New Developments in the treatment of Diabetic Retinopathy

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Topics

- Management of diabetic retinopathy
  - Interventions
    a. primary (prevention)
    b. secundary (treatment options for DRP)
  - What does it mean for everyday practice?

Management of diabetic retinopathy

Primary intervention

- Glycemic control

  Intensive control (HbA_{1c} = 7.2%) *vs* conventional control (HbA_{1c} = 9.1%)*
  - Reduction of incidence of DRP by 76%
  - Reduction of progression of DRP by 54%

- Blood pressure control

  Tight blood pressure (<150/<85 mm Hg) control *vs* conventional control (<180/<105 mm Hg) **
  - 34% reduction in DRP progression
  - 47% reduction in visual actuity deterioration
  - 35% reduction in laser photocoagulation

- Lipid-lowering therapy

  Dyslipidemia increases the risk of DRP, especially diabetic macular edema

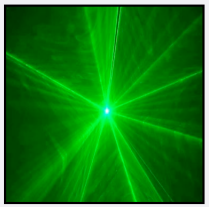
* *The Diabetes Control and Complications Trial (DCCT) - 6.5 years of follow-up*

* * *United Kingdom Prospective Diabetes Study (UKPD) – 9 years of follow-up*

Management of diabetic retinopathy

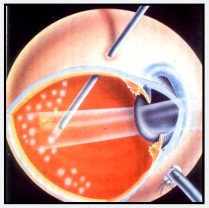
Secundary intervention

- Laser intervention
  - Severe nonproliferative and proliferative DRP
  - Diabetic macular edema



- Interventions with intravitreal agents
  - Corticosteroids
  - Anti-angiogenesis agents

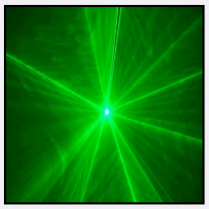
- Surgical intervention
  - Vitrectomy for vitreous hemorrhage and proliferatieve DRP
  - Vitrectomy for other reasons such as diabetic macular edema

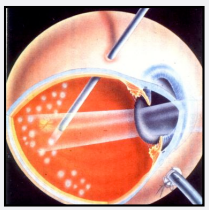


Management of diabetic retinopathy

Secundary intervention

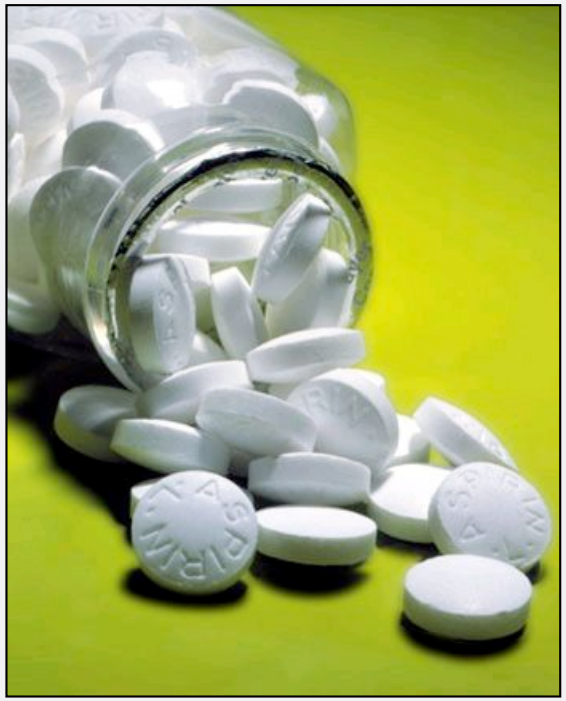
- Medical intervention
  - Anti-platelet agents
  - Protein Kinase C inhibitors (Ruboxystaurin)
- Laser intervention
  - Severe nonproliferative and proliferative DRP
  - Diabetic macular edema
- Interventions with intravitreal agents
  - Corticosteroids
  - Anti-angiogenesis agents
- Surgical intervention
  - Vitrectomy for diabetic macular edema
  - Vitrectomy for vitreous hemorrhage and proliferatieve DRP





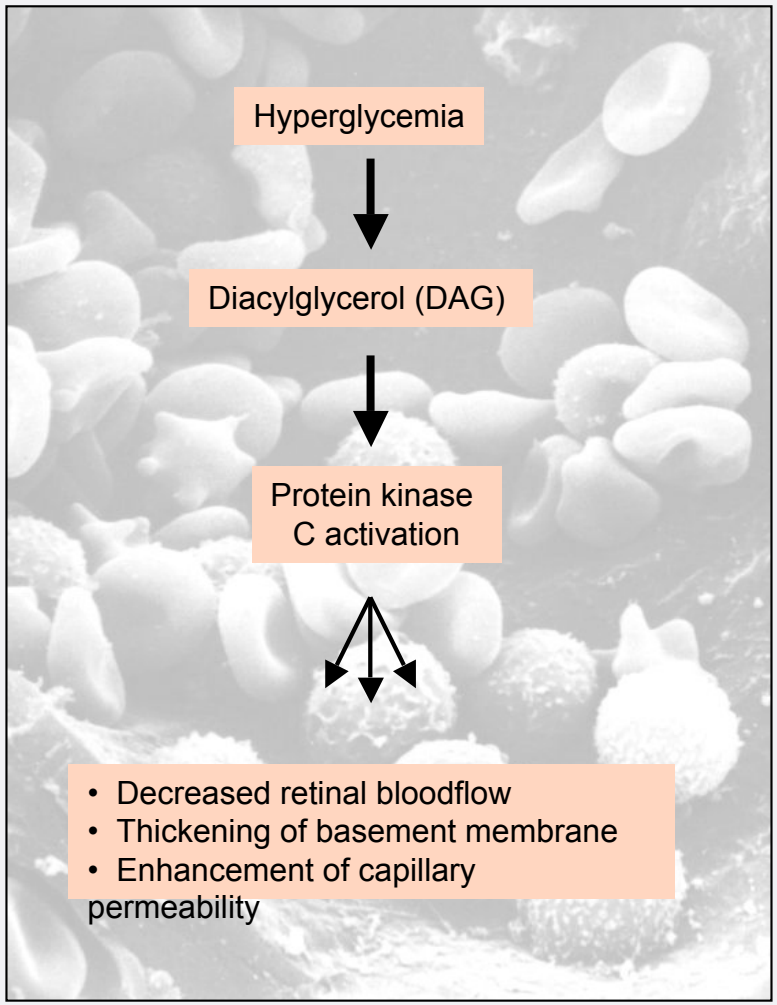
Medical intervention

- Antiplatelet agents
  - 650 mg aspirin has no effect on DRP (positive or negative) – ETDRS
  - Circumstantial evidence that aspirin may delay the incidence of DRP



Medical intervention

- Protein kinase C (PKC) inhibitors



Non-selective PKC inhibitors: side-effects

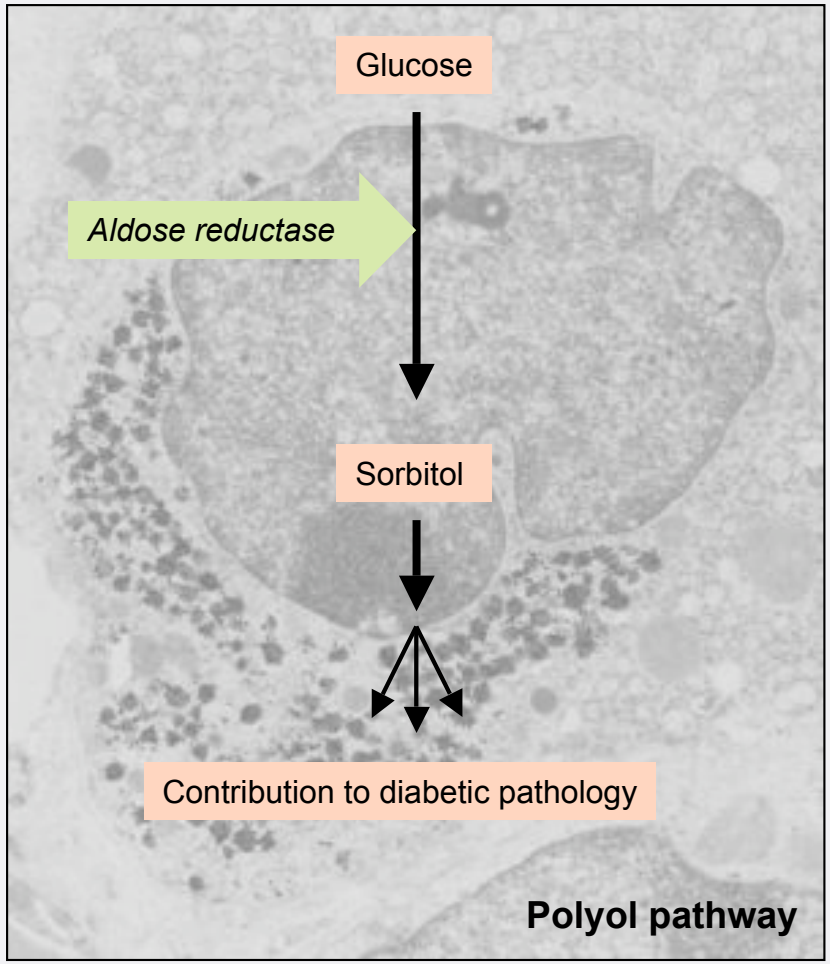
Ruboxistaurin (PKC-β inhibitor)

- Phase II and III
- Therapeutically effective:
  - Preventing visual loss
  - Resolution of macular edema
  - No effect on progression from NPDR to PDR
- Limited side-effects

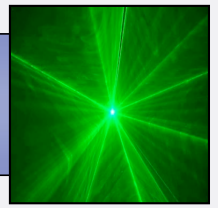
Medical intervention

- Octreotride (synthetic analogue of somatostatine)

- Aldose reductase inhibitors
  - RCTs: sordinil and tolrestat
  - No effect on DRP incidence or progression 3-5 years



Laser intervention



Nonproliferative and proliferative DRP

Mild and moderate nonproliferative DRP

- No photocoagulation (unless for macular edema)

Severe and very severe nonproliferative DRP (4-2-1 rule)

- Consider panretinal photocoagulation, especially for:
  - Type II diabetes
  - Impending cataract surgery
  - Pregnancy

Proliferative DRP

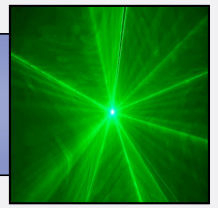
- Panretinal photocoagulation generally indicated.

High risk proliferative DRP

- Panretinal photocoagulation
- Vitrectomy

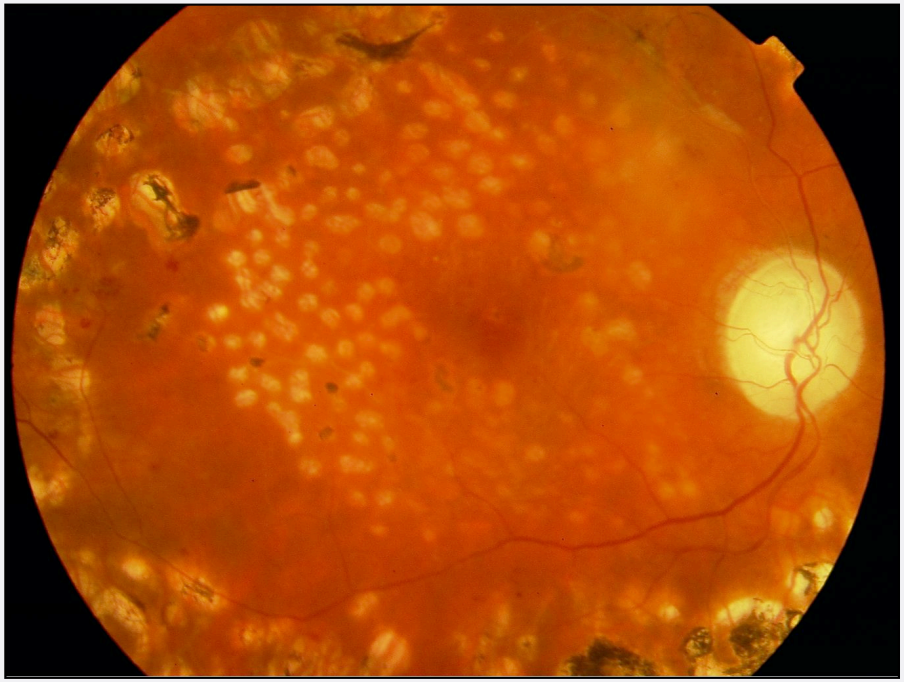
Severe NPDR

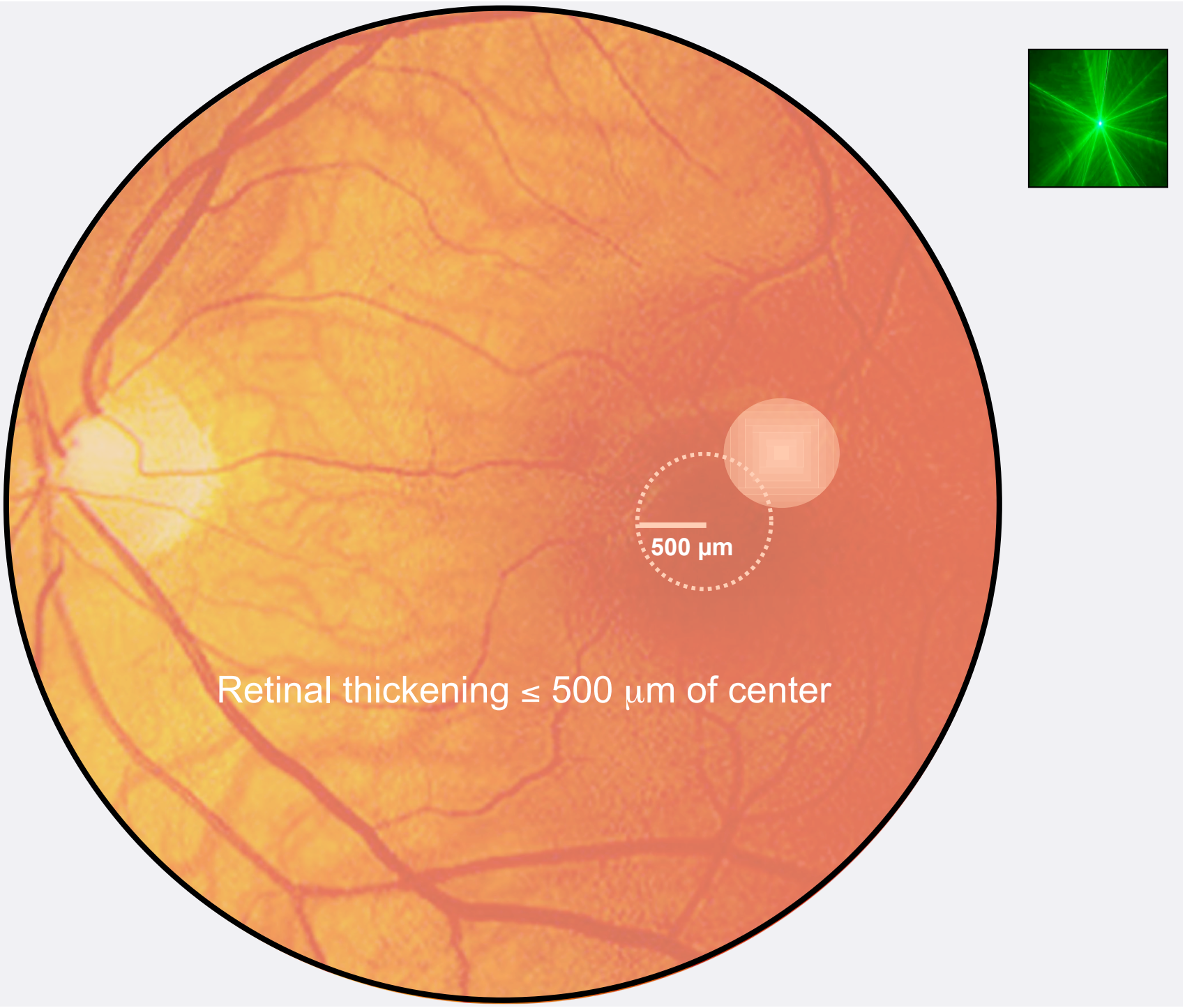
Laser intervention

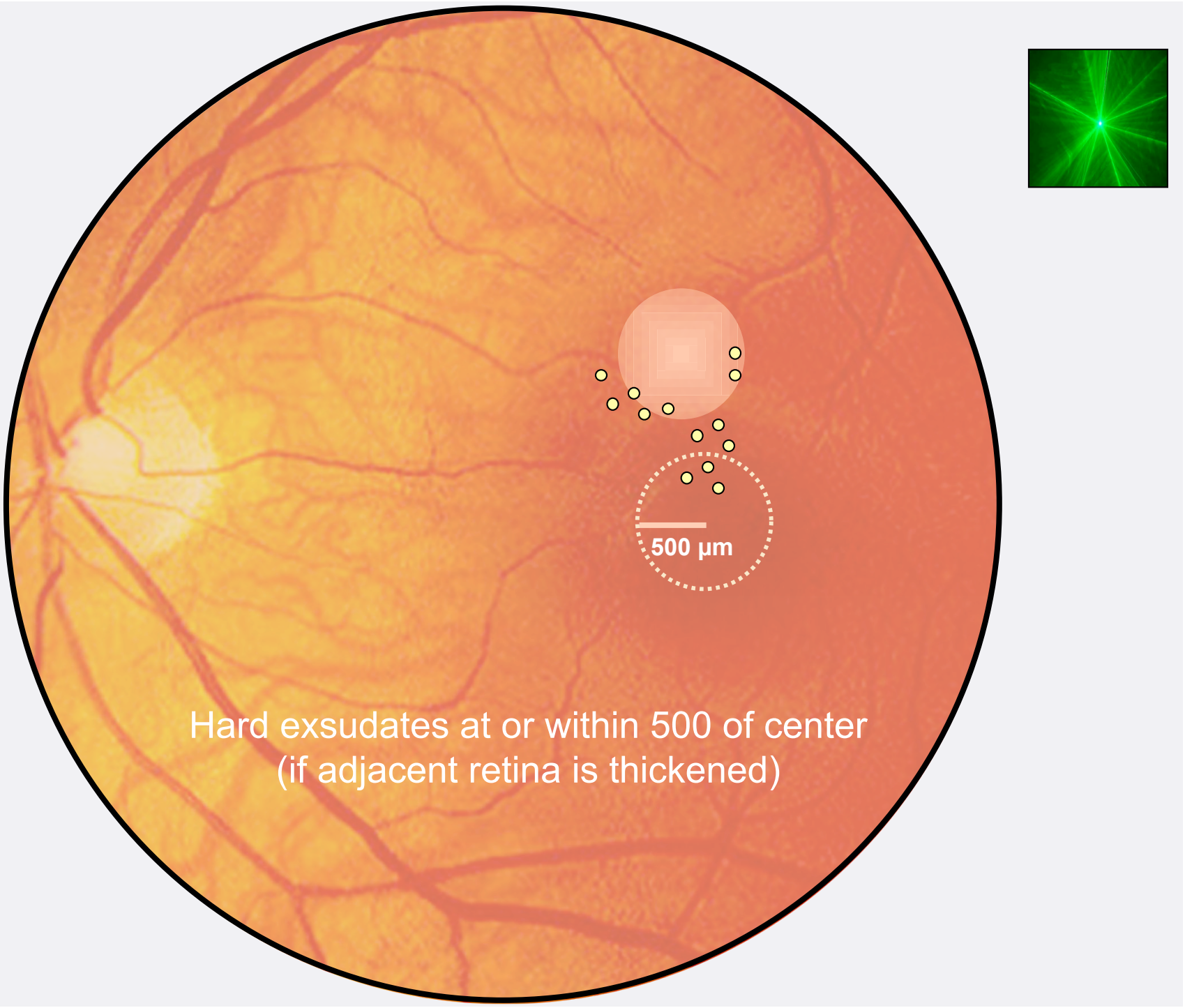


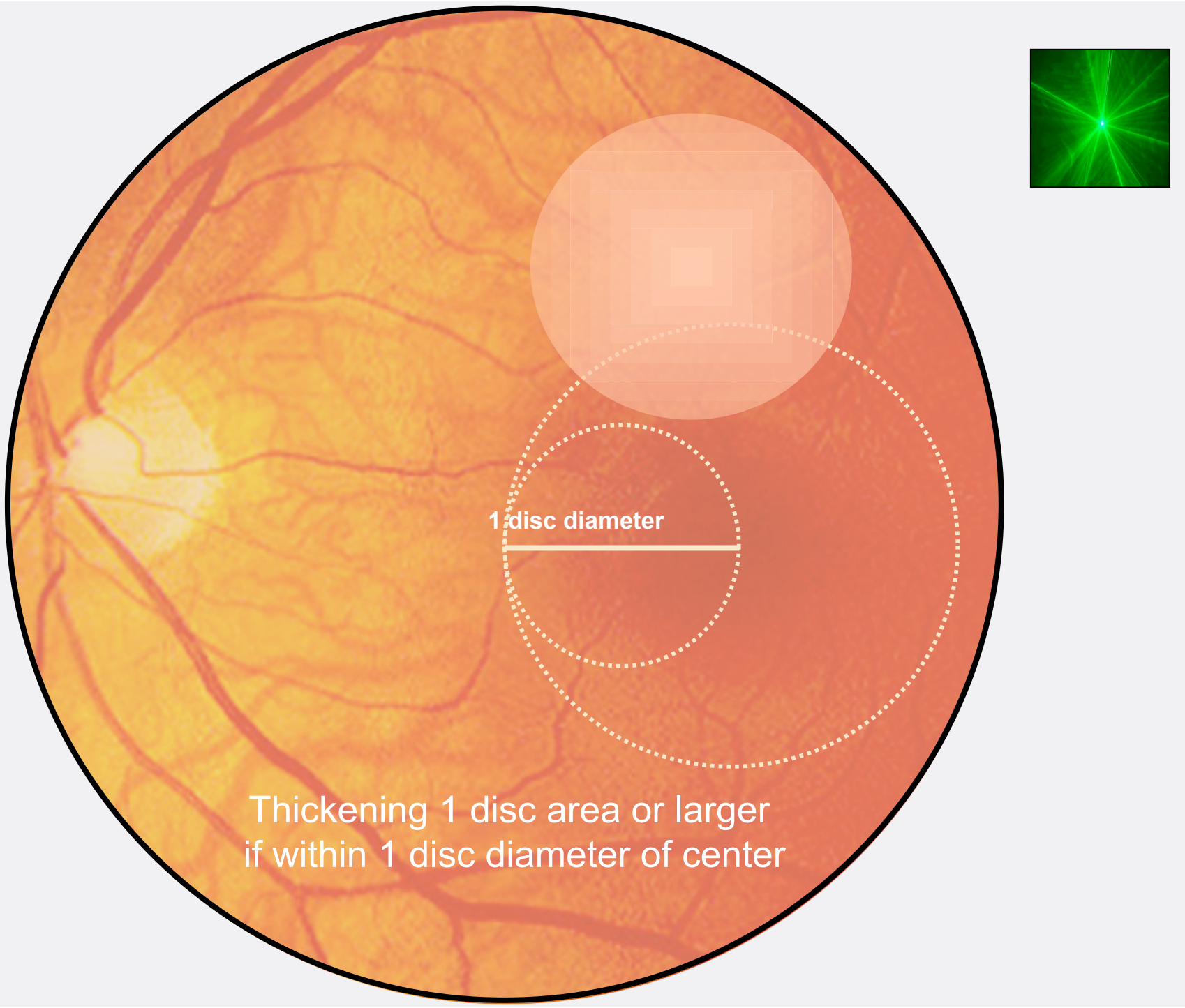
Diabetic macular edema

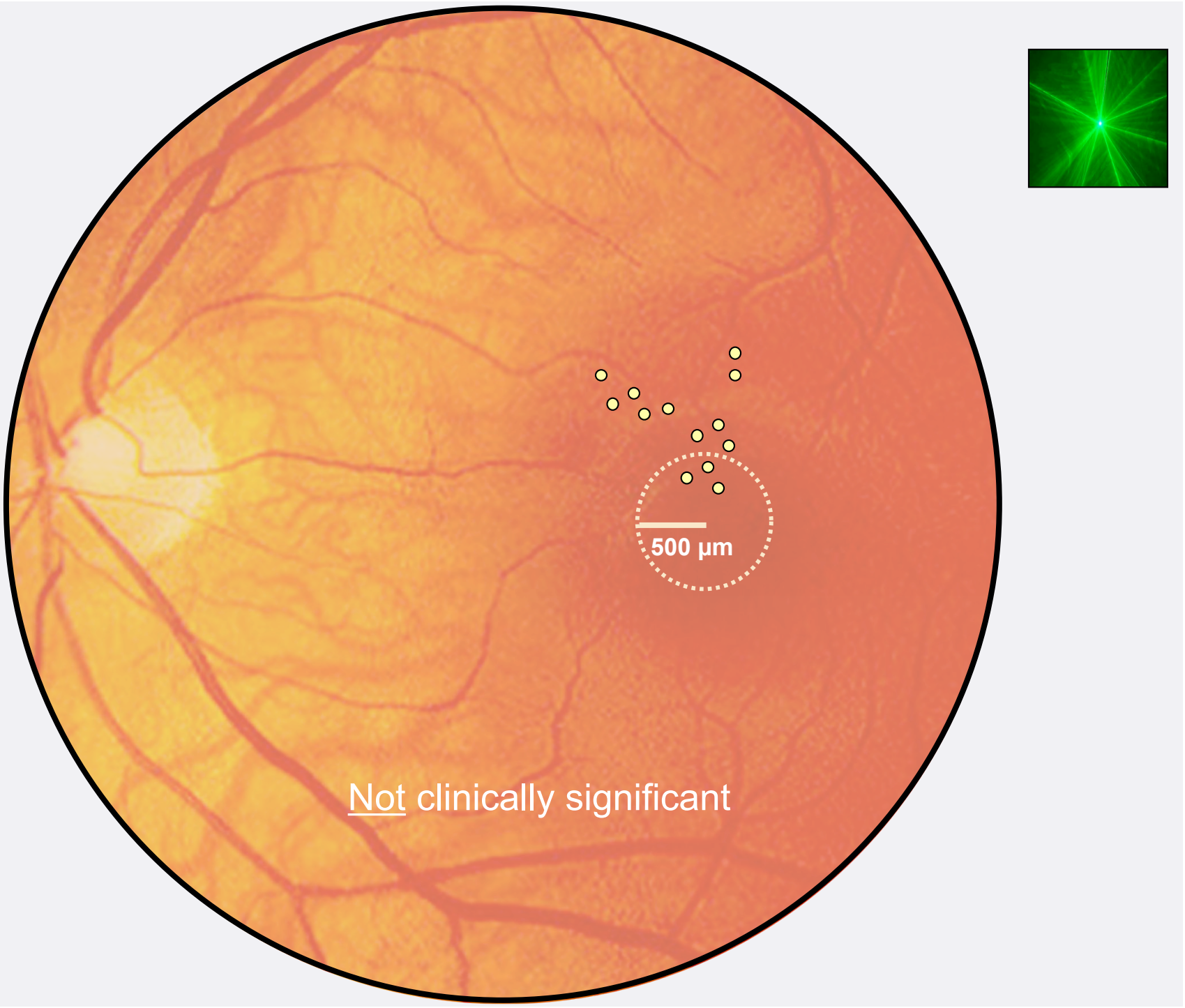
- Clinical significant macular edema (CSME)
  - Focal laser treatment
  - Grid laser treatment

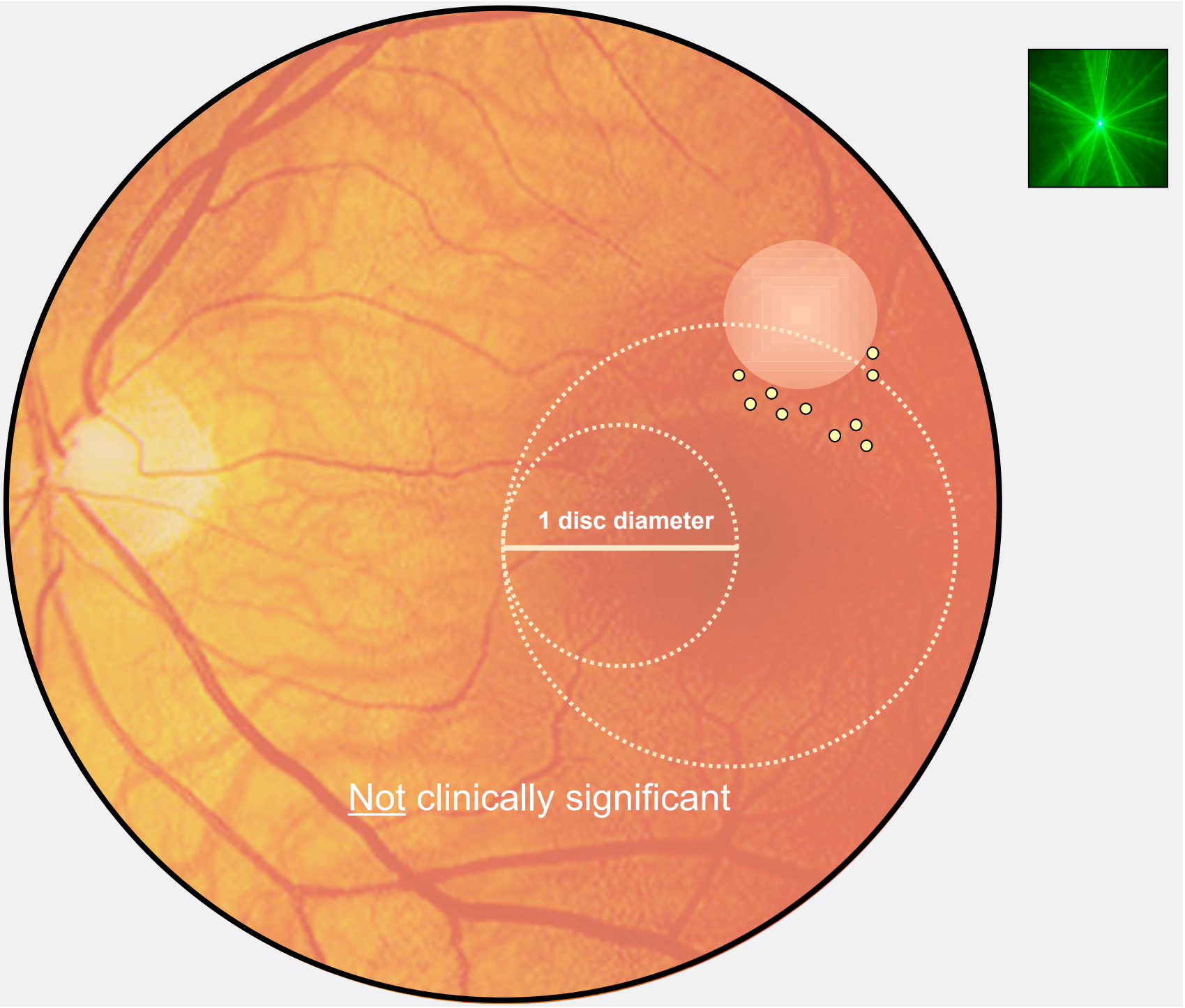



500 µm
Retinal thickening ≤ 500 µm of center


500 µm
Hard exsudates at or within 500 of center
(if adjacent retina is thickened)


1 disc diameter
Thickening 1 disc area or larger
if within 1 disc diameter of center

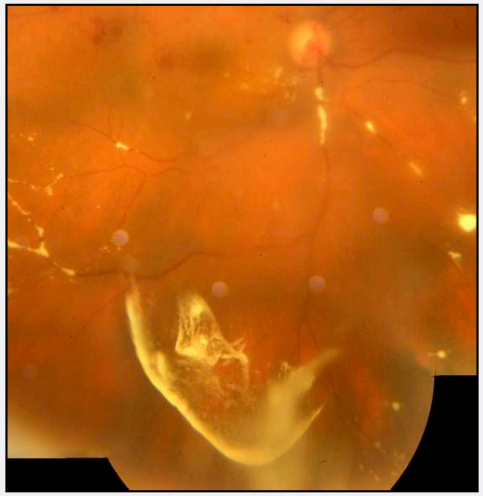

500 µm
Not clinically significant


1 disc diameter
Not clinically significant

Intravitreal agents

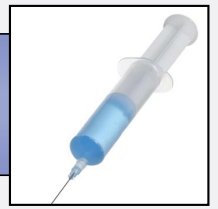
Triamcinolon (IVTA)

- Several small RCTs show improvement in macular edema and visual acuity



- RCT (n=69, follow-up 2 years)
  - Twice the chance of improved visual acuity
  - Half the chance of visual loss
- Significant disadvantages
  - Significant side-effects
    - Cataract (50%)
    - Elevated intraocular pressure (40%)
    - Medically uncontrollable glaucoma (1-2%)
    - Endophthalmitis (1:1000)
  - Repeat injections may be necessary (duration of effect is approximately 6-9 months for 20 mg – 2-4 months for 4 mg)

Intravitreal agents



Triamcinolon (IVTA)

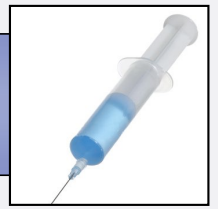
- Suggestions for use:
  - In diabetic macula edema
  - An option in refractory cases
  - An option in very pronounced, diffuse edema
  - Consider a combination with focal / grid laser after 4-6 weeks

Intravitreal agents

Anti-angiogenic agents

- Three trials
  - Finished (phase II) Pegaptanip (Macugen®)
    - 172 patients with DME
    - 34% versus 10% improvement of ≥ 10 letters
    - decrease in macular thickness
  - Ongoing Ranibizumab (Lucentis®) - RESOLVE study
    Bevacizumab (Avastin®) - US National Eye Institute

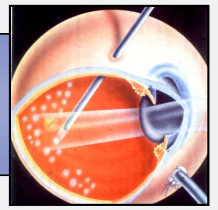
Intravitreal agents



Anti-angiogenic agents

- Suggestions for use:
  - Perhaps in diabetic macular edema (glaucoma patients / steroid responders)
  - In case of very severe proliferations
    a. Neovascular glaucoma
    b. Very severe retinal proliferaties
    c. Always additional treatment necessary!

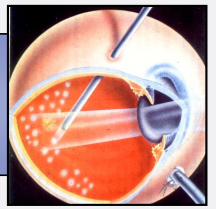
Surgical intervention



Vitrectomy

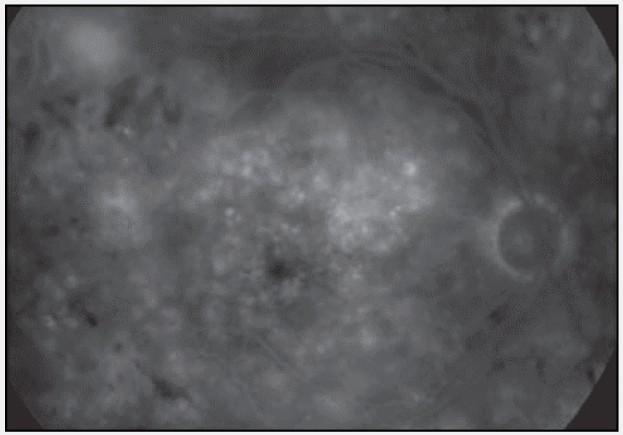
- Guideline indications
  - Dense nonclearing vitreous hemorrhage
  - Tractional retinal detachment involving or threatening the macula

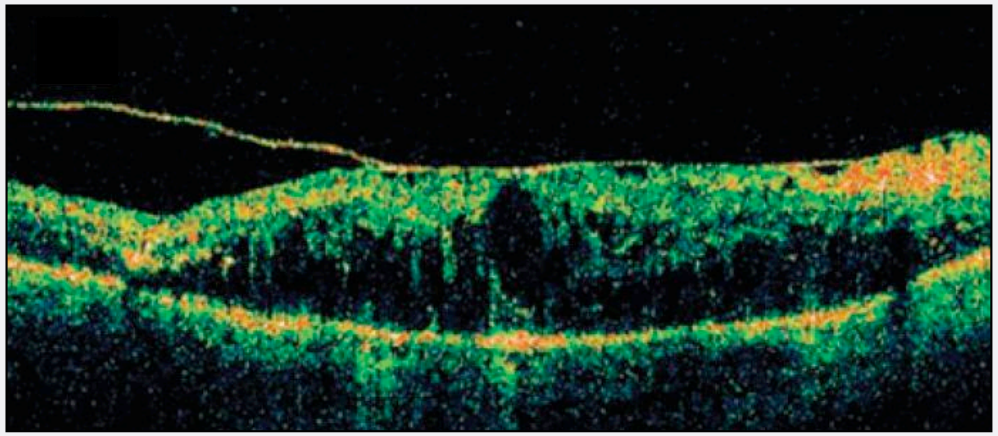
Surgical intervention



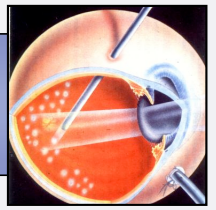
Vitrectomy

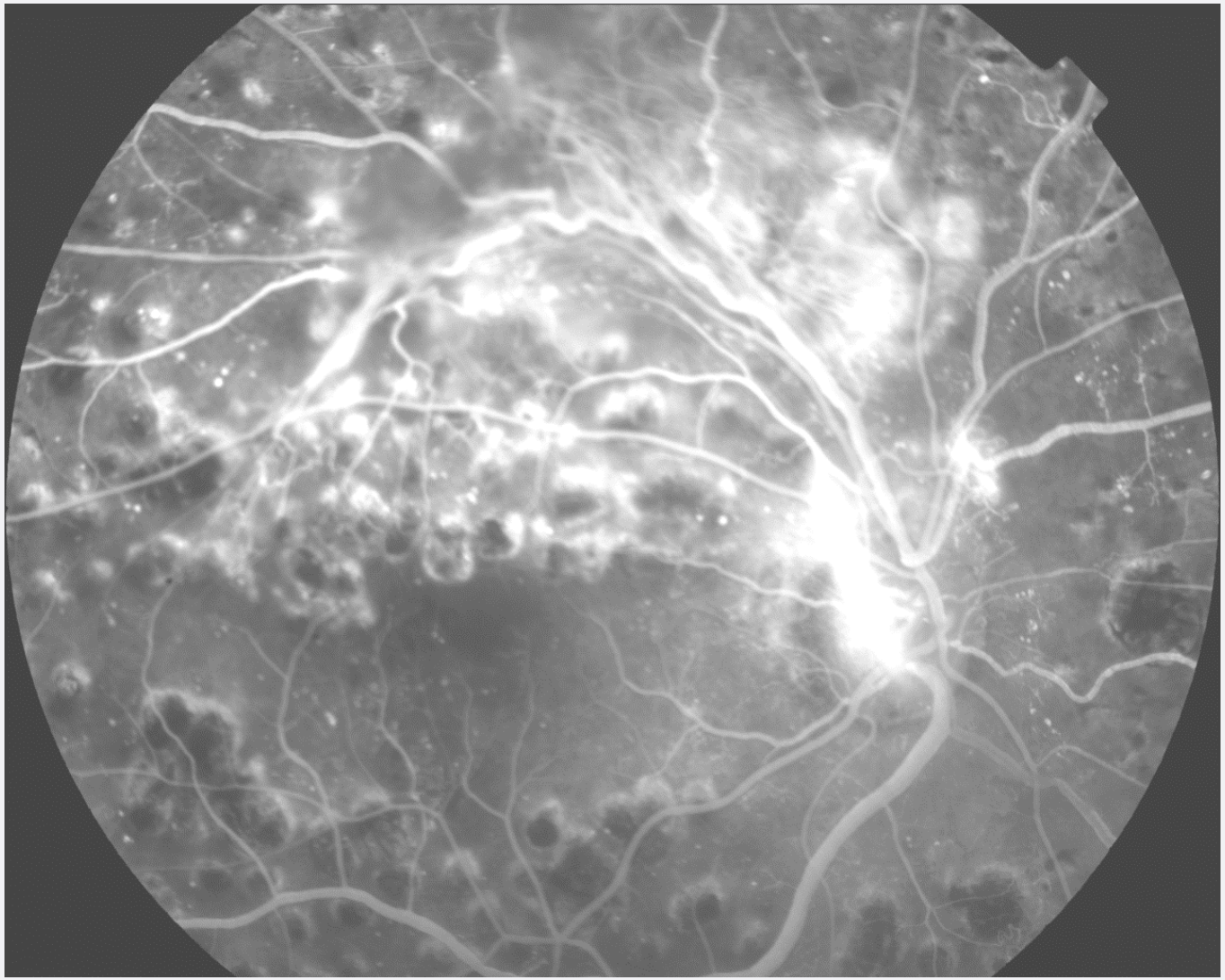
- The role of vitrectomy has expanded:
  - Recurrent vitreous hemorrhage despite maximal PRP
  - Diabetic macular edema in combination with vitreous traction
  - Diabetic macular edema evidence of traction
  - Progressive PDR despite laser (especially type I)



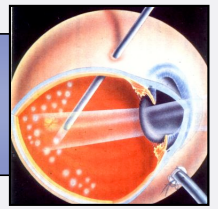


Surgical intervention





Surgical intervention

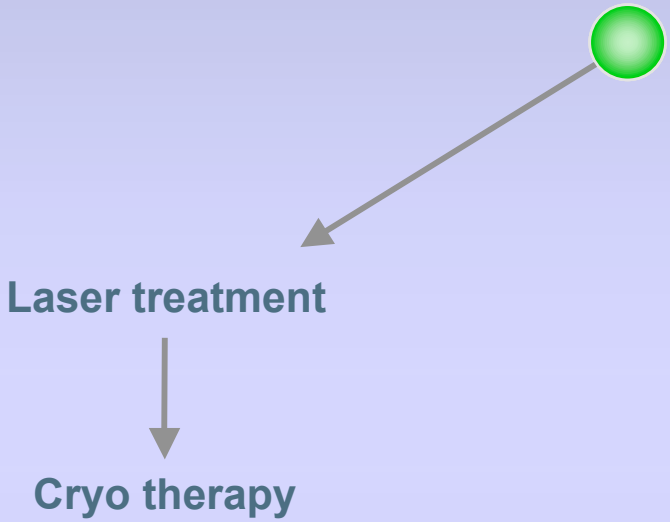


Vitrectomy

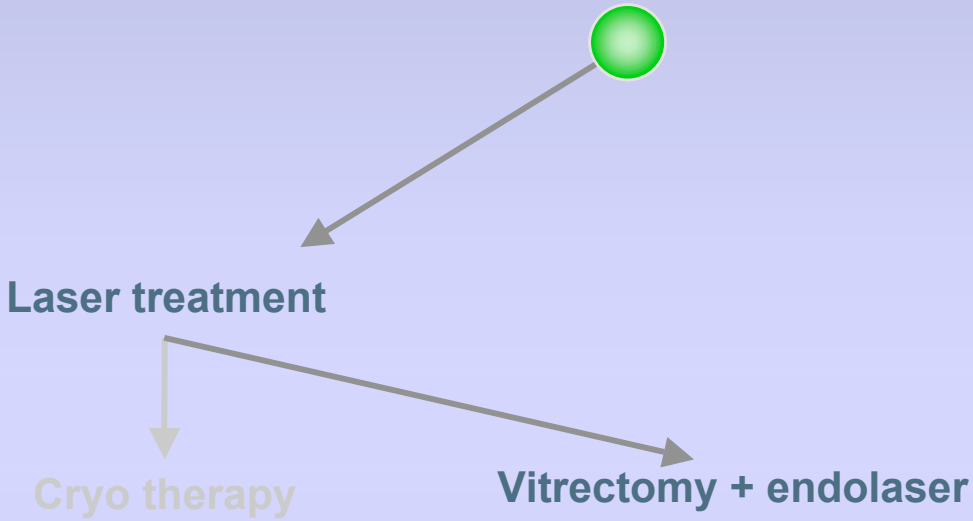
- Important:
  - Create a posterior vitreous detachmant
  - In case of traction, consider removing the ILM to ensure complete removal of tractional membranes
  - Consider very peripheral laser

Ischemia and proliferations

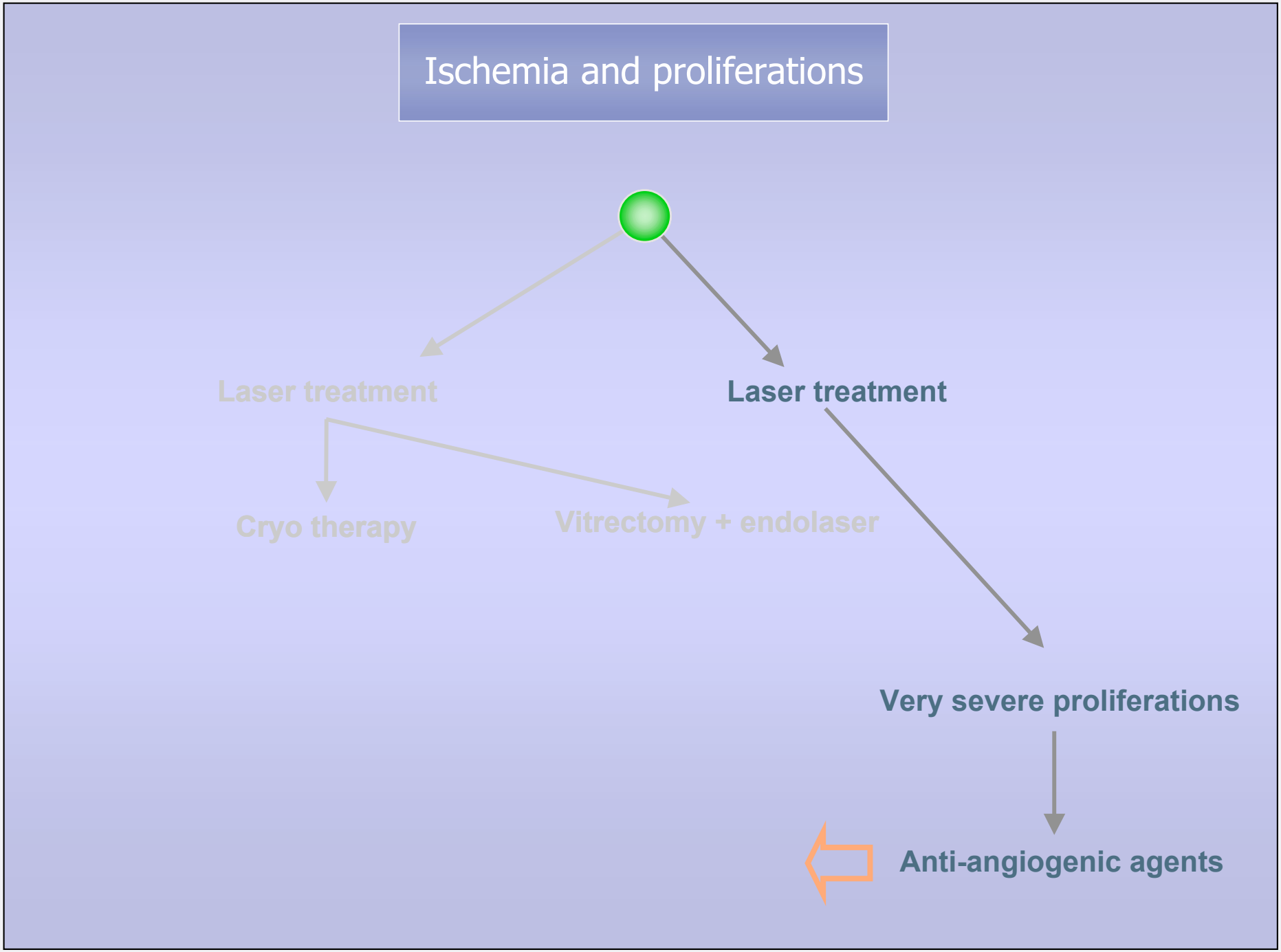
Ischemia and proliferations



Ischemia and proliferations

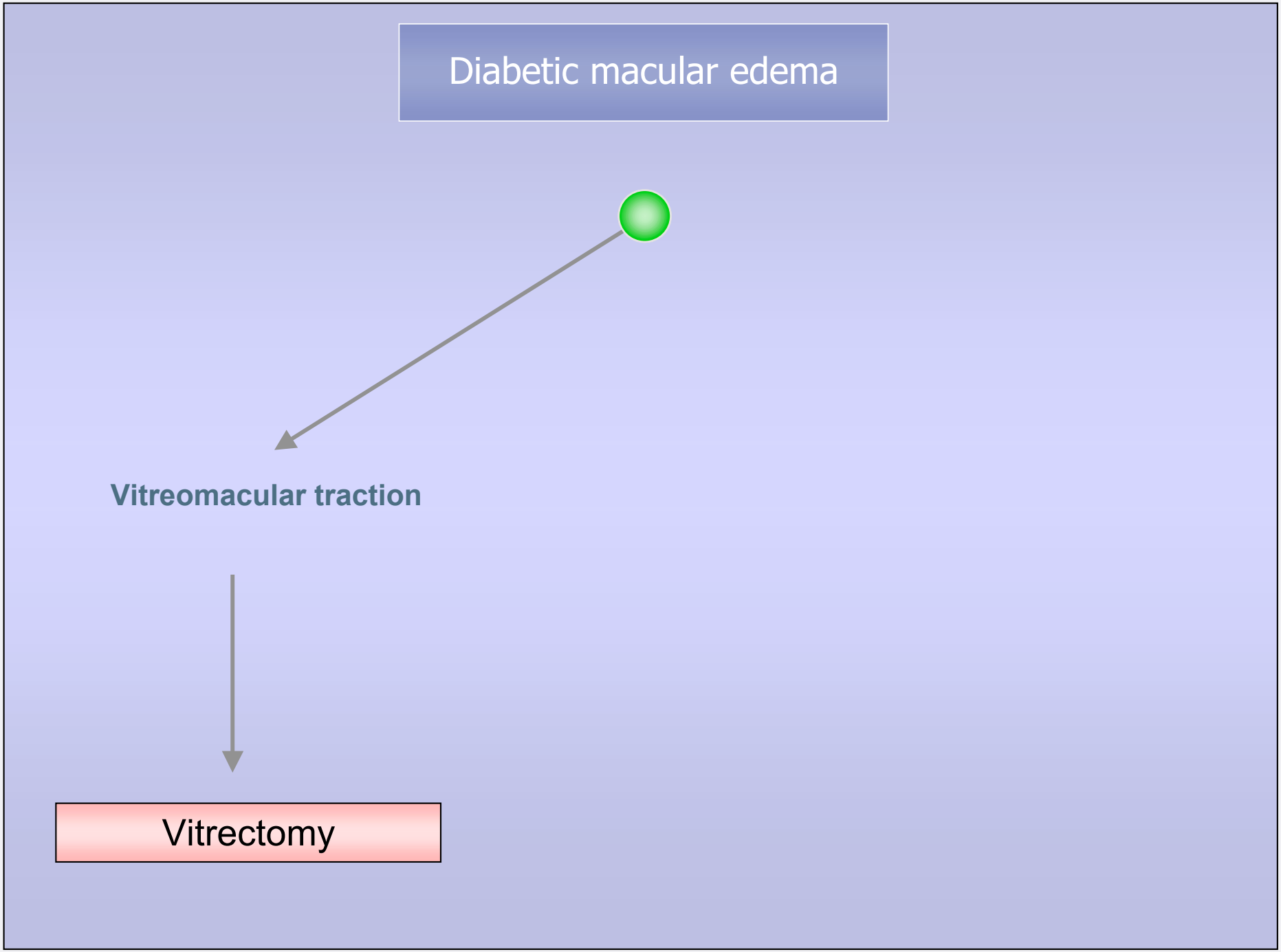


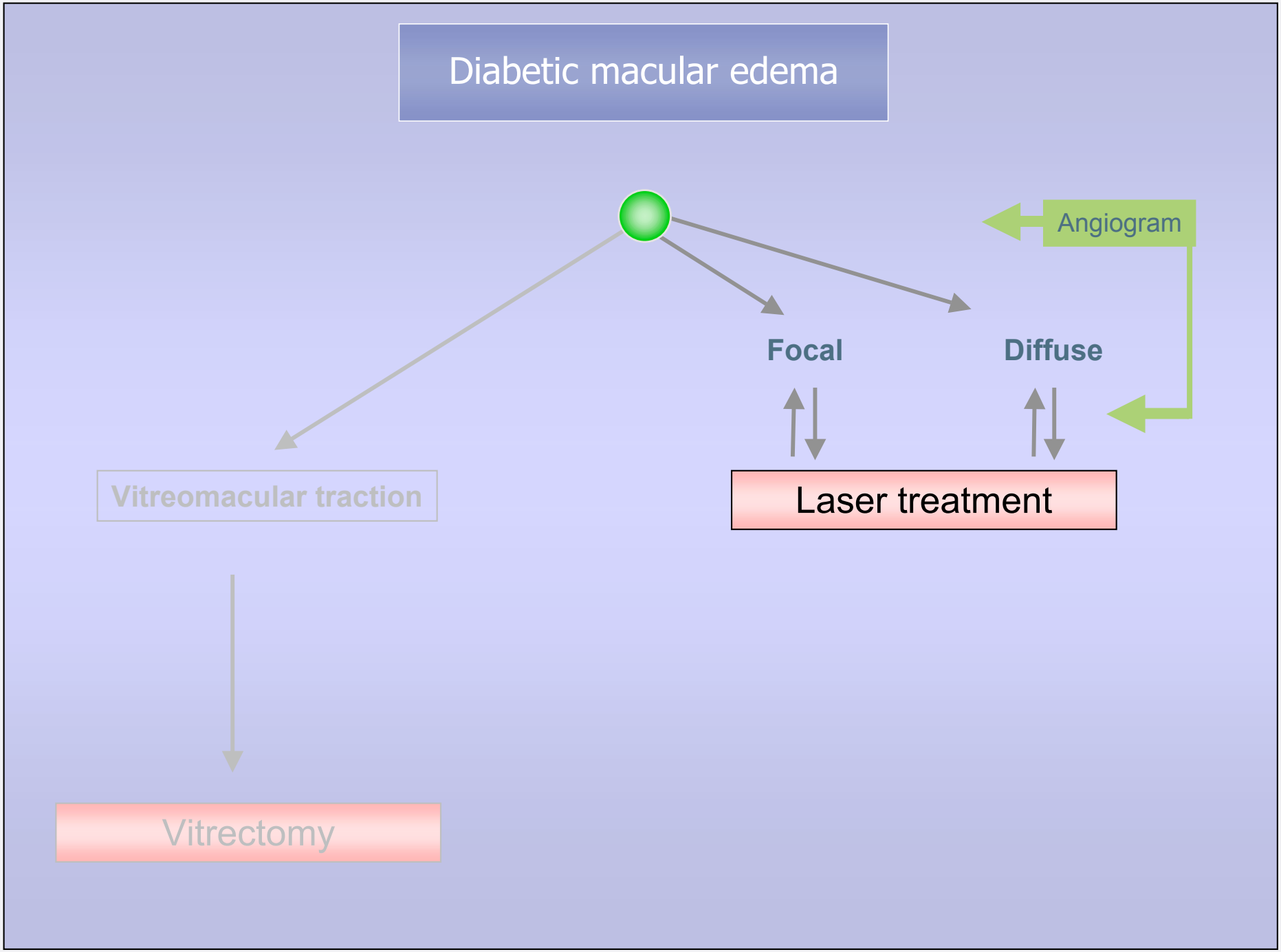
Ischemia and proliferations

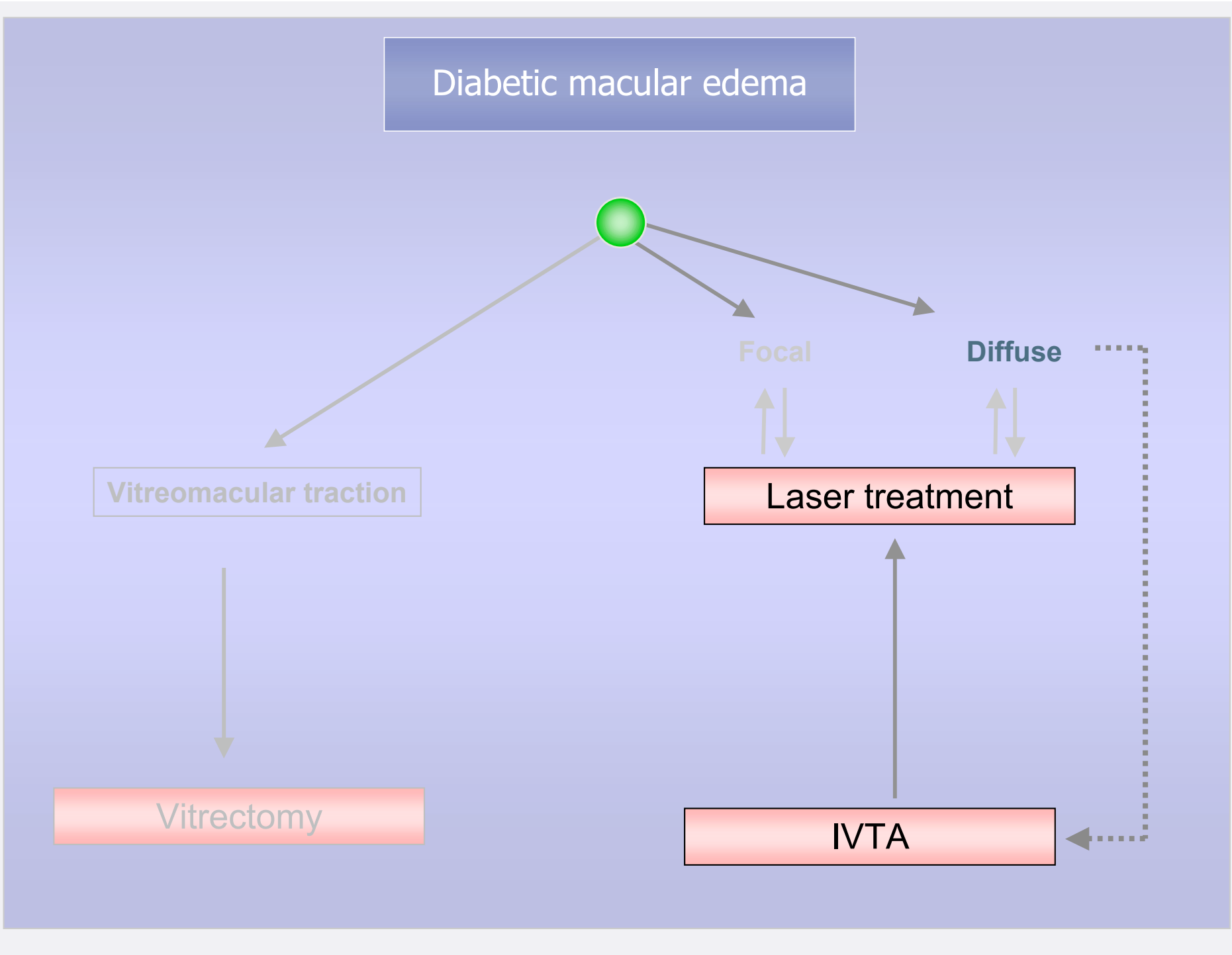


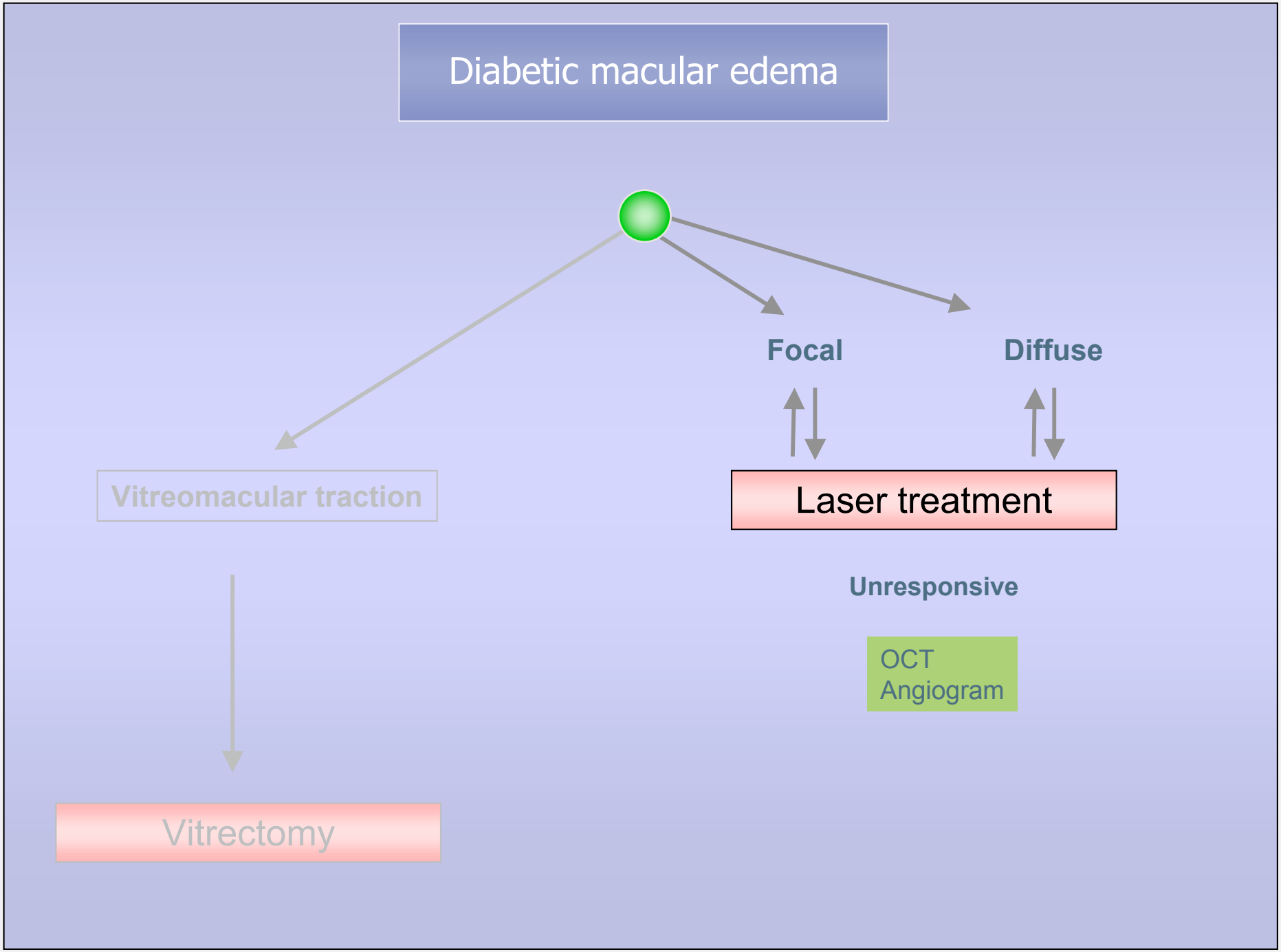
Diabetic macular edema

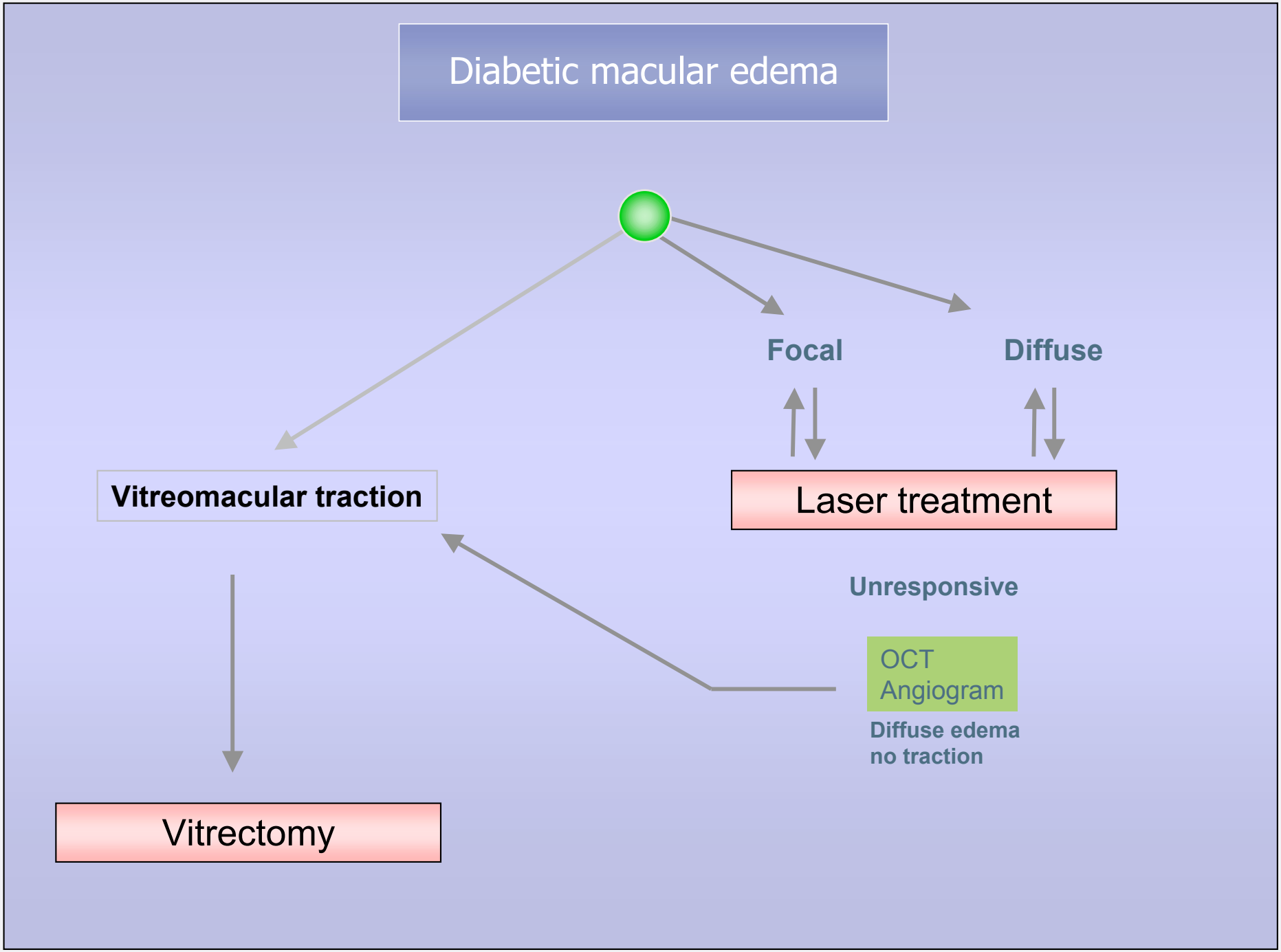
?

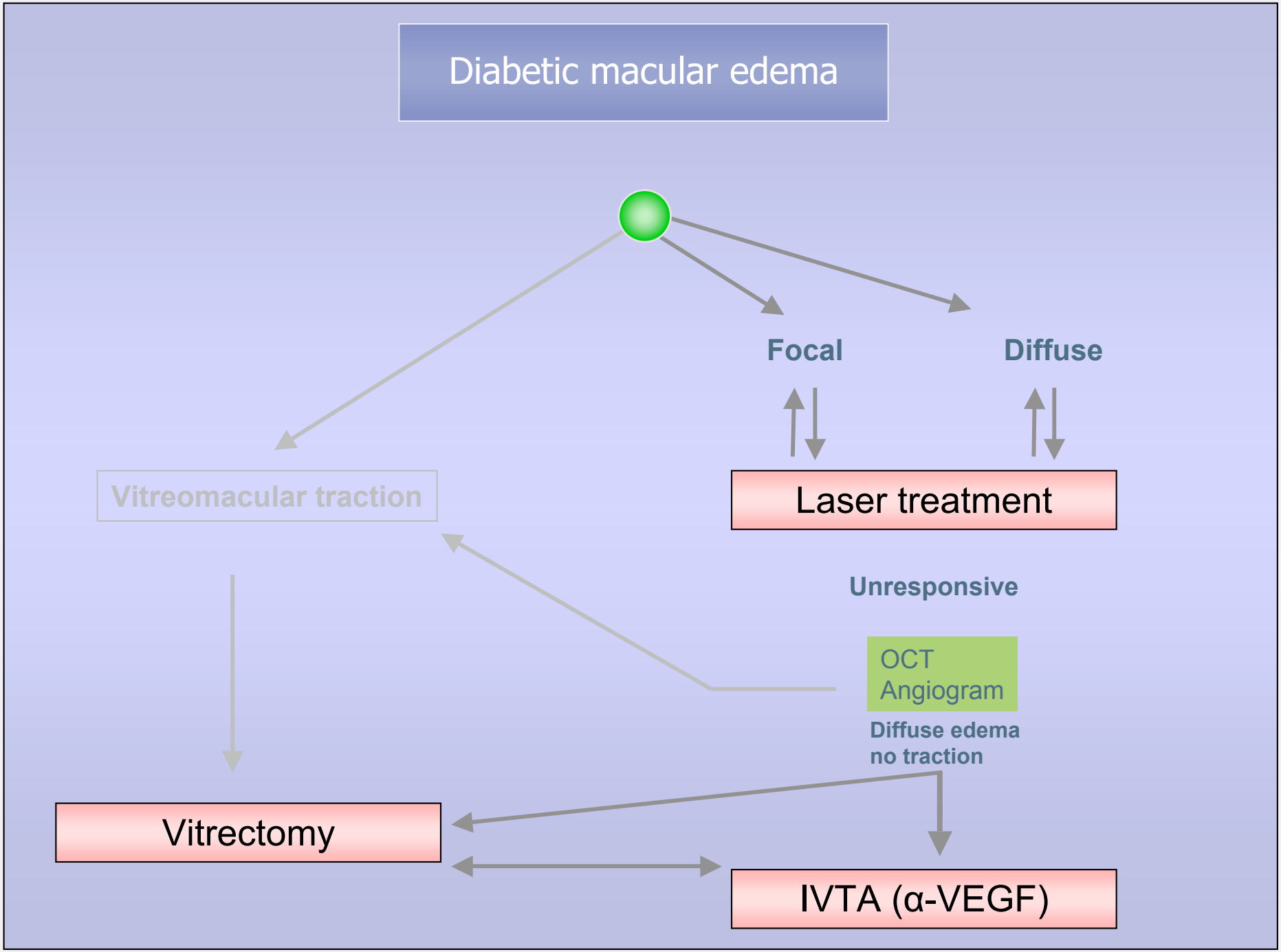

Diabetic macular edema
Vitreomacular traction
Vitrectomy


Diabetic macular edema
Angiogram
Focal
Diffuse
Vitreomacular traction
Laser treatment
Vitrectomy


Diabetic macular edema
Focal
Diffuse
Vitreomacular traction
Laser treatment
Vitrectomy
IVTA


Diabetic macular edema
Focal
Diffuse
Vitreomacular traction
Laser treatment
Unresponsive
OCT
Angiogram
Vitrectomy


Diabetic macular edema
Focal
Diffuse
Vitreomacular traction
Laser treatment
Unresponsive
OCT Angiogram
Diffuse edema no traction
Vitrectomy


Diabetic macular edema
Focal
Diffuse
Vitreomacular traction
Laser treatment
Unresponsive
OCT
Angiogram
Diffuse edema
no traction
Vitrectomy
IVTA (α-VEGF)


The End