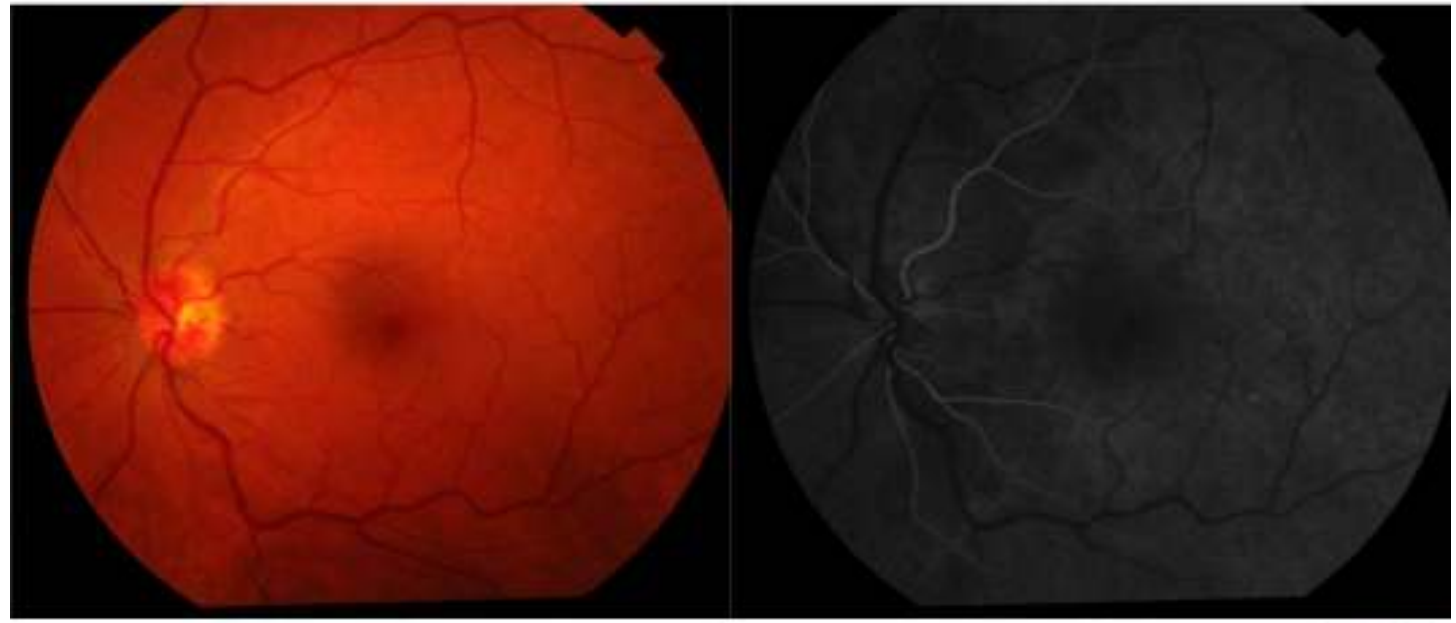

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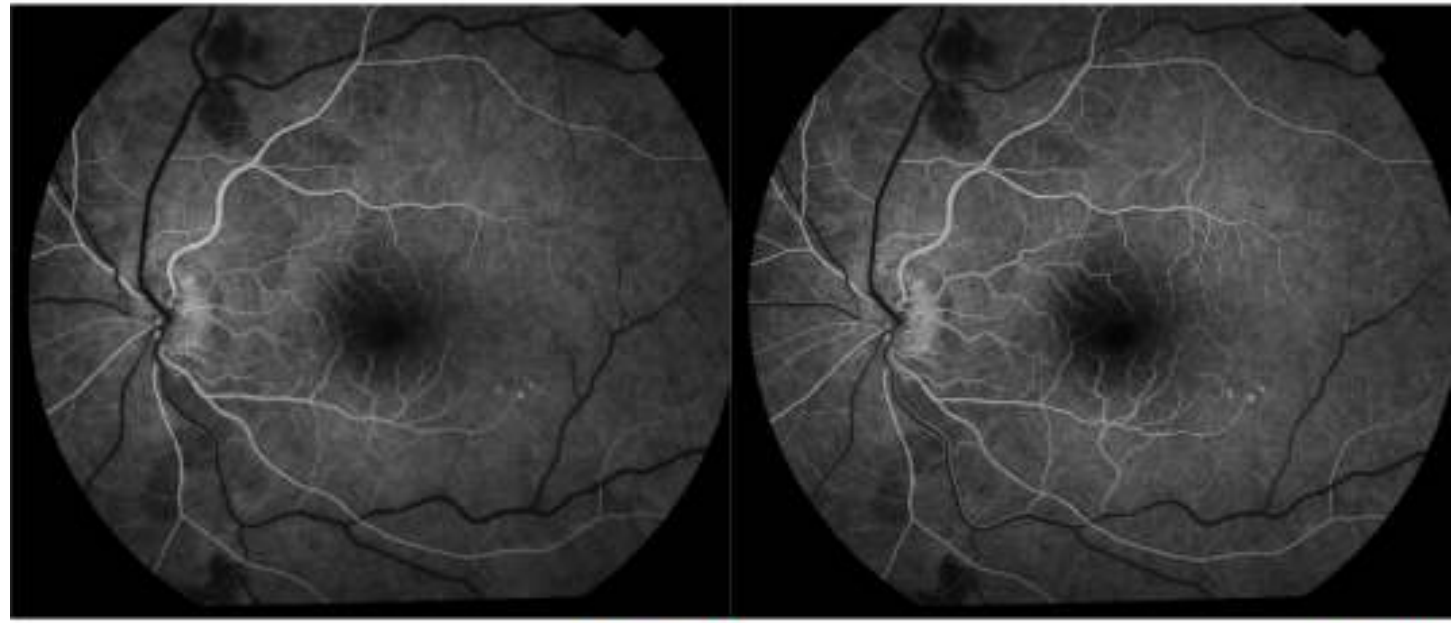

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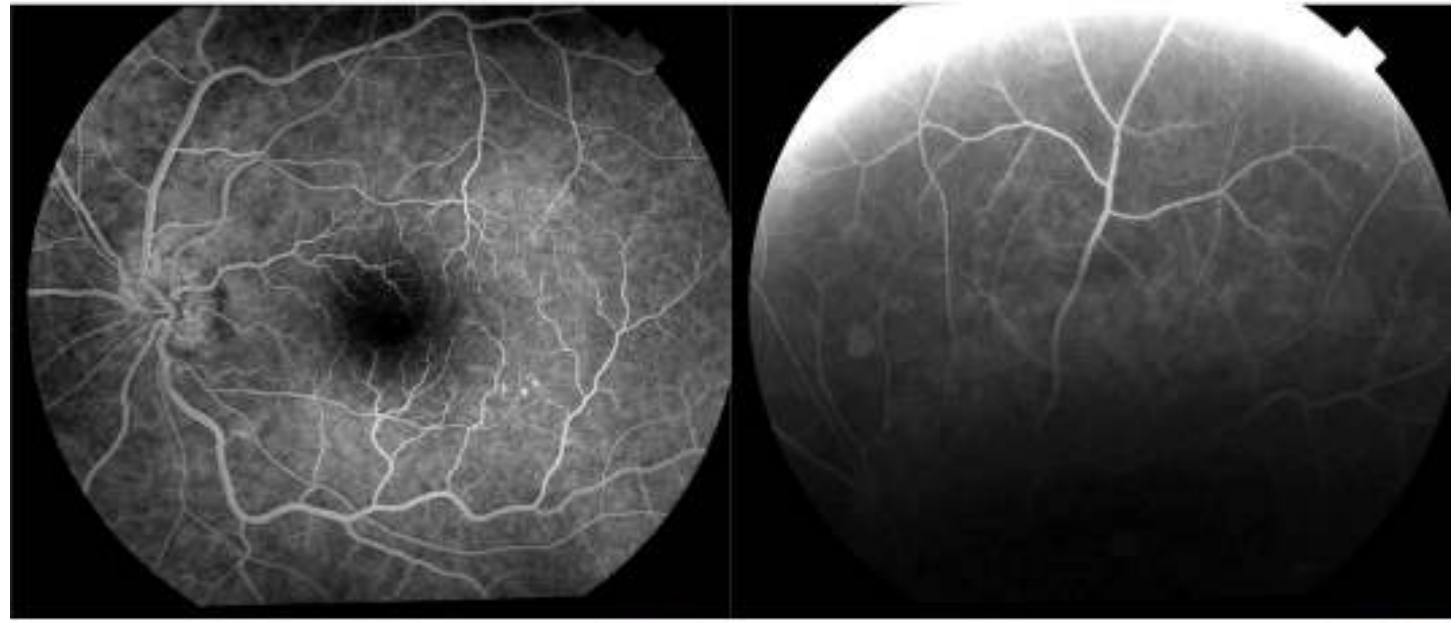

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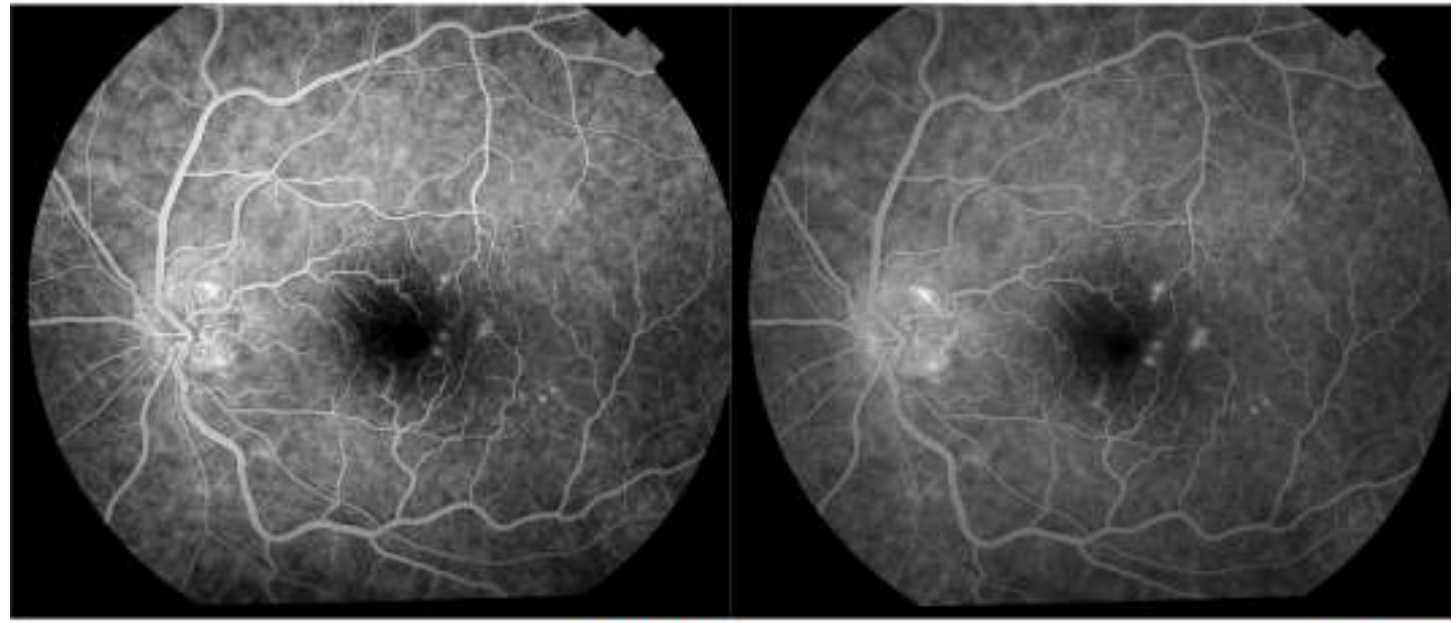

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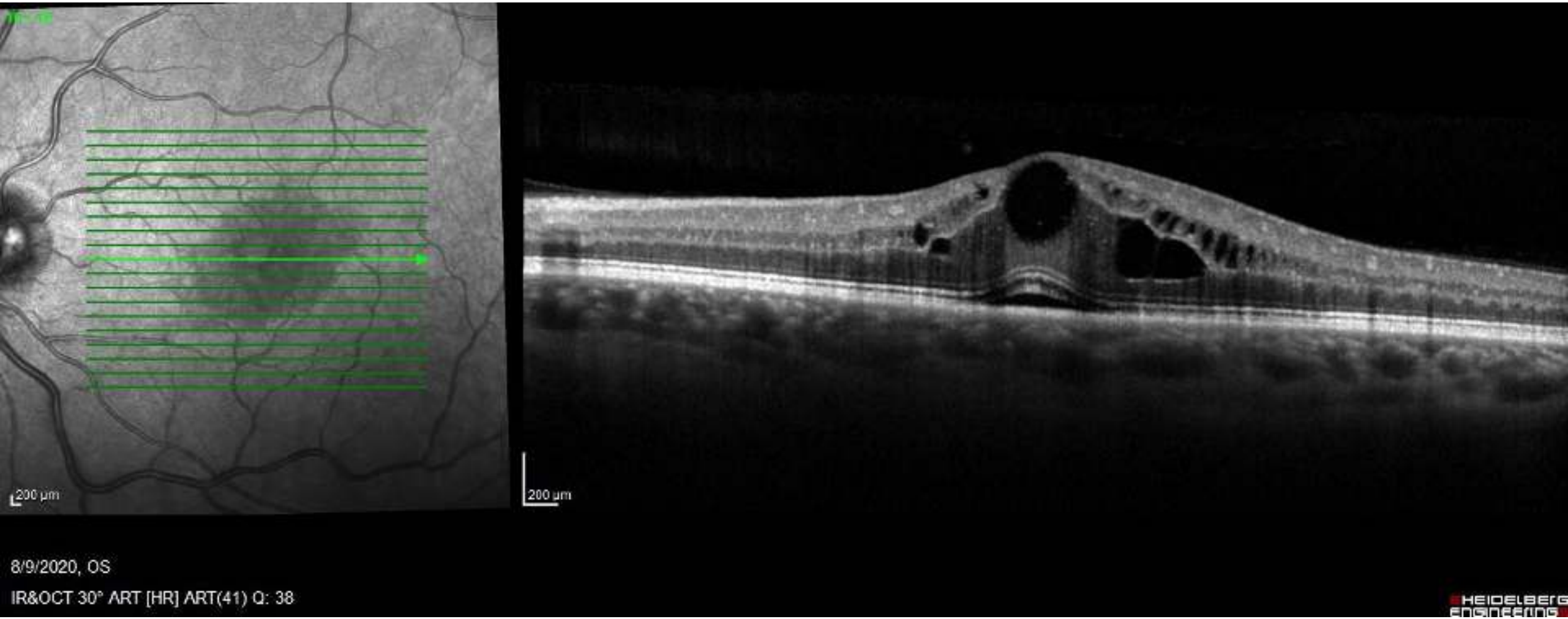
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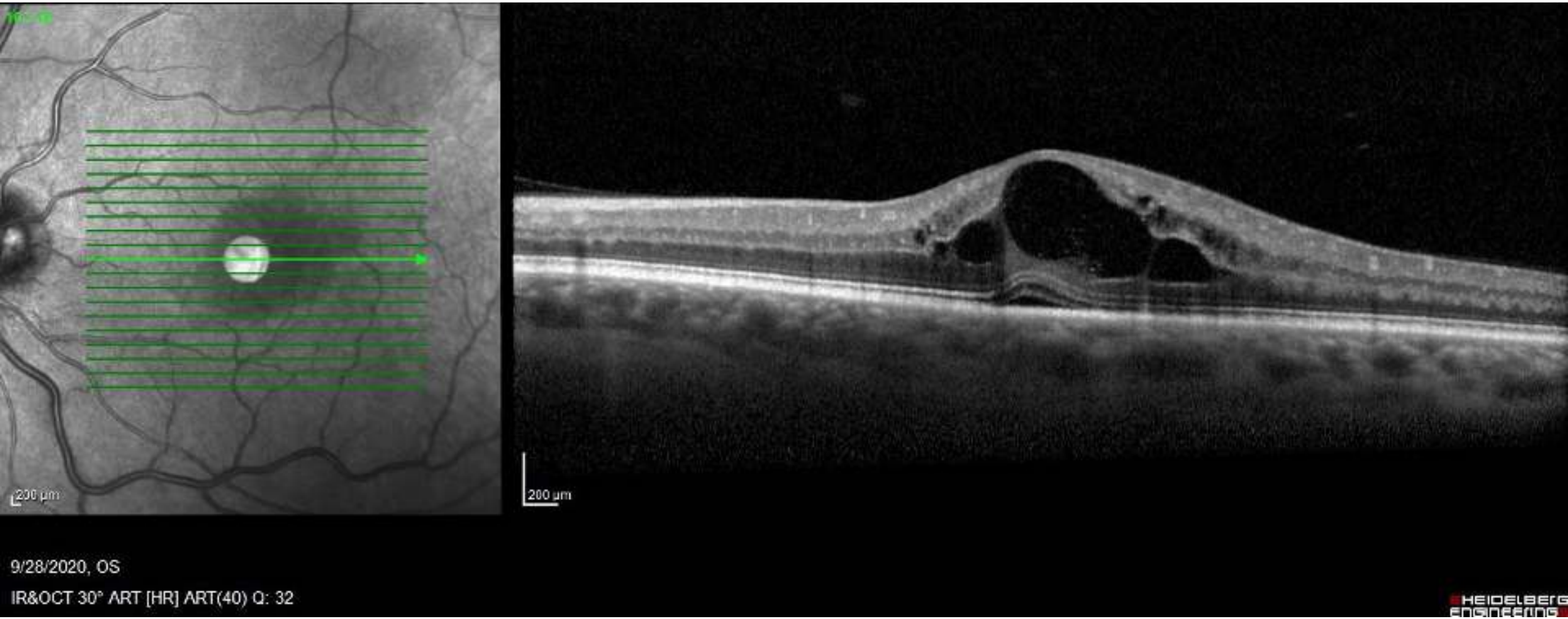
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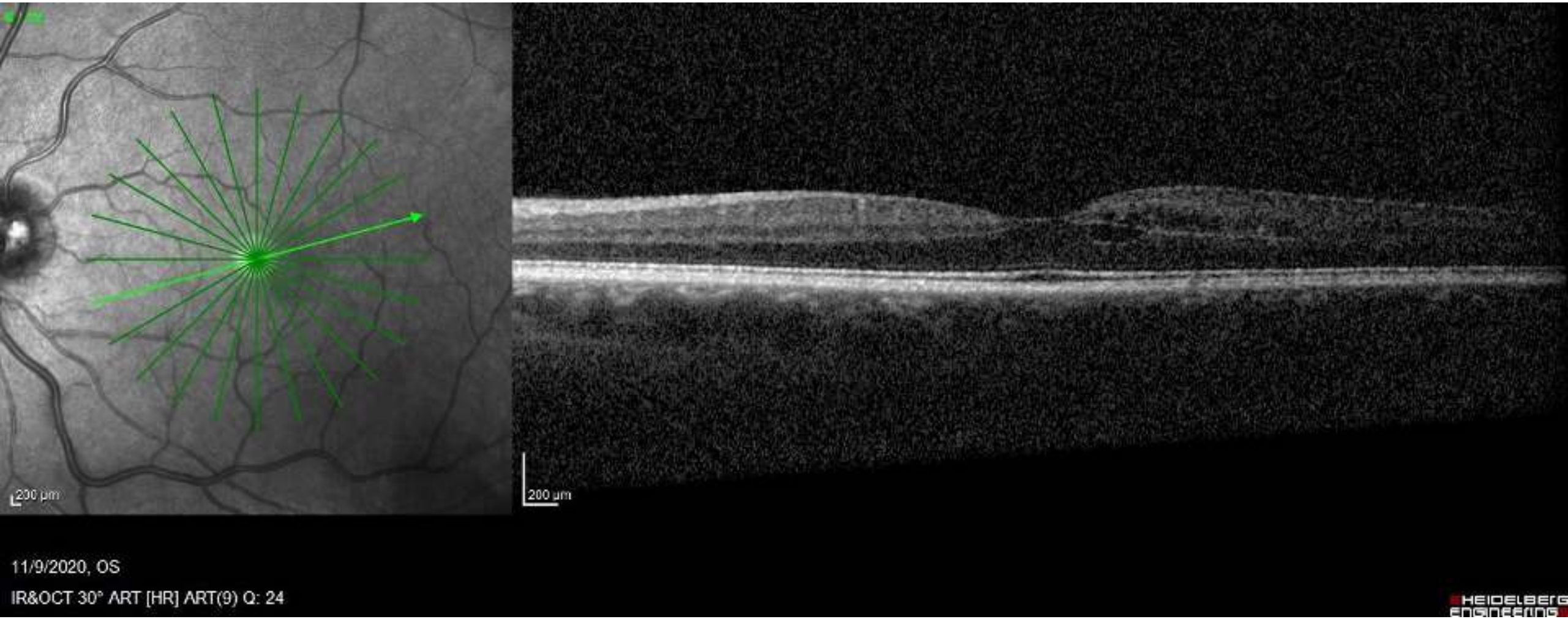
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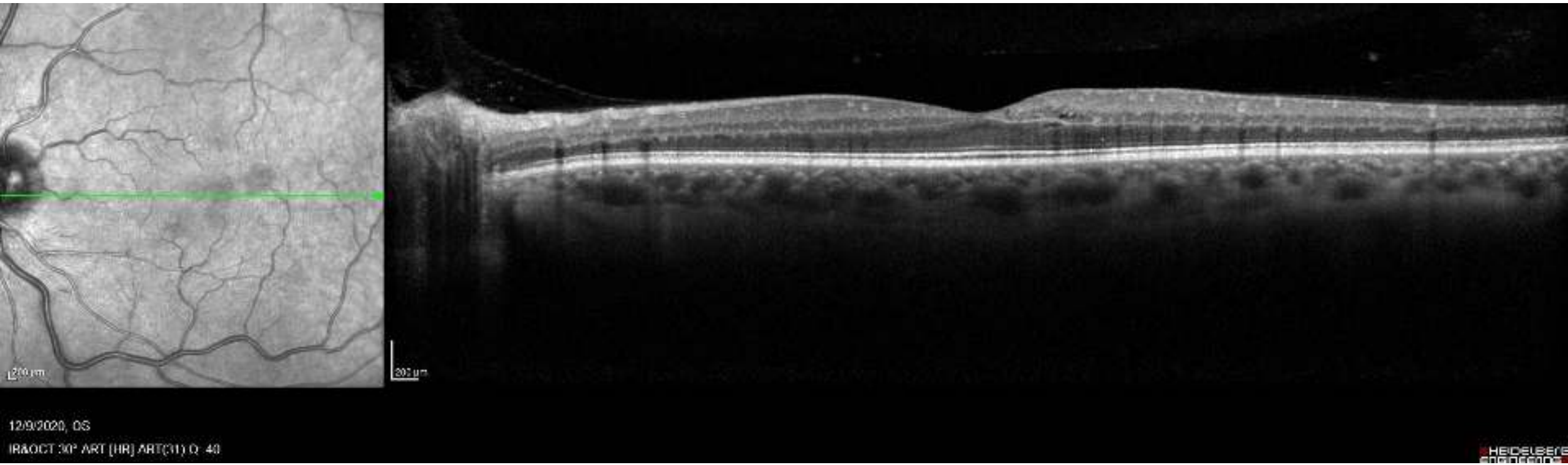
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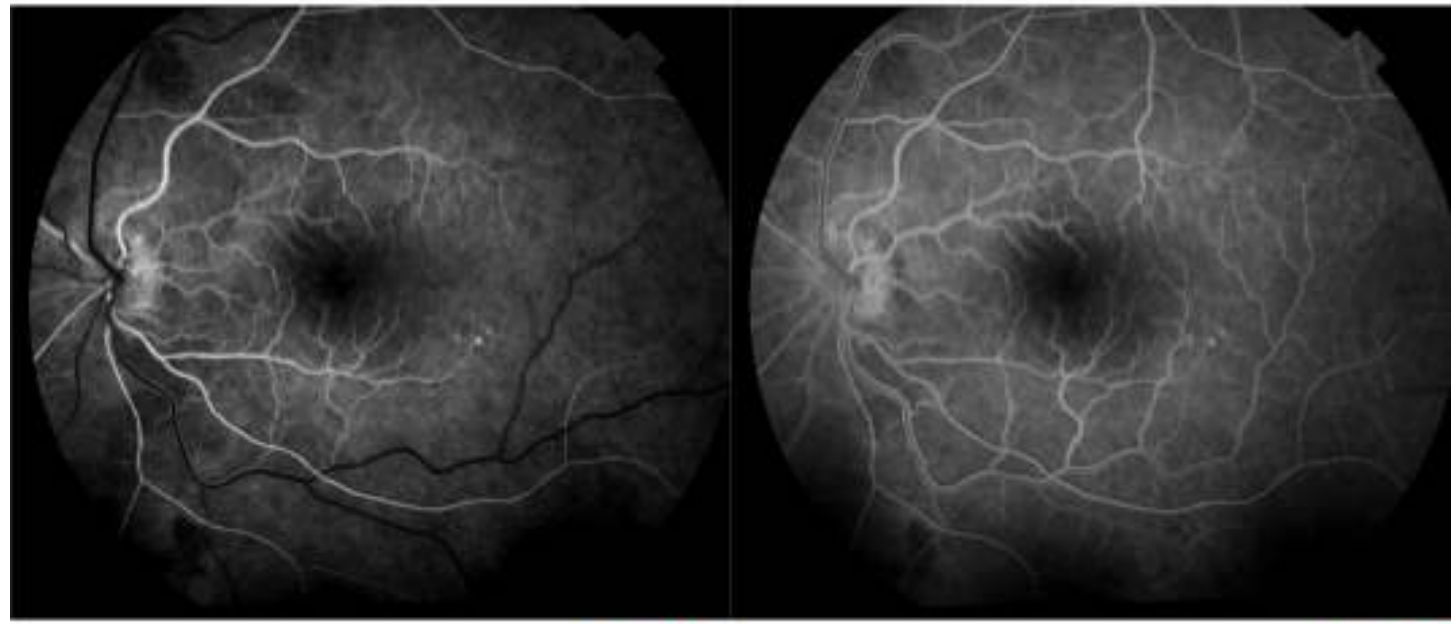

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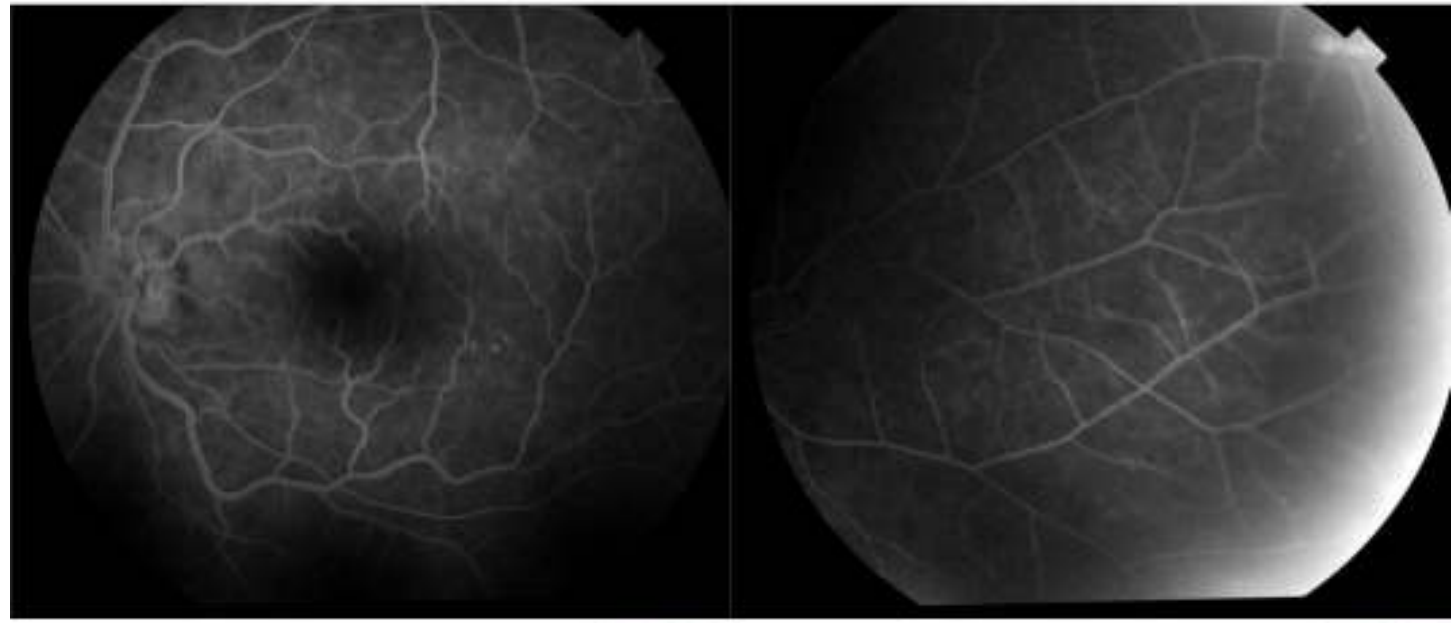

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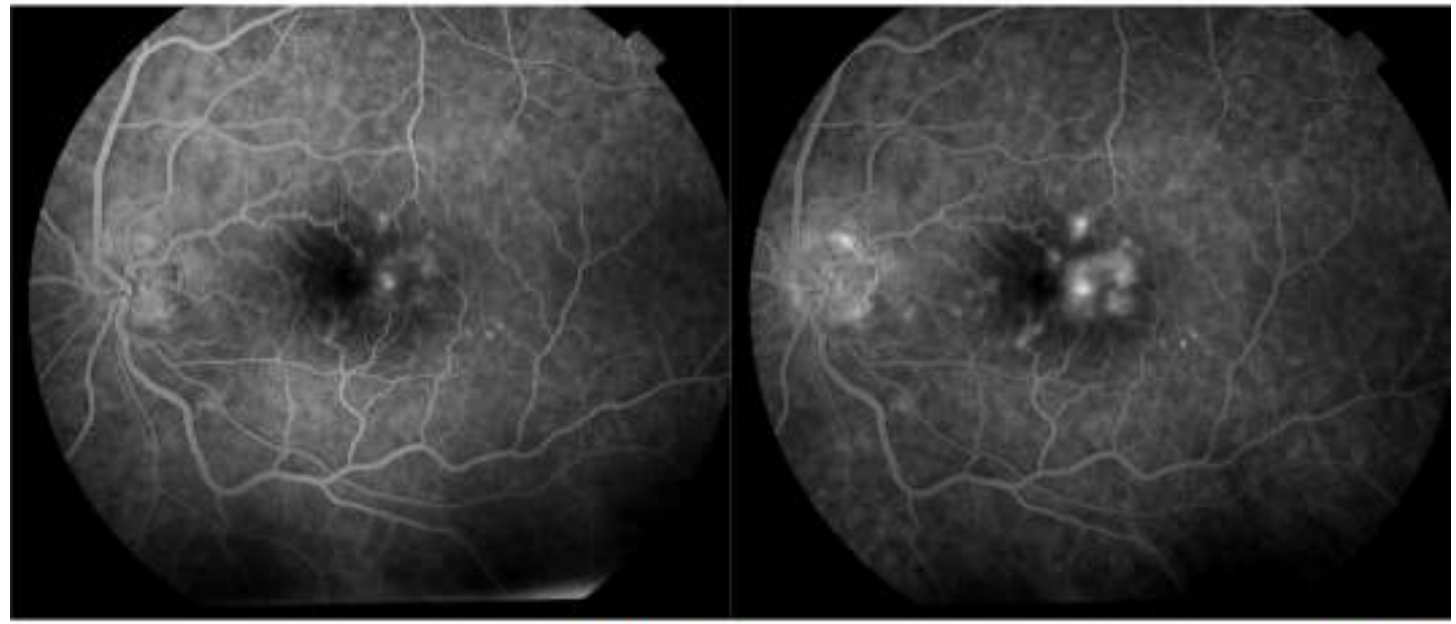

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Steroids

The breakdown of the blood-retina barrier in RVO is mediated in part by VEGF and in part by inflammatory cytokines .

Although the mean vitreal levels of VEGF are elevated in both disease states (CRVO and BRVO) , in one-third of the eyes, these may fall within the normal range despite the presence of macular edema .

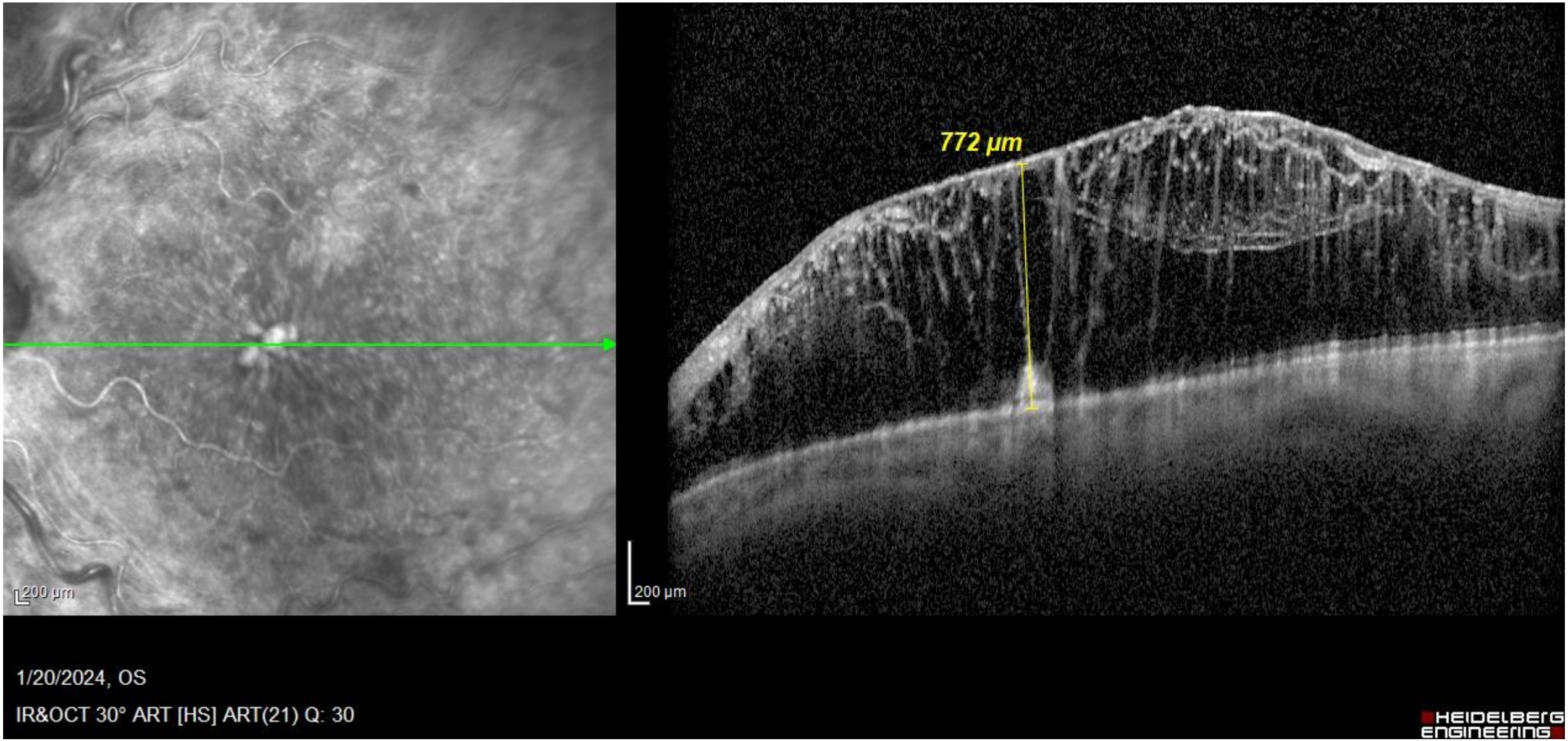
This finding indicates the existence of VEGF-independent pathways leading to macular edema that may be the reason why some patients are less responsive to anti-VEGF therapy alone.


MECHANISM OF ACTION

Steroids inhibit the expression of the VEGF gene and the metabolic pathways of VEGF, and, in addition, that of inflammatory cytokines .

Steroids may also have a neuroprotective effect that is beneficial in eyes with RVO .

Steroids may increase arteriovenous oxygen saturation measurement in patients with RVO, indicating improved retinal oxygenation , the exact mechanism is unknown.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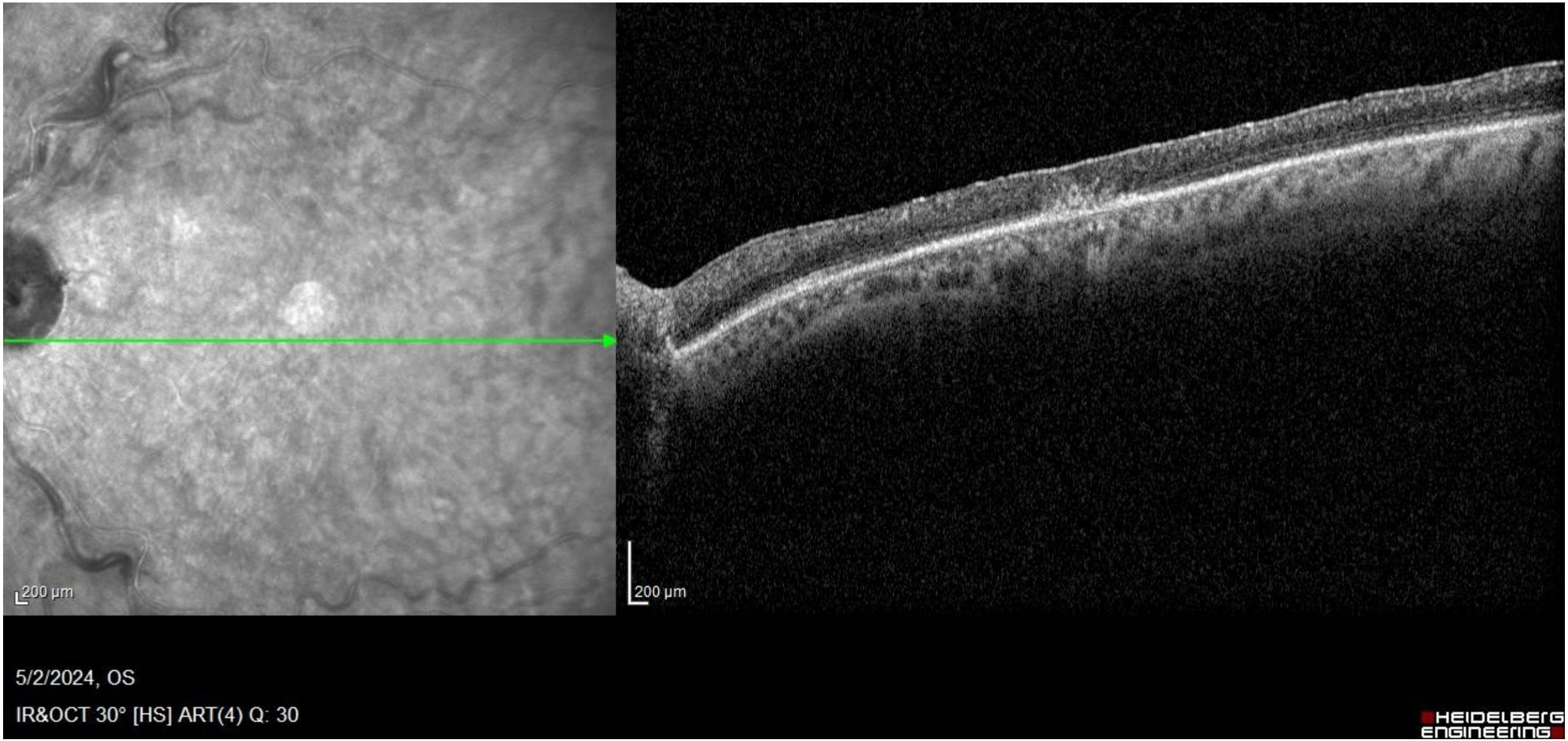
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- Commercially available corticosteroid compounds for intravitreal use include triamcinolone acetonide & dexamethasone (Ozurdex).

- ***The only FDA approved corticosteroid compounds for intravitreal use is Dexamethasone (Ozurdex).***

Recommendation

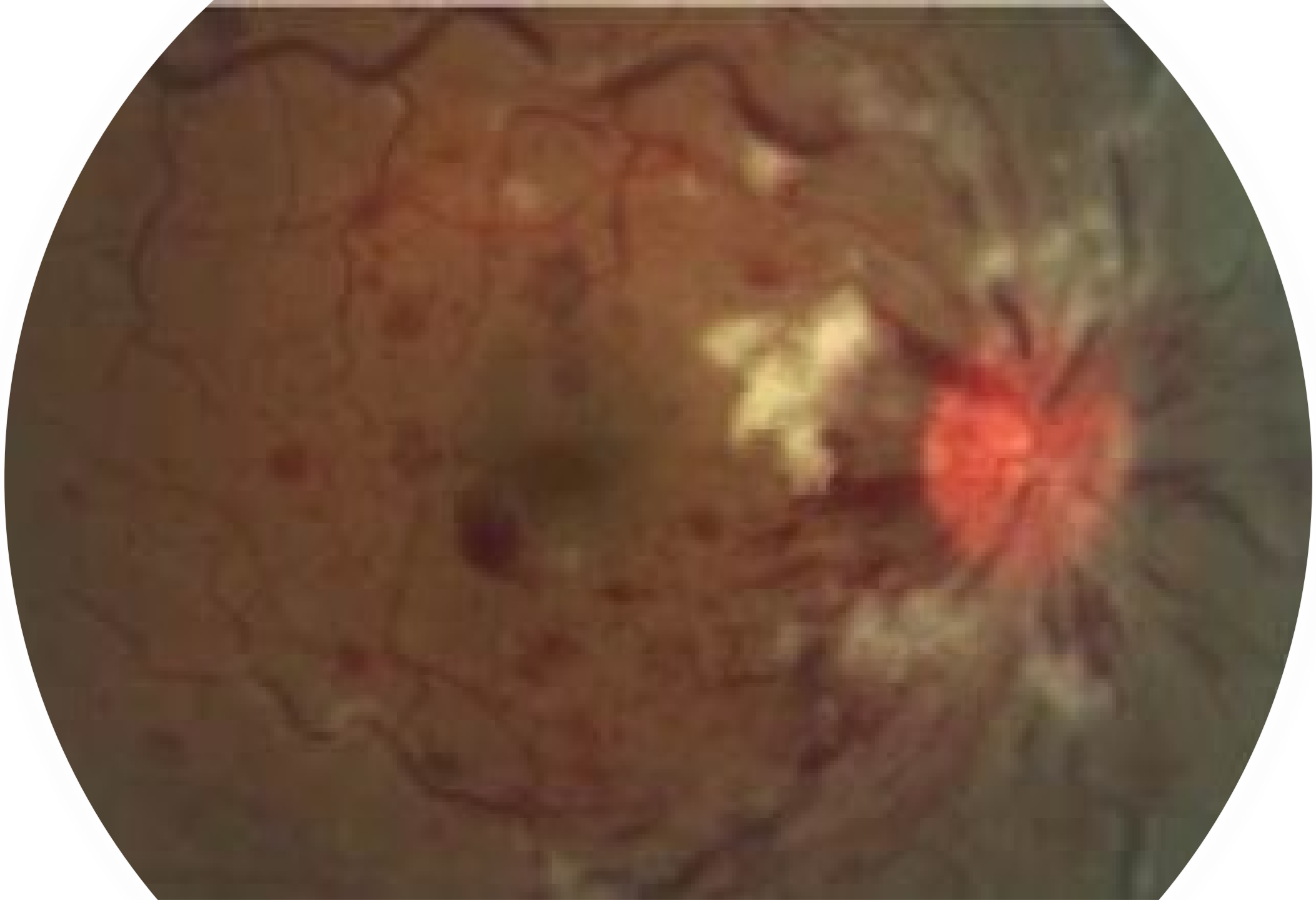
- Based on the data that exist thus far, corticosteroids are important in our armamentarium of drugs for treating patients with RVO, but largely ***on a second-choice level.***

Steroids may be considered as a first-line therapy for patients who have :-

- Recent history of a major cardiovascular or cerebrovascular event.
- Patients who are unwilling to come for monthly injections (and/or monitoring) in the first 6 months of therapy.

Pregnant females.

Is there any role for systemic steroids??



Laser Therapy

Laser photocoagulation is the standard of care for the treatment of iris or retinal NV.

Prophylactic PRP

For eyes initially categorized as nonperfused or indeterminate, 35% developed INV/ANV, compared with 10% for eyes initially categorized as perfused.

Therefore, PRP was recommended only after iris neovascularization was visible.

Where close follow-up is not possible, prophylactic PRP should be considered as early PRP can prevent iris neovascularization in ischemic CRVO


thank you