Laser in Ophthalmology

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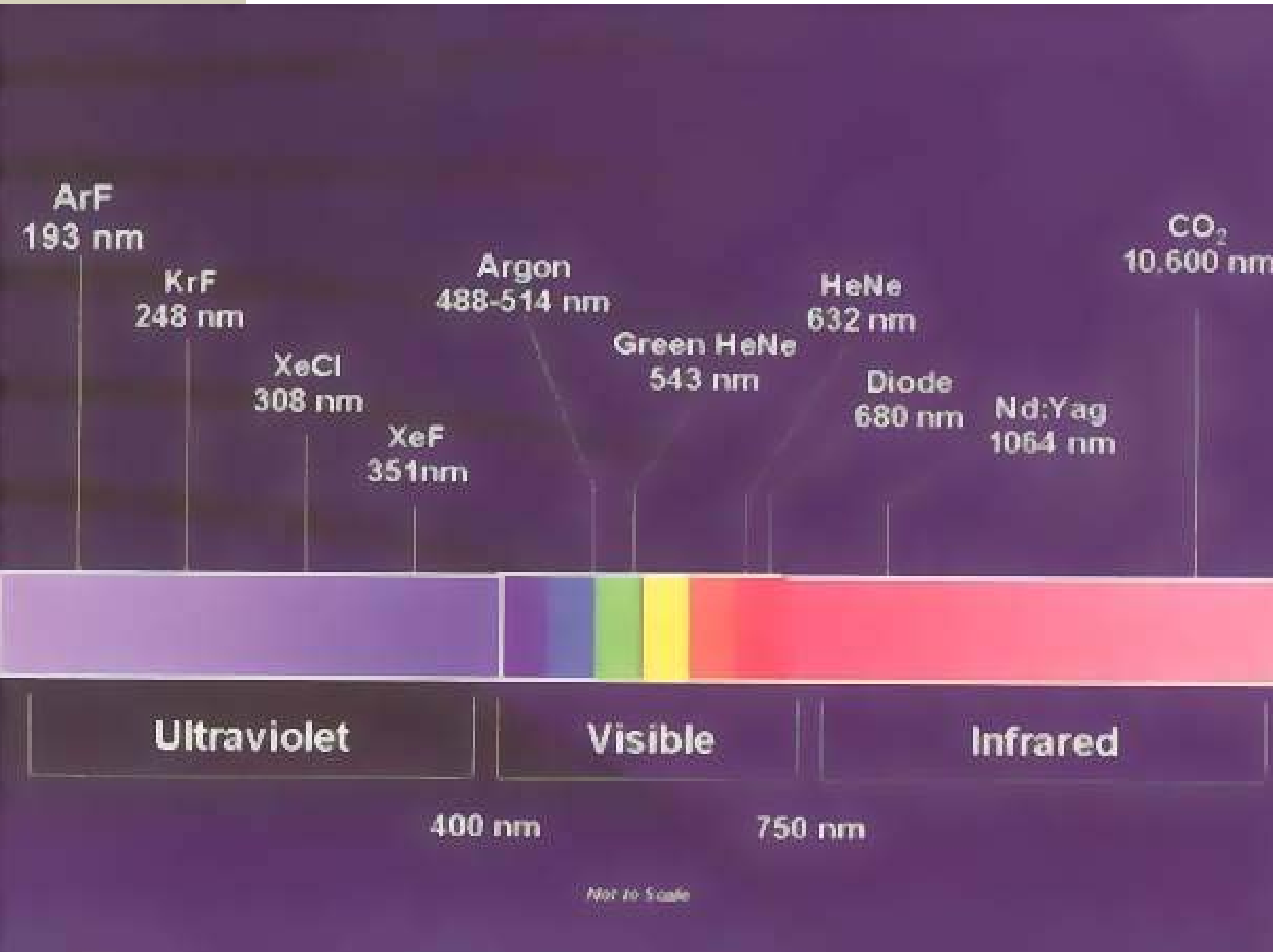
2004 3 29

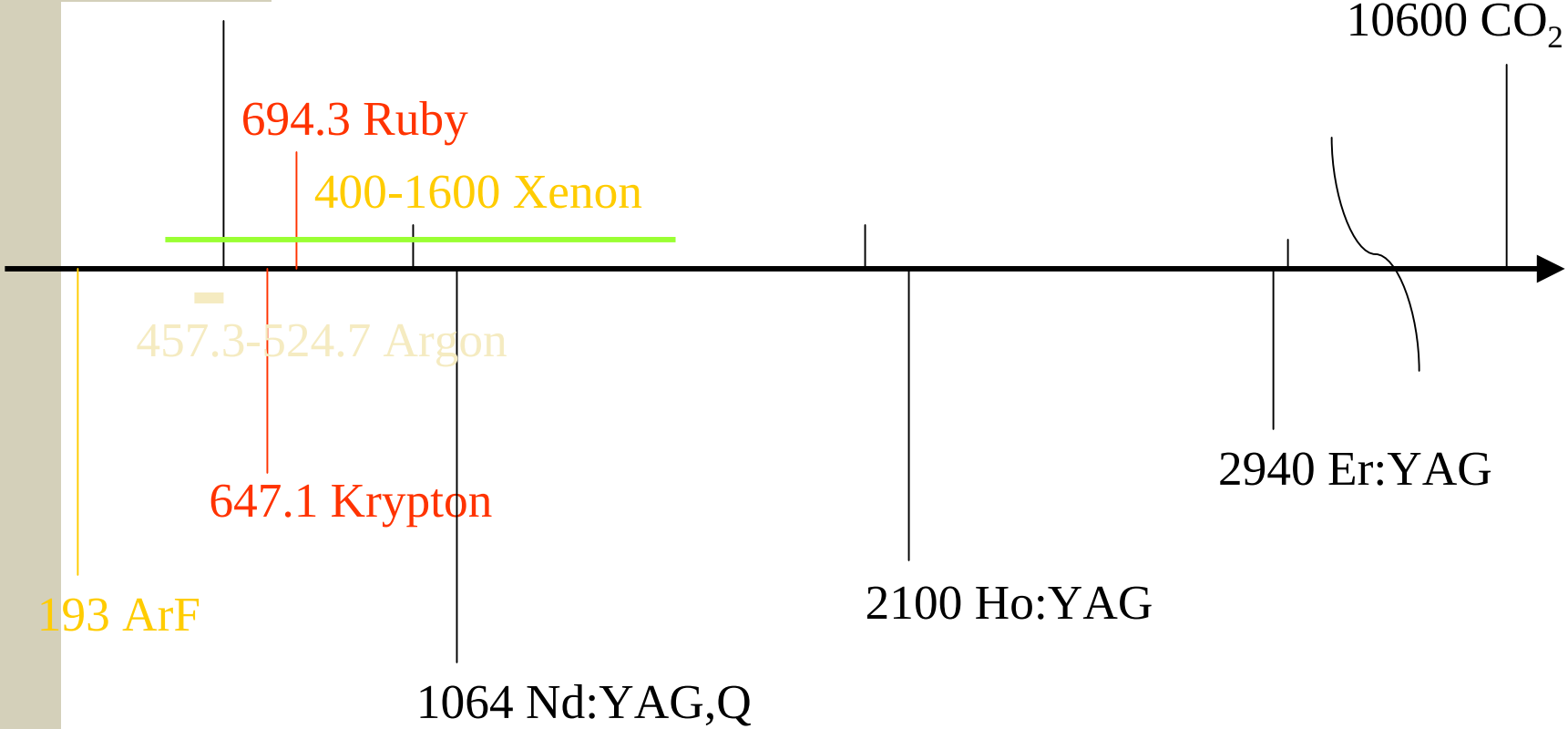
Introduction

- 1960 Maiman: Ruby laser
- 1960~1980 photocoagulation
  - eg; diabetic retinopathy, glaucoma
- Early 1980 photodisruption
- Recent phototablation→photochemical interaction, diagnostic laser

Different Laser applications in Ophthalmology

	Wave length (nm)
Xenon-arc system	400.0-1600
Ruby laser	694.3
Argon laser	457.3-524.7
Nd:YAG laser	
frequency doubled	532
Q-switched	1054
Krypton laser	647.1
Carbon dioxide laser	10600
Dye laser	multiple
Ho:YAG	2100
Er:YAG	2940
Excimer laser	193


ArF
193 nm
KrF
248 nm
XeCl
308 nm
XeF
351nm
Argon
488-514 nm
Green HeNe
543 nm
HeNe
632 nm
Diode
680 nm
Nd:Yag
1064 nm
CO_2
10.600 nm
Ultraviolet
Visible
Infrared
400 nm
750 nm
Not to Scale


532 Nd:YAG
10600 CO_2
694.3 Ruby
400-1600 Xenon
457.3-524.7 Argon
647.1 Krypton
193 ArF
1064 Nd:YAG,Q
2100 Ho:YAG
2940 Er:YAG

Laser tissue interactions

- Laser
  - Wavelength: $E=h\nu=hc/\lambda$
  - Duration
  - power
- Target
  - Absorbance, $A=\log[I_0/I(d)]=\varepsilon cd$
  - Transmission, $T(d)= 10 -A(d)=e^{-\alpha d}=10^{-2.3A}$

Laser tissue interaction

- Photothermal interaction
  - Photocoagulation, melting, carbonization, vaporization,
- Photoablation
- Optical breakdown
- Photochemical interaction
- Laser diagnostics
- Optical tweezers & optical scissors

Photothermal interaction

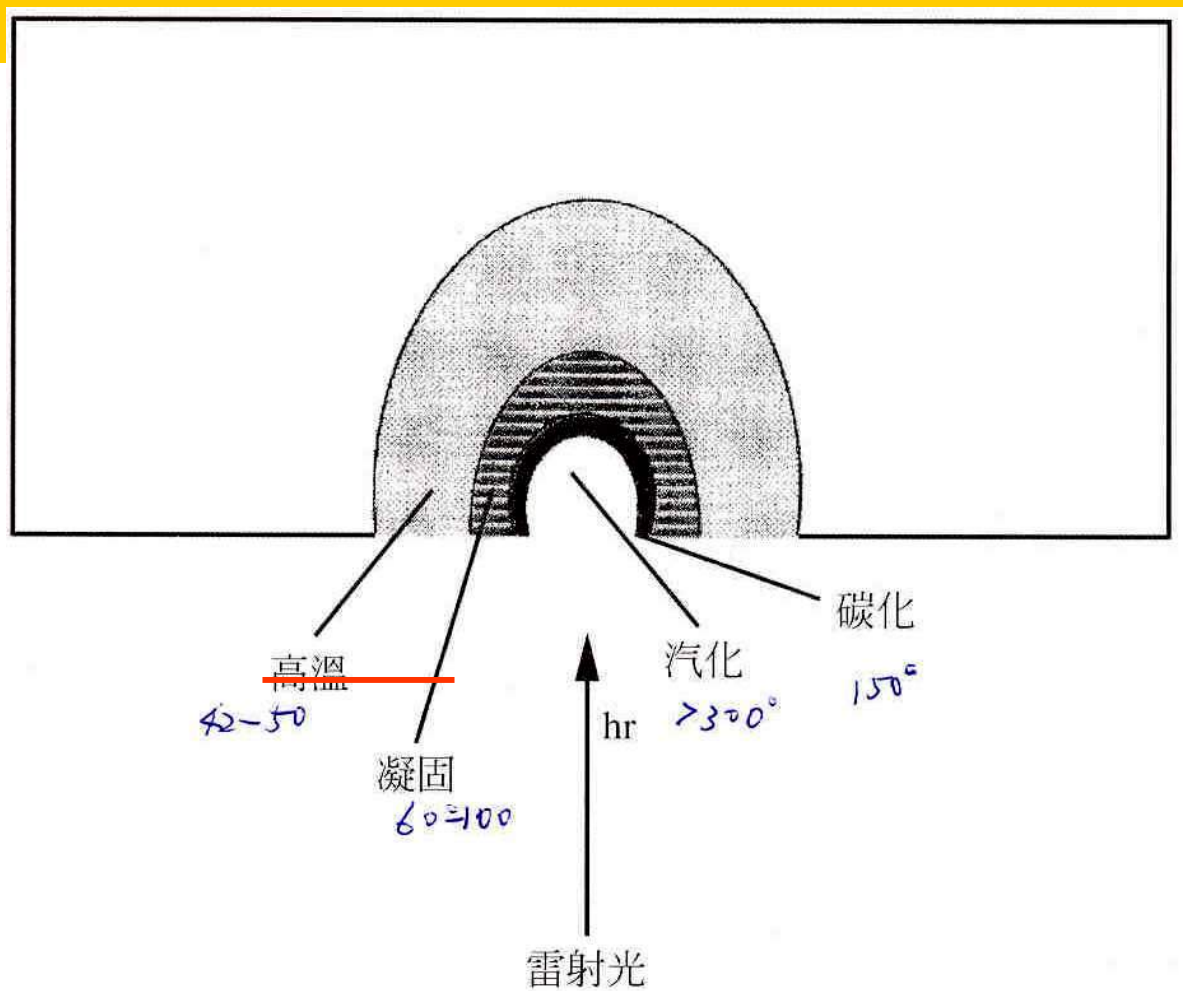


圖2-2：組織內部受到雷射照射後局部的熱效應變化

	Phtothermal interaction	photoablation	Plasma-induced ablation	Mechanical photodisuption
duration	1μs~1 min	10-100ns	100-500fs	100ns-100fs
Power density W/cm^2	$10\sim10^6$	10^7-10^{10}	10^{11}-10^{13}	10^{11}-10^{16}
kinds	Nd:YAG Er:YAG Ho:YAG Argon ion Diode lasers	Excimer lasers	Nd:YAG Nd:YLF Titanium:sapphire	Nd:YAG Nd:YLF Titanium:sapphire

Photocoagulation

- Non-laser photocoagulation
  - 1945 Meyer-Schwickerath : sunlight
  - 1956 Meyer-Schwickerath: xenon arc
- Laser photocoagulation
  - 1968 L'Esperance: argon laser
  - 1972 krypton laser
  - 1981 tunable laser
  - 1990~ diode laser

photocoagulation

- Duration: 100-200~500ms
- Power: mW
  - ↓ duration, ↑tissue rupture & hemorrhage
- Spot size: 50-500 μm
- Temperature
  - ↑ 10-20 °C: inactivation of enzymes, protein & nucleic acid denaturation→ necrosis, hemostasis, coagulation
  - ↑ ↑: water vaporization , gas bubble formation
  - ↑ 100 °C: loss of structure

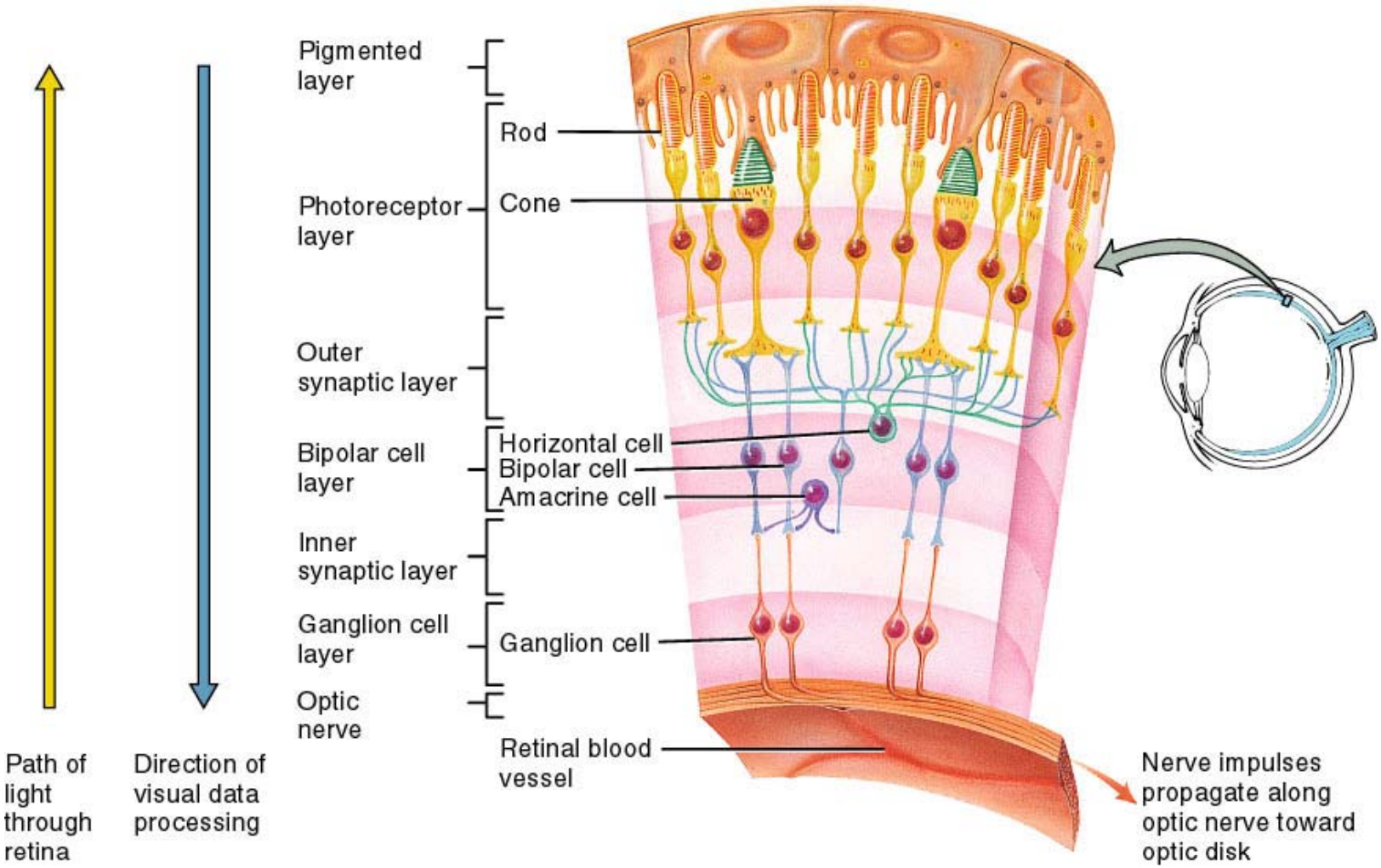
Principle wavelengths of common photocoagulation lasers

Laser	Wavelength(nm)
Argon(blue-green)	488.0
Argon(green)	514.5
Frequency doubled Nd:YAG	532.0
Krypton (yellow)	568.2
Krypton (red)	647.1
Tunable dye	Variable(most 570-630) depending on dye
Diode	Variable (most 780-850) depending on diode
Nd:YAG	1064

photocoagulation

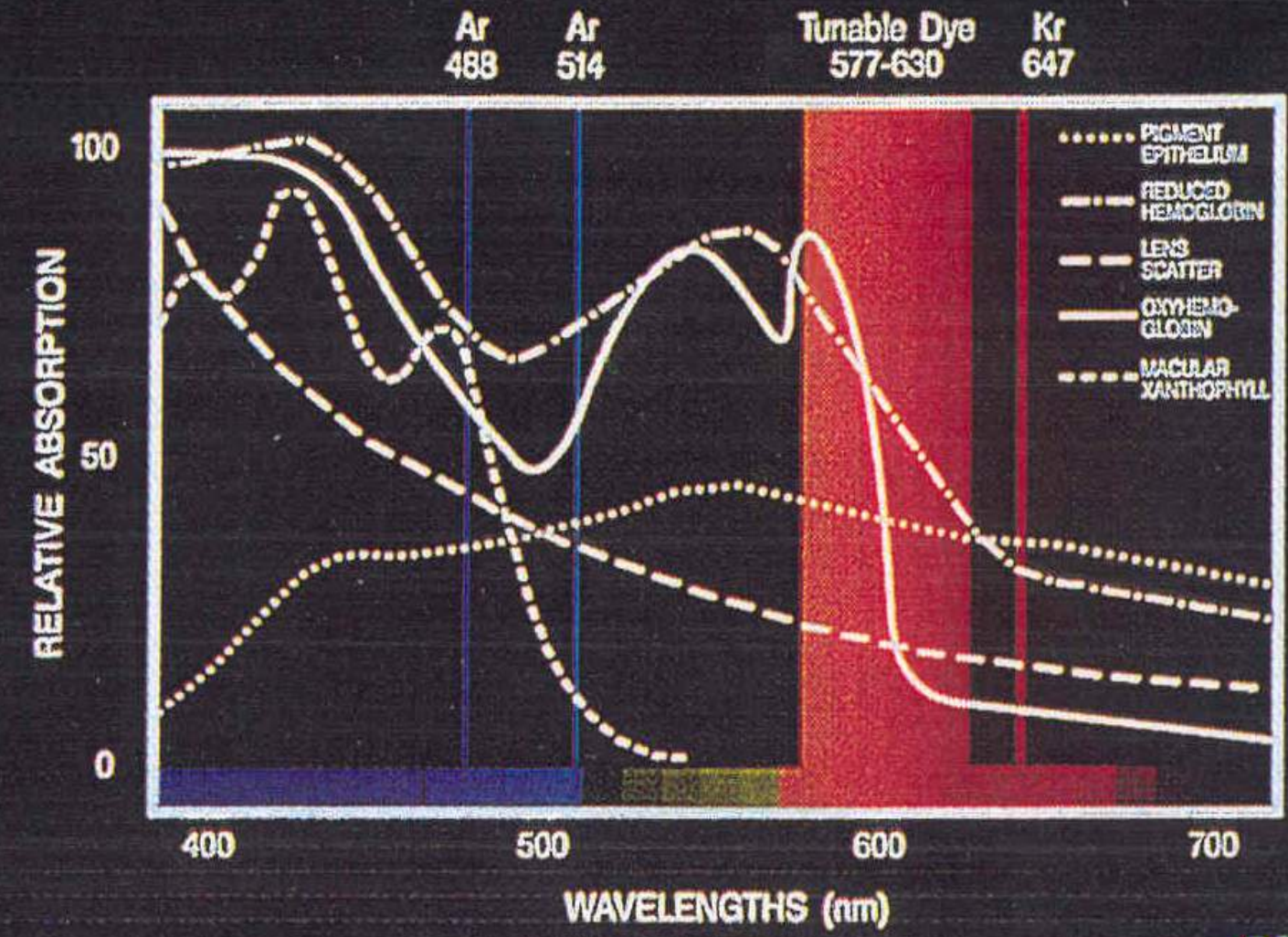
- Chromophore
  - Melanin: 400-700 nm
    - retinal pigment epithelium, uvea, trabecular meshwork
  - Xanthophyll
    - macula
    - Argon (green); 514.5 nm, minimal absorption
  - Hemoglobin
    - Shorter than red light: strong absorption, useful for blood vessel closure
    - Krypton red: absorption in RPE layer & choroid
      - ↑ discomfort, deep penetration, choroidal hemorrhage,

Fig. 16.09



16.09

LASER LIGHT IN OCULAR MEDIA



V

A

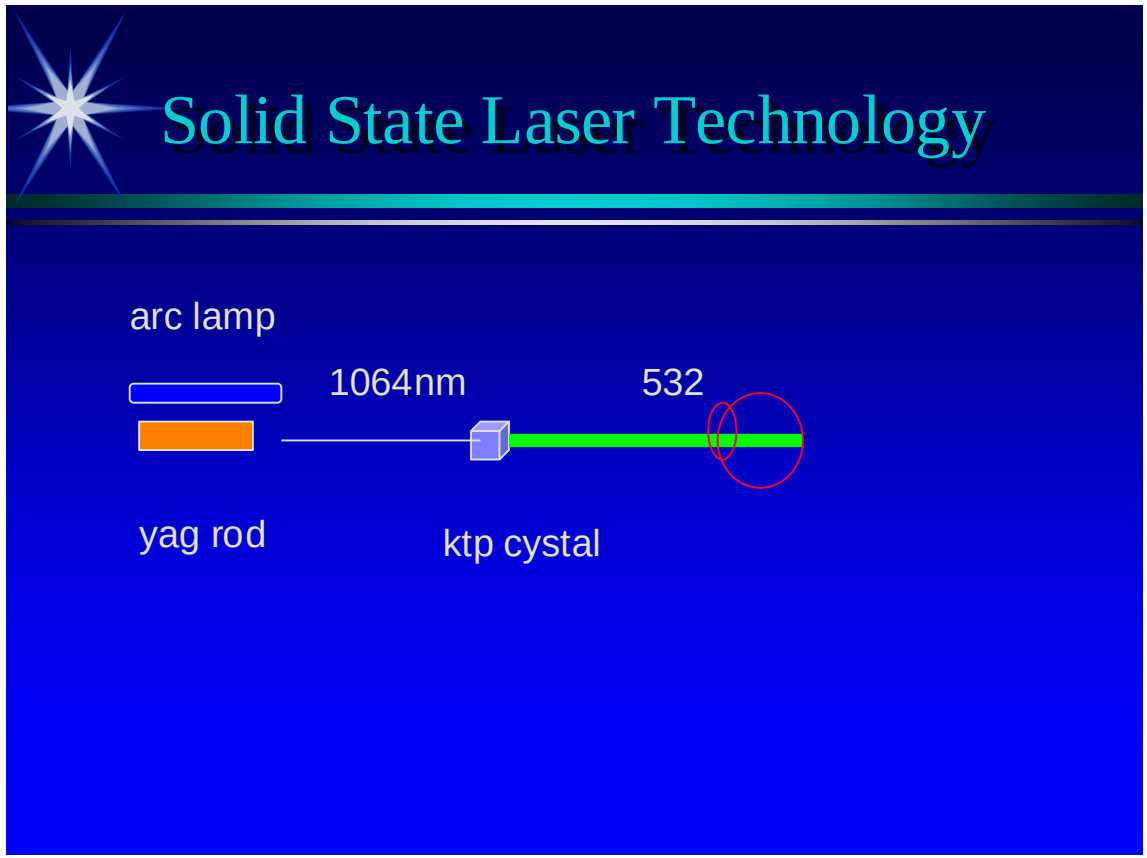
COHERENT

photocoagulation

- Nd:YAG laser
  - Radiation at 1064 nm
  - Deeper penetration
  - Lower absorption of melanin
  - Greater absorption by other the ocular media
  - Higher power needed

EyeLite 532 Laser

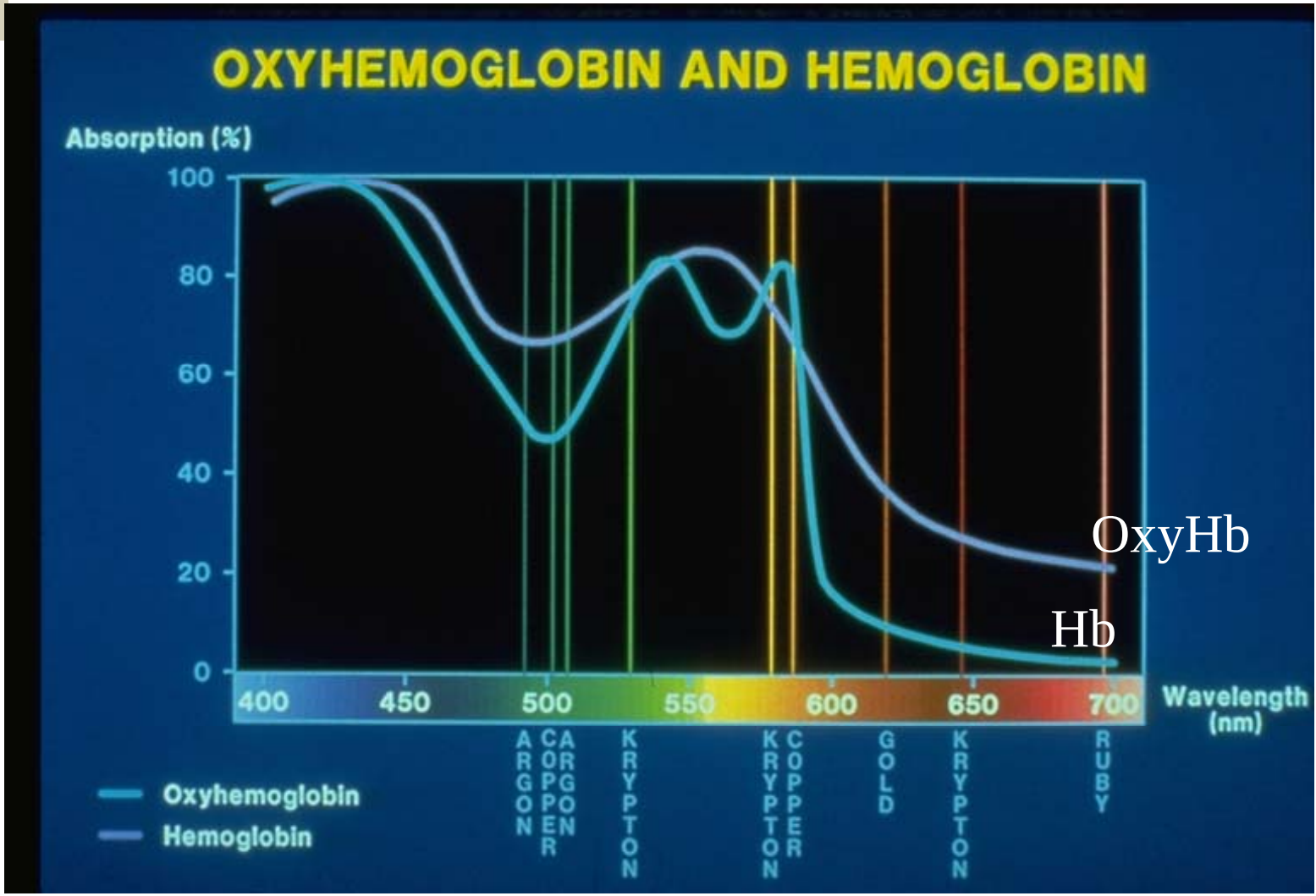
Diode pumped frequency doubled - YAG



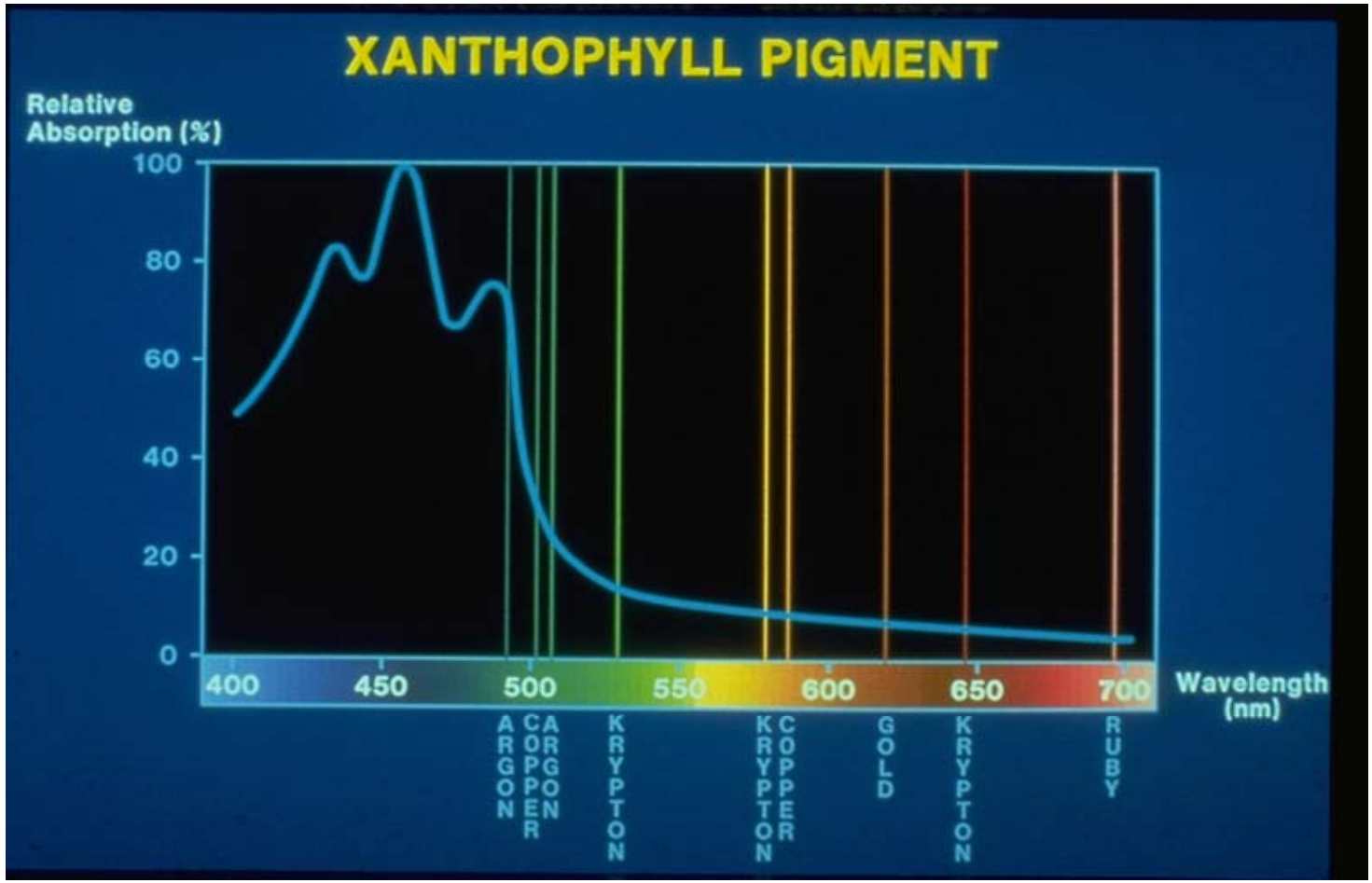
- DIODE PUMPED, FREQUENCY DOUBLED YAG TECHNOLOGY
  二極體激發光源及倍頻雅格雷射技術
  更有效率的雷射激發
  更低的熱能損耗
  更長的雷射管壽命
- THERMAL ELECTRIC COOLER
  半導體電子式冷卻系統(TEC)
  不再使用液體冷卻系統==>節省空間
  更有效率的帶走熱能==>節省電能
  不再需要任何調整==>節省保養時間
- 532 nanometer 波長
- 連續波輸出, CW
- 臨床測試中性質與argon laser相似但擁有532 nm吸收特性優點

- 532 Laser在血紅素的吸收比514 Laser還好==>凝結效果好 (30- 50 % less power required)
- 532 Laser 在Xanthophyll的吸收比514 Laser還低==>Pigment傷害低
- 532 nm波長接近於550 nm之黑色素吸收效果==>較少能量需求於chorioretinal效果.
- PULSE REPEAT MODE
  Nine shots per second
  (≤100 ms exposure time)
- 治療效果好

Greater absorption in hemoglobin



Lesser absorption in xanthophyll



純 綠 光 (532nm)與 Argon laser 比較

- 優 點
  - 對血紅素較佳的吸收率(只需較低能量)
  - 對葉黃素較低的吸收率(減低對黃斑部的熱效應)
  - 波長很接近550nm(黑色素吸收長)(只須較低能量就能達到視網膜脈絡膜附著)
  - 雷射儀體積小,單相電壓提供,於維修上更方便
- 缺 點
  - 對視覺介質比黃光或紅光有較高的吸收率
  - 於白內障,血液及模糊的介質比黃或紅光較難使用

- **Laser Wavelength:** 532 nm
- **Laser Power**
  - 30 mW~1.7 Watts minimum at cornea - Slit Lamp mode
  - 50 mW~1.7 Watts minimum at cornea - ENDO mode
  - 100 mW~1.7 Watts minimum at cornea - LIO mode
- **Spot Size:** 50 - 1000 microns
- **Exposure Time (in seconds)**
  - 0.01 - 0.02 -0.05 - 0.1 - 0.15 - 0.2 - 0.25 - 0.3 - 0.4 - 0.5 - 0.7 -1.0 -1.5 -2.0
- **Repeat Interval**

  0.1 - 1.0 seconds in 0.1 second increments

photocoagulation

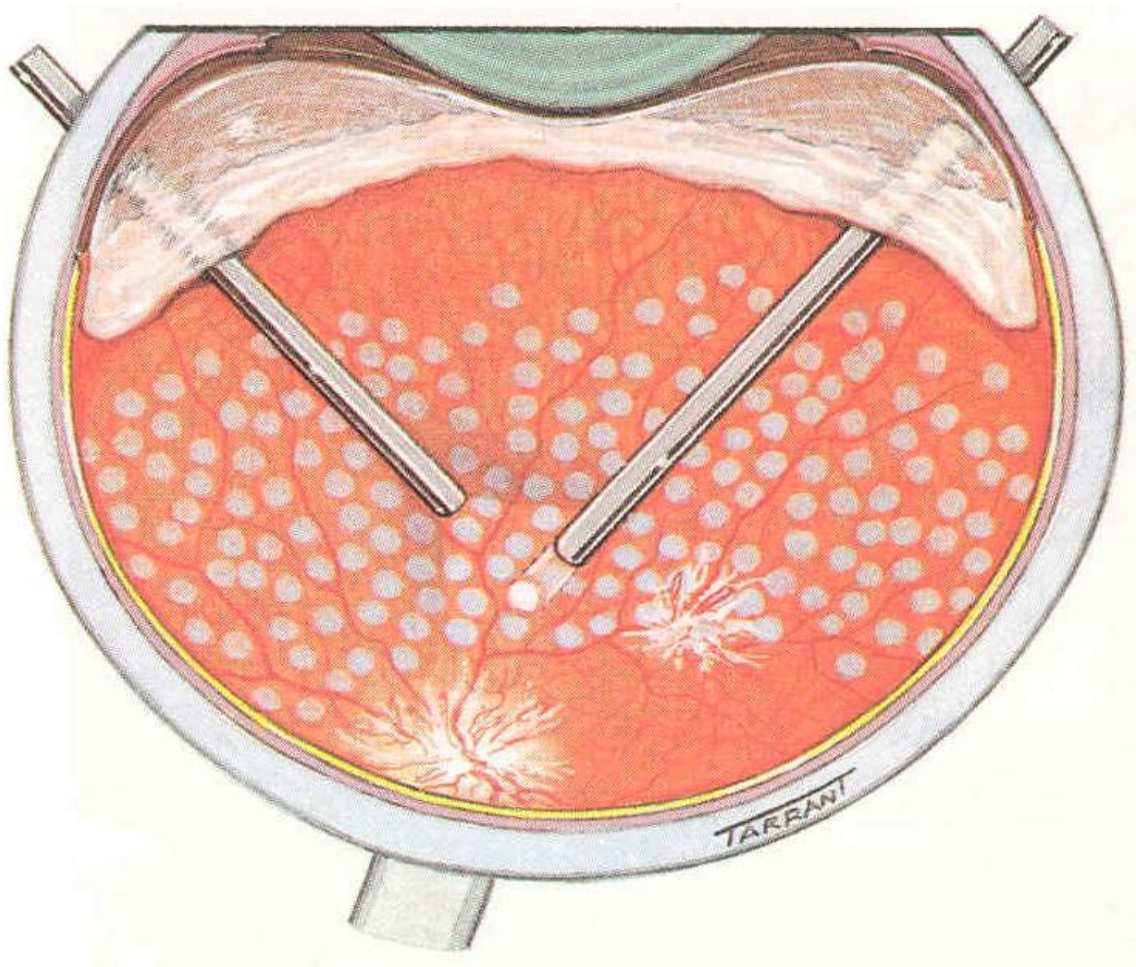
- Tunable dye laser
  - Pumped by other lasers
  - Select the desired wavelength
  - Most: 560-640 nm---argon laser
  - 560-580 nm: Targeted melanin and Hb:
  - 610-640 nm: RPE and choroidal melanin:
  - orange light 580-610nm:
    - RPE and underlying neovasculizaton
    - Retinal or vascular tumors

photocoagulation

- Diode laser
  - Emit between 780-810 nm (commercial 810 nm)
  - 優點
    - Exceptional electrical to optical efficiency
    - Smaller, less expensive, more portable lasers
    - Deeper penetration, through macular edema
    - Transmission through cataract, hemorrhage
    - Lesions similar to those with Krypton red light 647 nm
  - 缺點
    - More energy, more irradiance and exposure time
    - Limited peripheral treatment
    - More discomfort

- Laser indirect ophthalmoloscopy
  - Spot size不易標準化
  - Useful for far peripheral treatment eg: ROP
- Endophotocoagulation system
  - Histological damage limited to outer retina
  - Mild burn: outer nuclear layer
  - Moderate burn: inner nuclear layer
  - Severe burn: ganglion cell loss, scarring
- Transscleral retinal photocoagulation
  - Retinal photocoagulation
  - cyclophotocoagulation

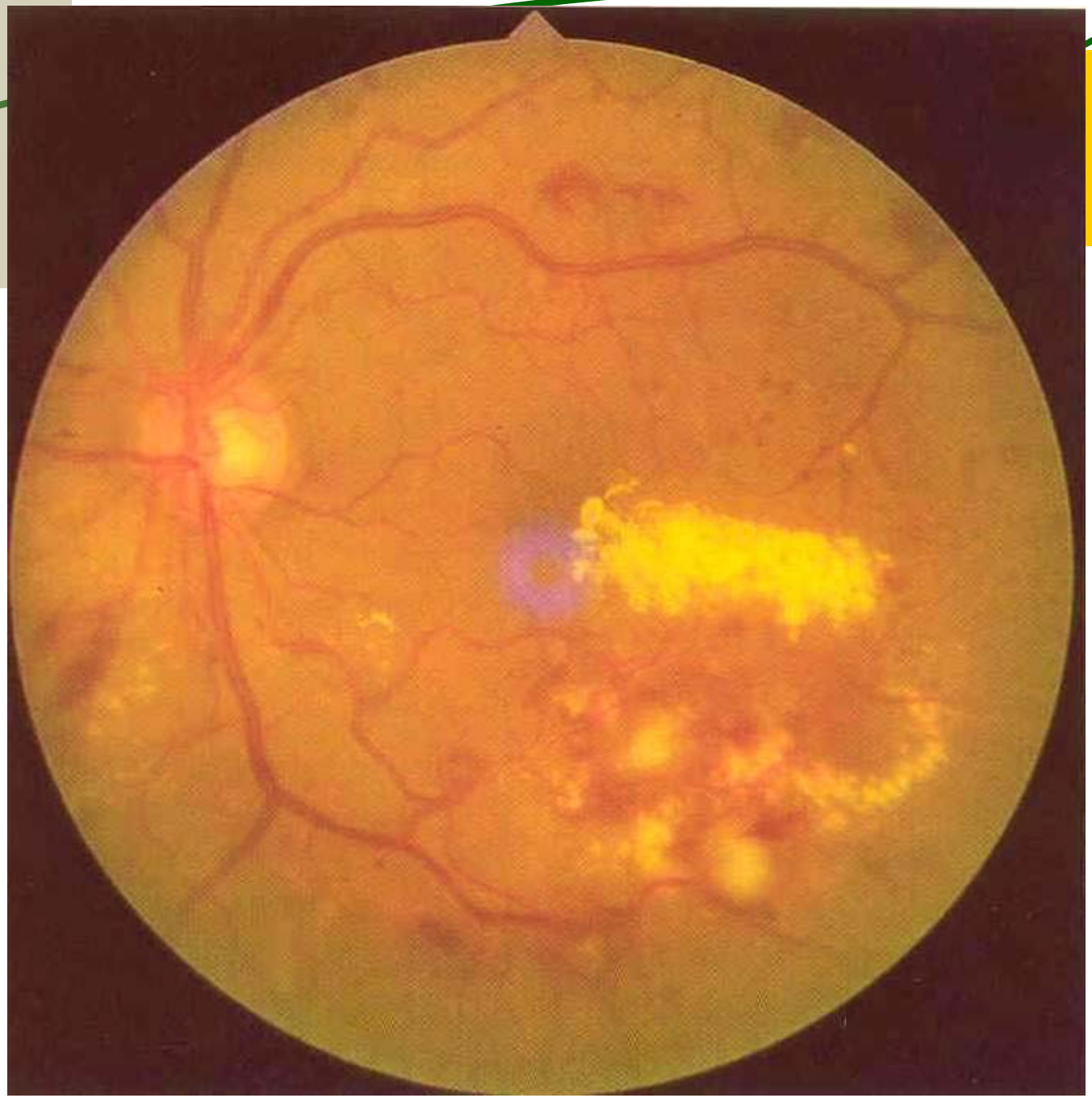
endophotocoagulation

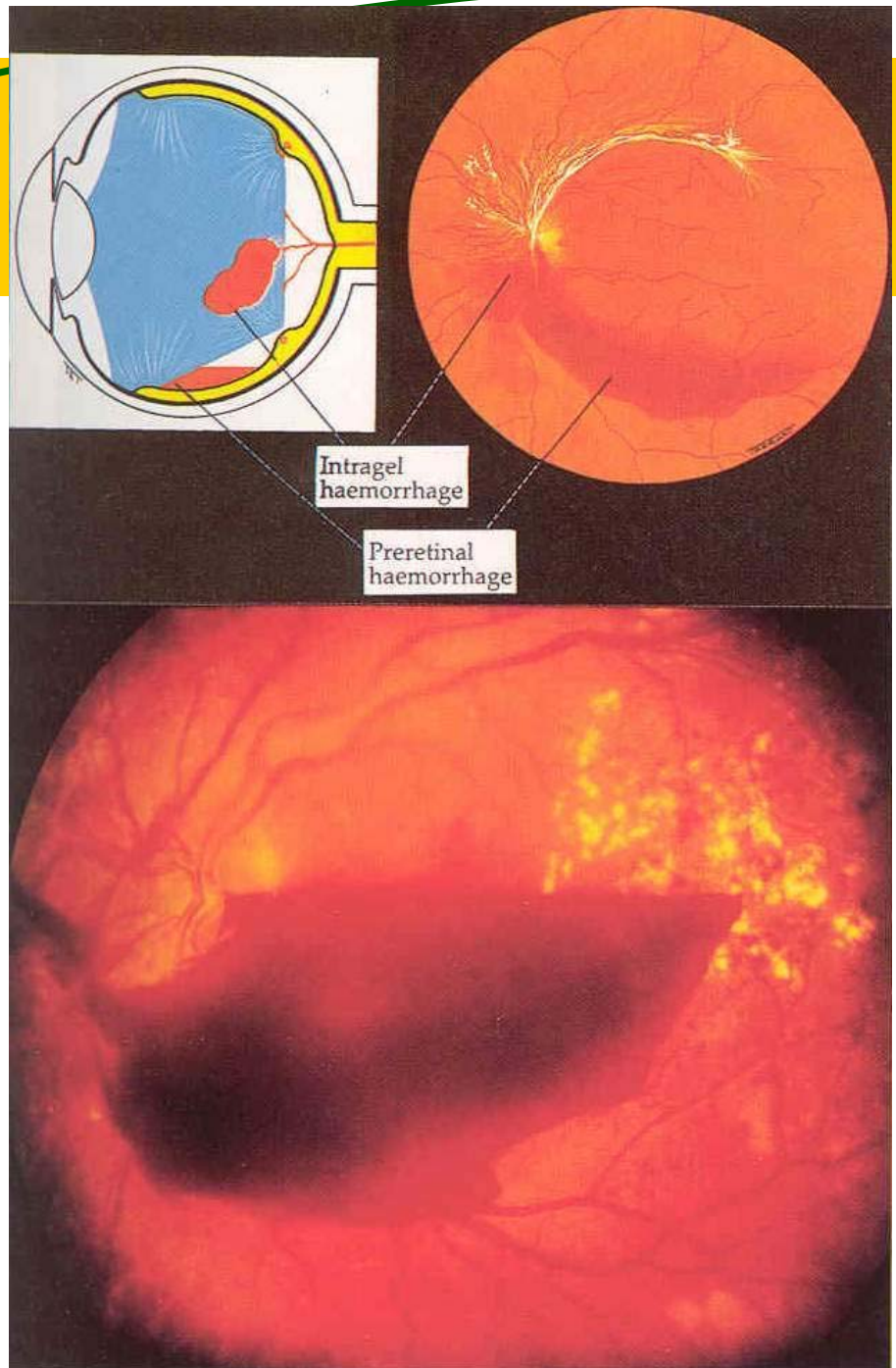


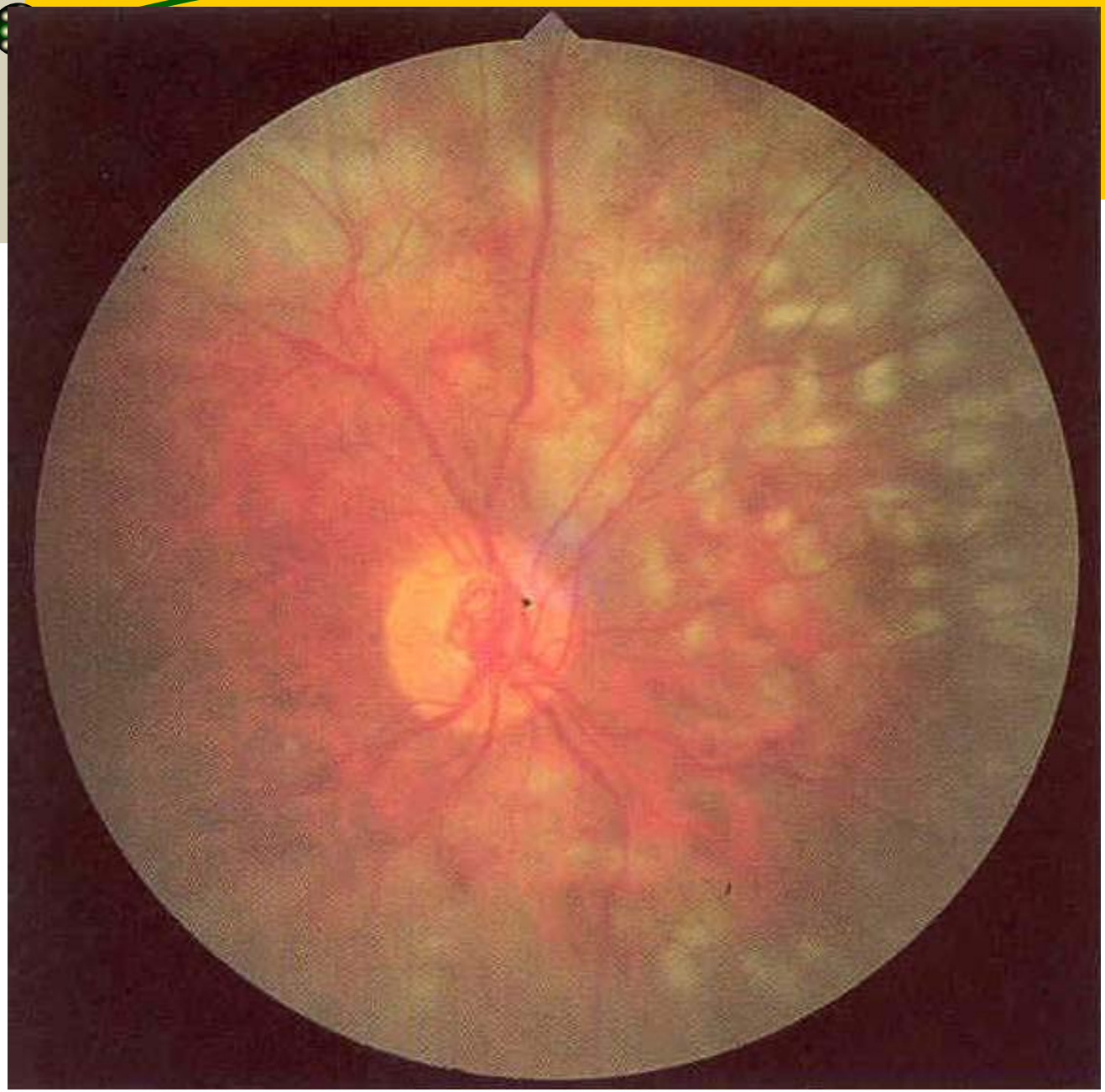
Photocoagulation

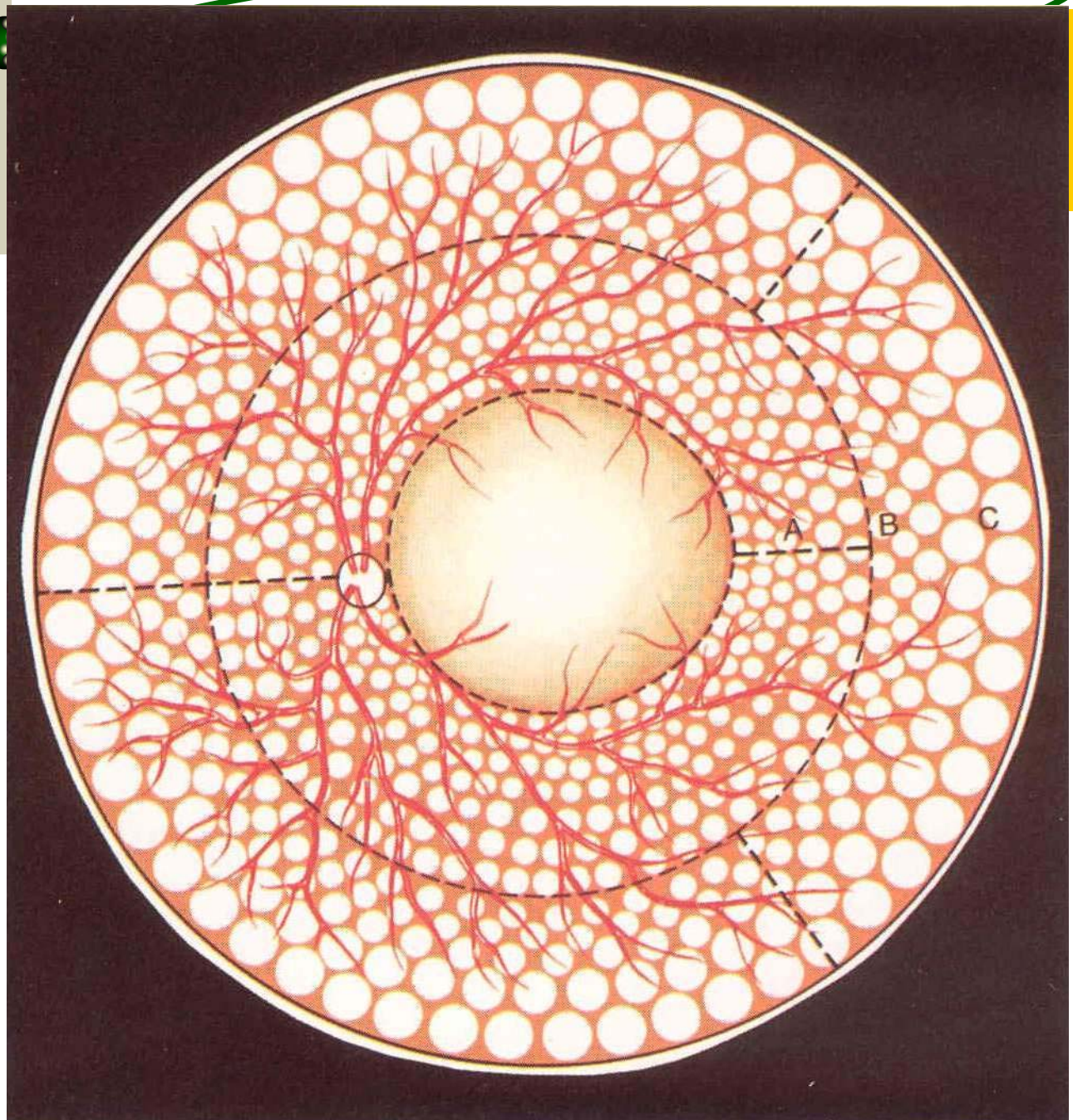
- Clinical applications
  - Diabetic retinopathy
  - Retinal vein occlusion
  - Macular degeneration
  - Focal Retinal detachment
  - Retinopathy of prematurity
  - Glaucoma
  - Oculoplastic surgery: trichiasis, capillary hemangioma
  - Ophthalmic oncology

- Diabetic retinopathy
  - Early proliferative diabetic retinopathy (PDR)
  - Panretinal photocoagulation(PRP)
    - Targeting of neovascular elements
    - Destruction of hypoxic retina
    - Improved oxygen diffusion
      - Creating tighter adhesion to choriocapillaries
    - Decreased vasoproliferative tendencies




Intragel haemorrhage
Preretinal haemorrhage



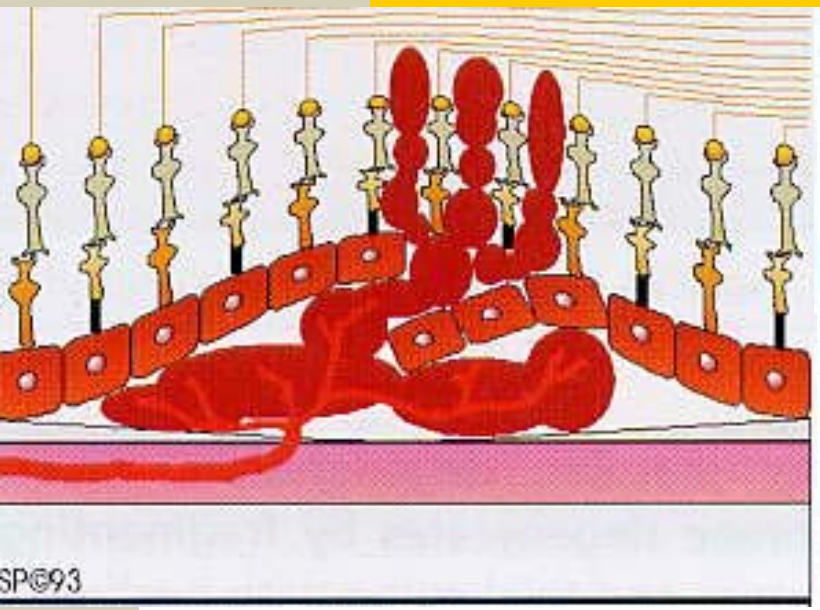

A
B
C

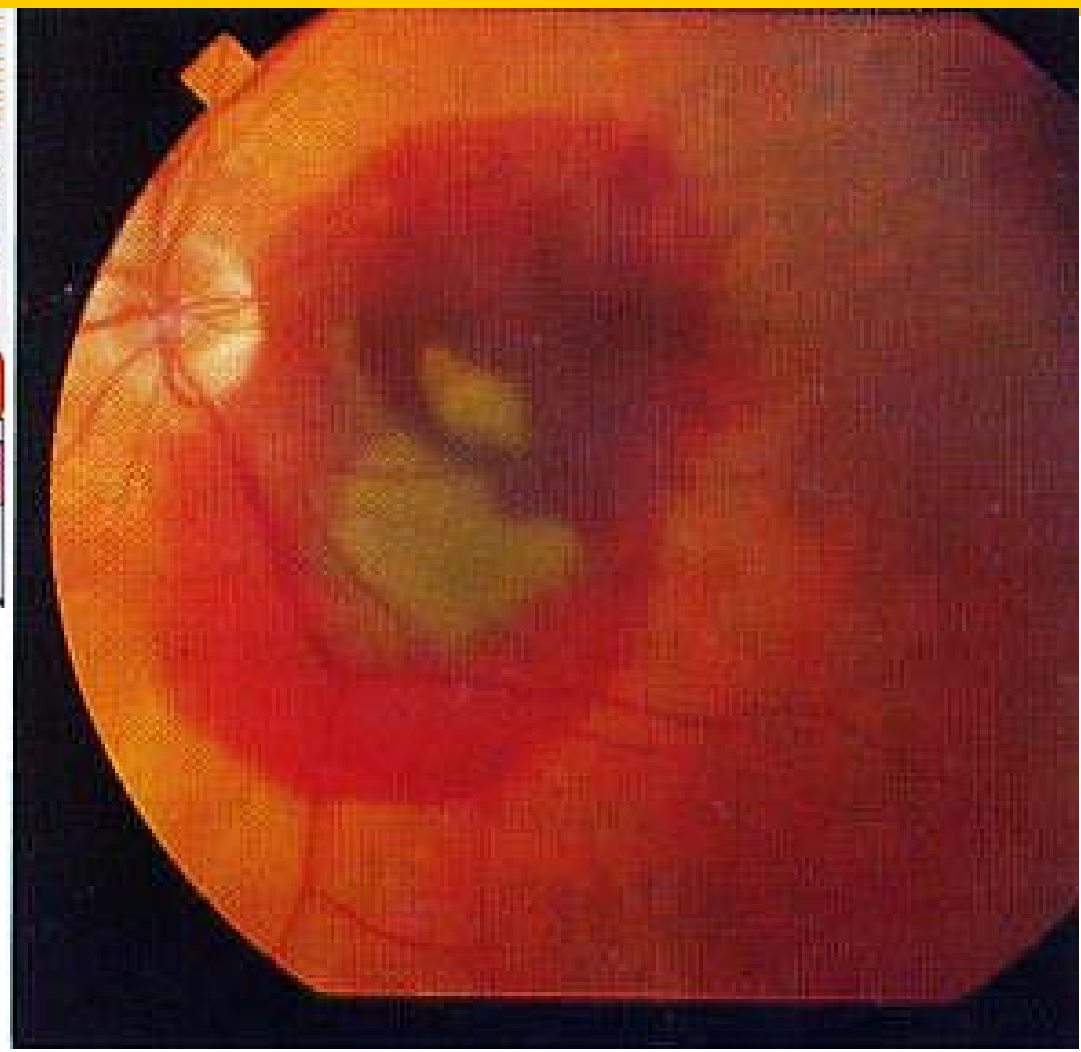
- Macular edema
  - The most common manifestation of DR
  - Treated with focal or grid laser
    - Preventing fluid passage from subretinal space through the RPE
    - Sealing leaking microaneurysms or capillaries
    - Damaged RPE (?)
      - Reduction of blood flow, ↑inner retinal oxygen, replacement of coagulated RPE, proliferation of endothelial cell (capillaries, venules), ↑ blood retinal barriers

Central retinal vein occlusion

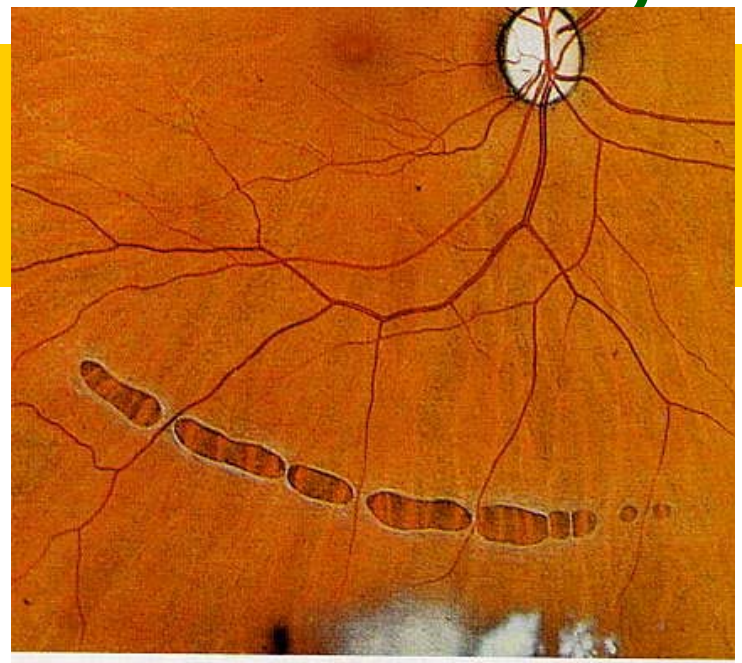
- Aged related macular degeneration (ARMD)
  - Heated-induced closure of the new vessels
  - Release of angiogenesis-inhibiting factors
  - Seals breaks in Bruch’s membrane

Macular degeneration with Subretinal vascularization

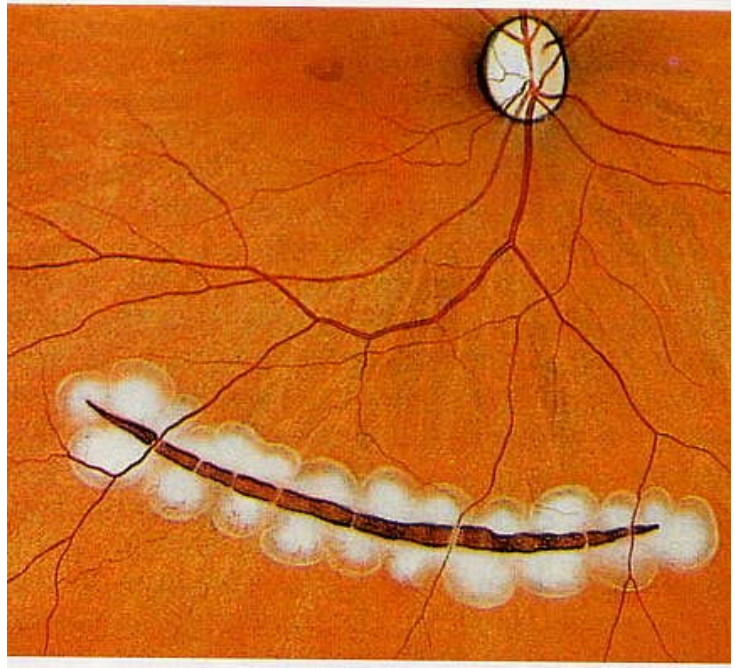


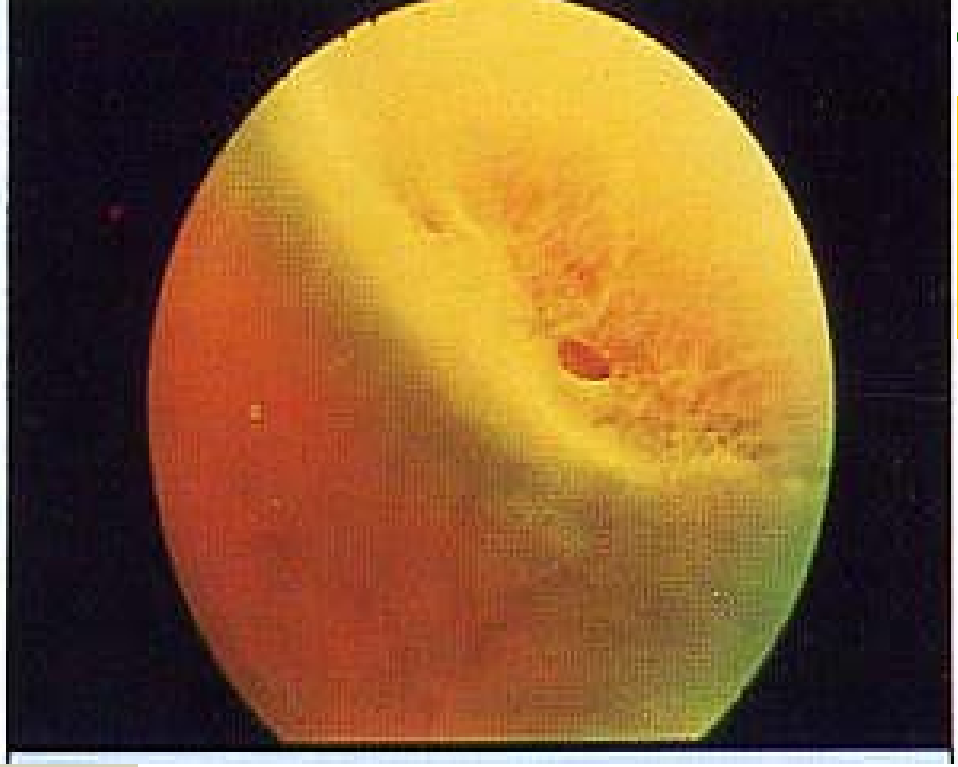


Retinal holes

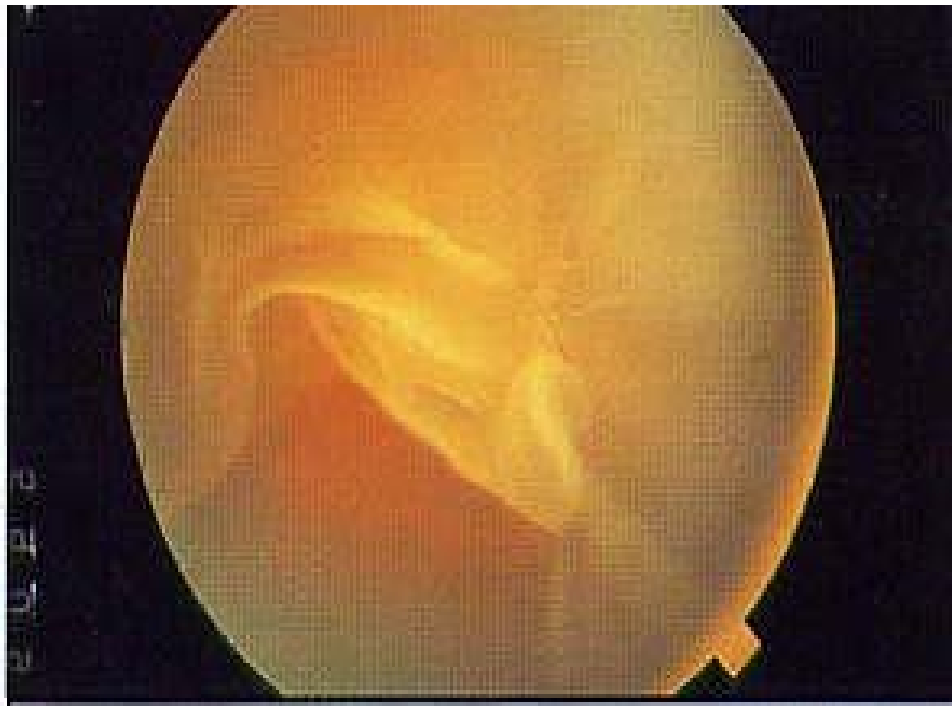


Prophylatic photocoagulation

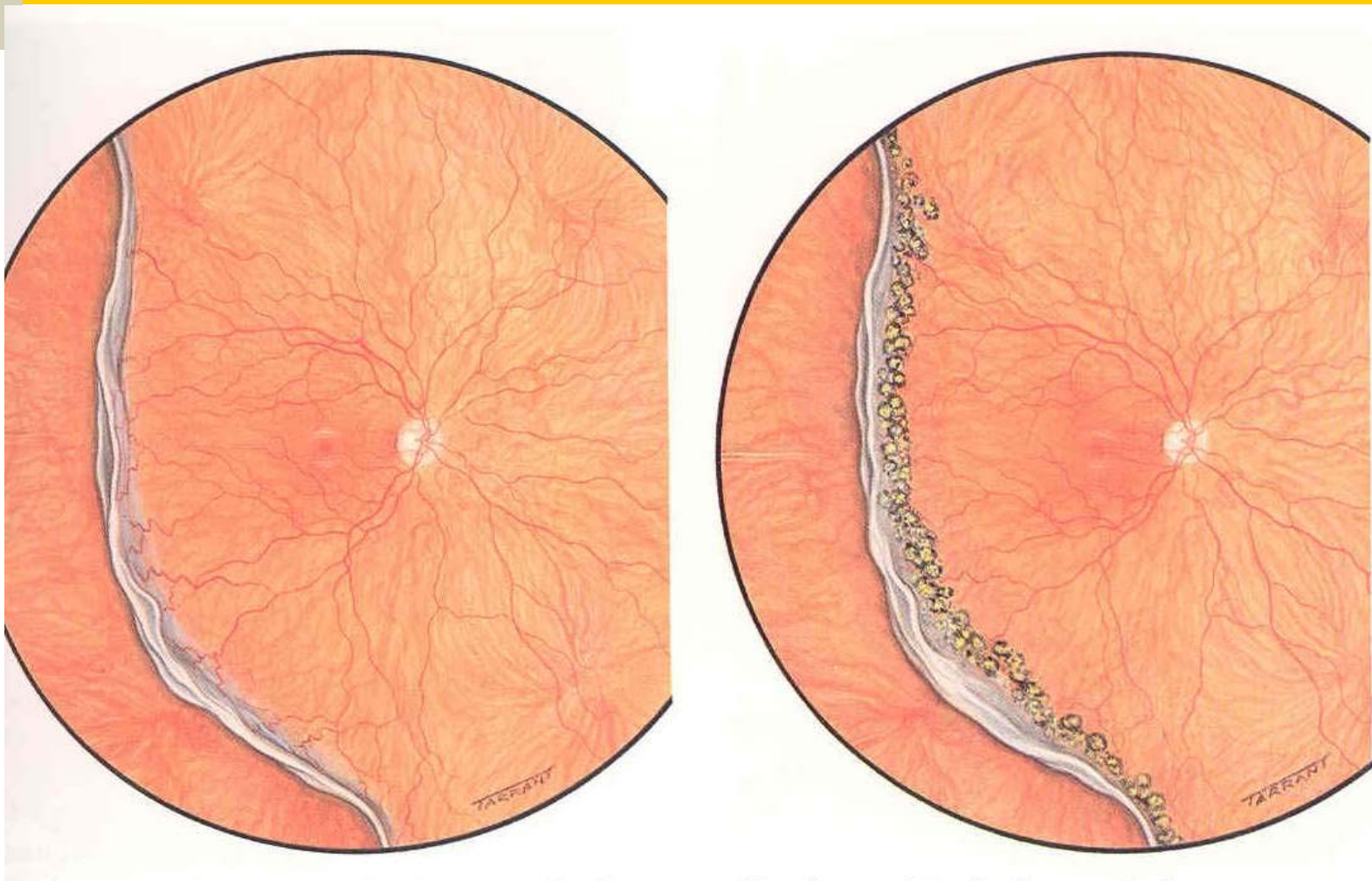




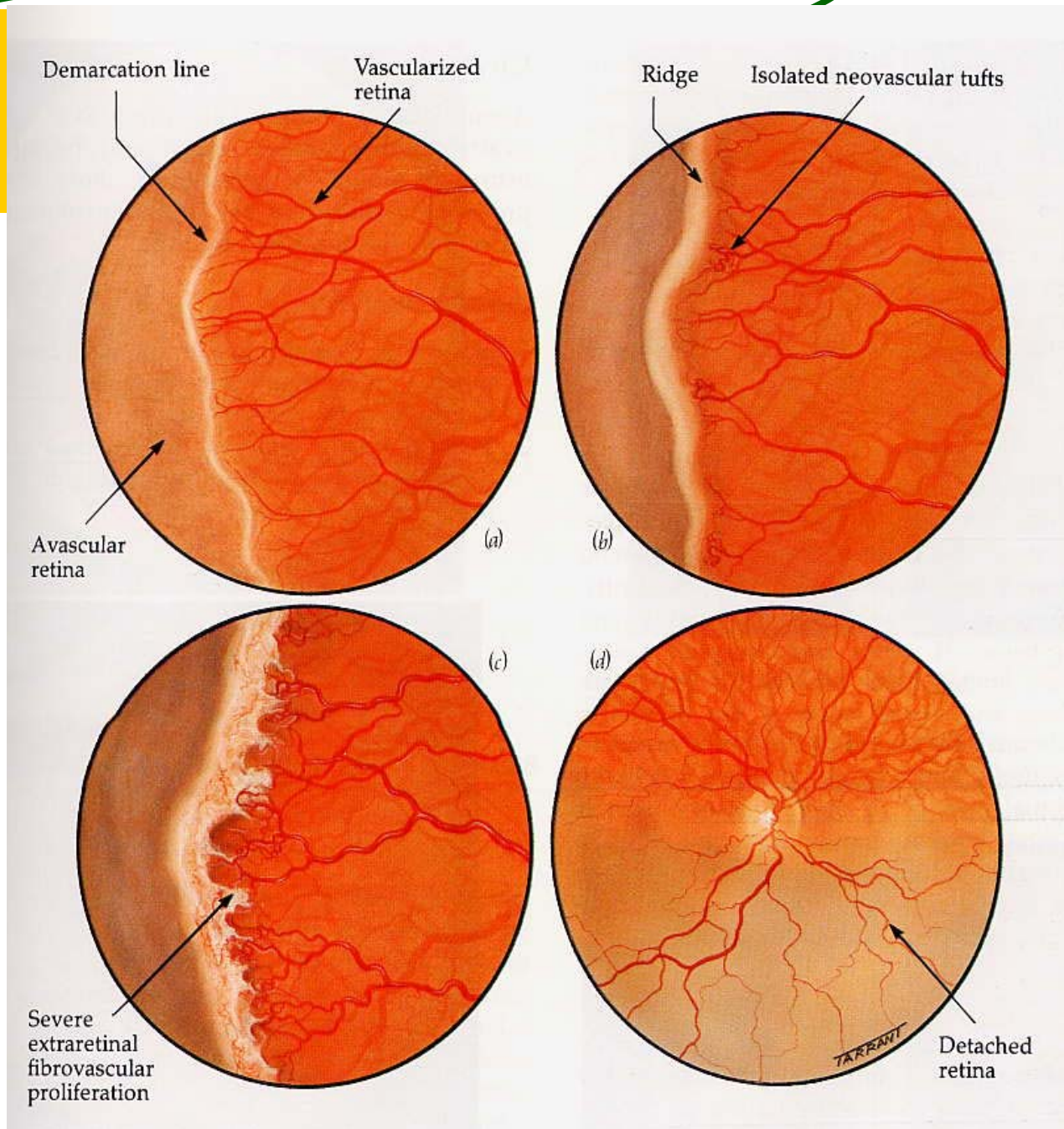
Retinal detachment

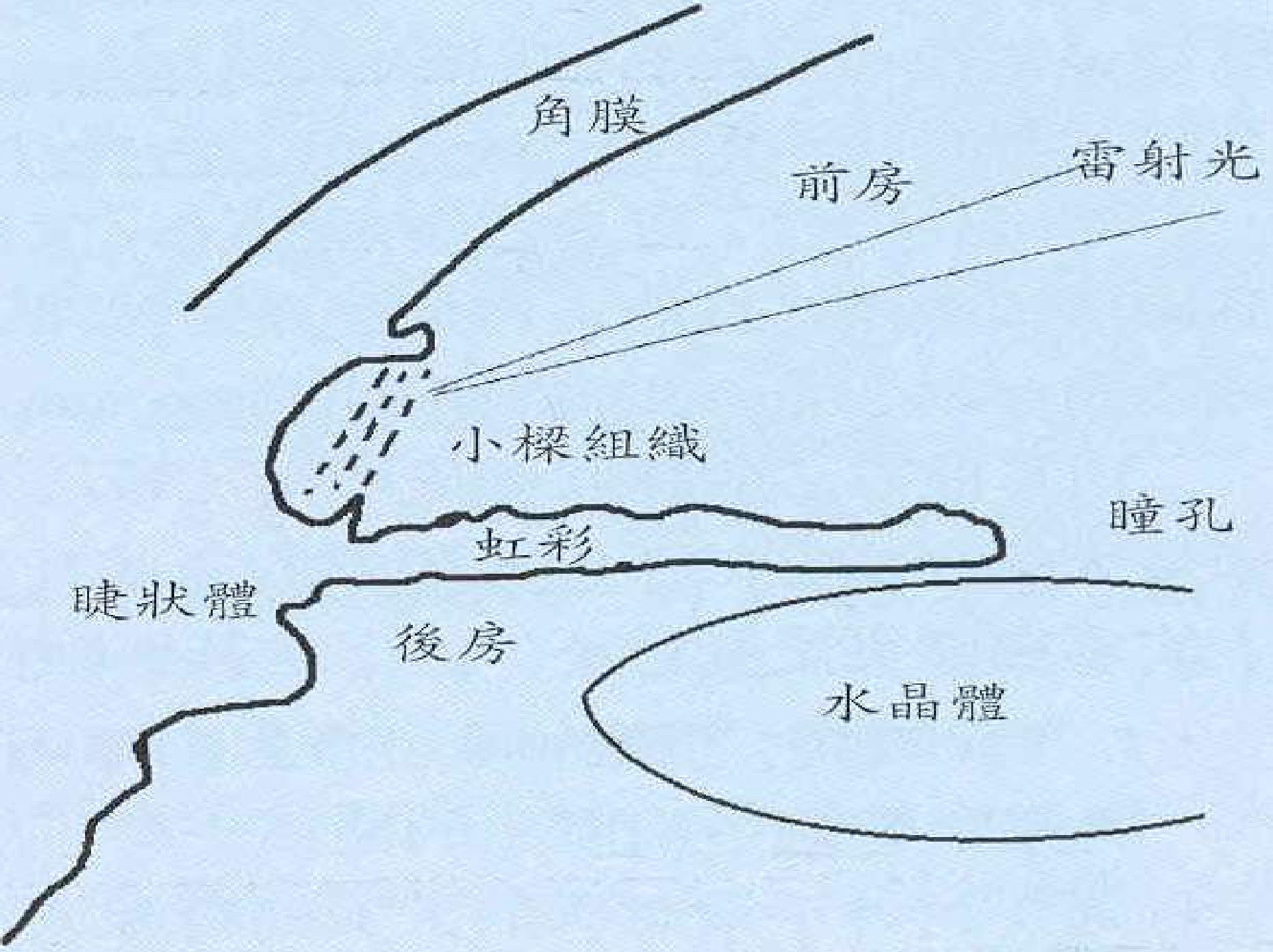


Retinal dialysis caused by blunt trauma



Retinopathy of prematurity (ROP)




角膜
前房
雷射光
小樑組織
瞳孔
虹彩
睫狀體
後房
水晶體

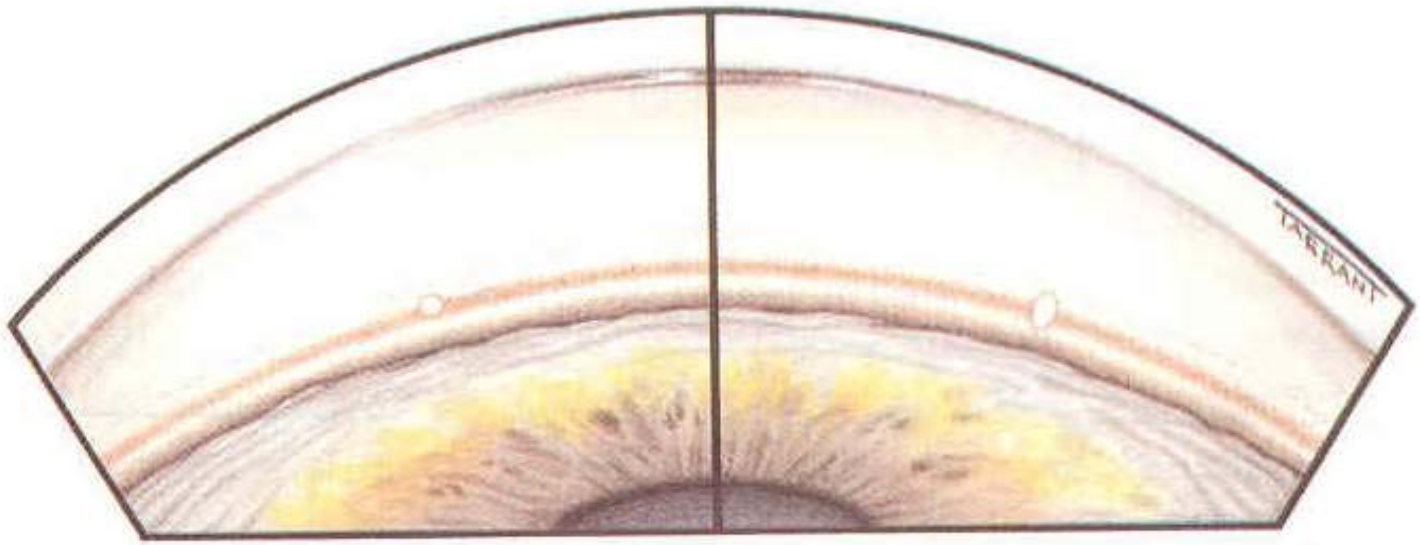


Figure 8.57 Argon laser trabeculoplasty. Left: correct focus with round aiming beam; right: incorrect focus with oval aiming beam

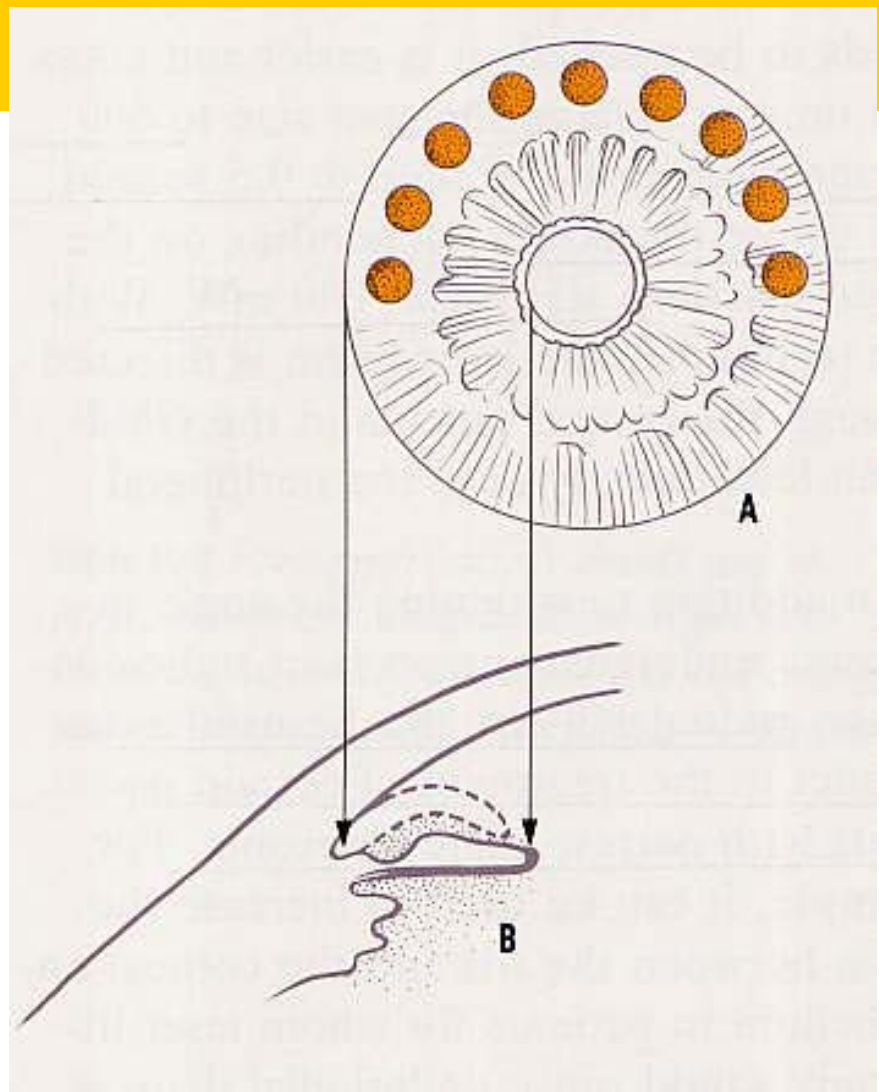
Laser trabeculopasty (ALT)

- argon or diode lasers
- shrinking the superfical collagen of trabecular work
- biochemical changes: phagocytic action
- 800-1200mW × 0.2s ×100μm × 50 burs/180º

Peripheral iridoplasty

200 mW × 0.2 s ×200μm

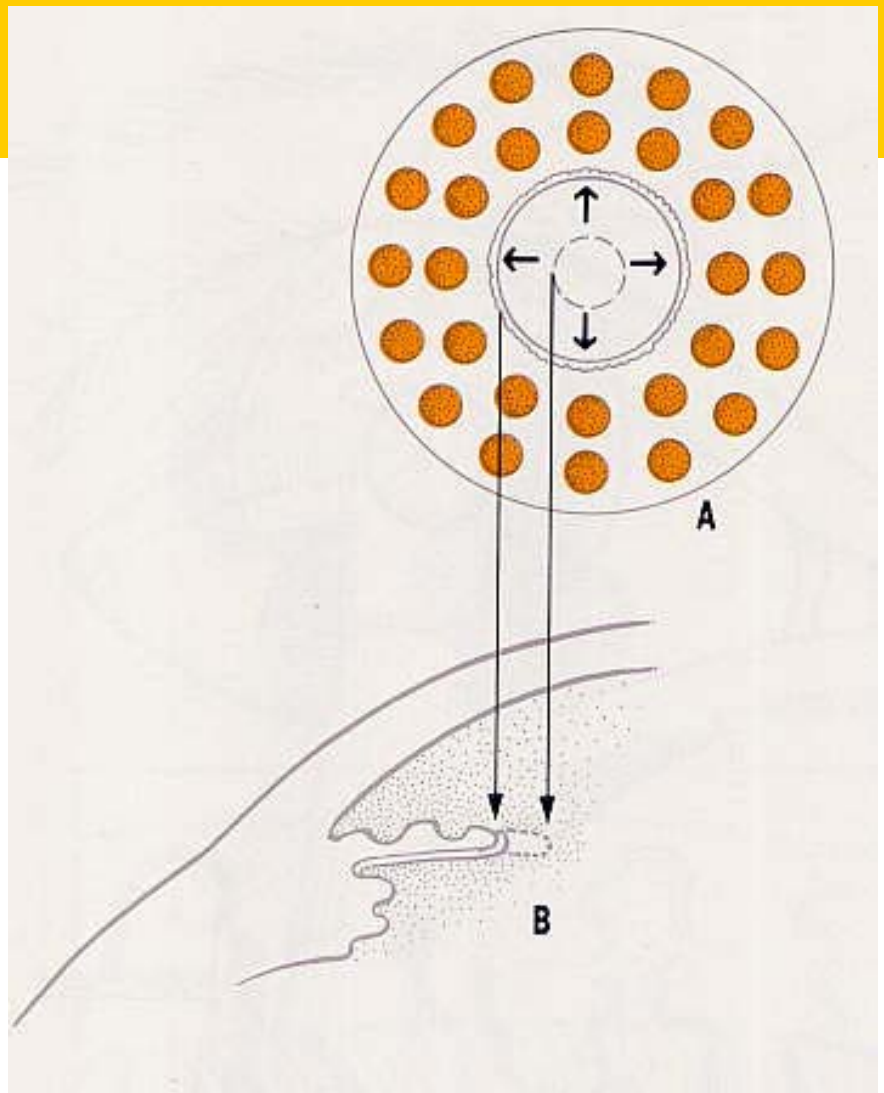
200 mW × 0.5 s ×500μm



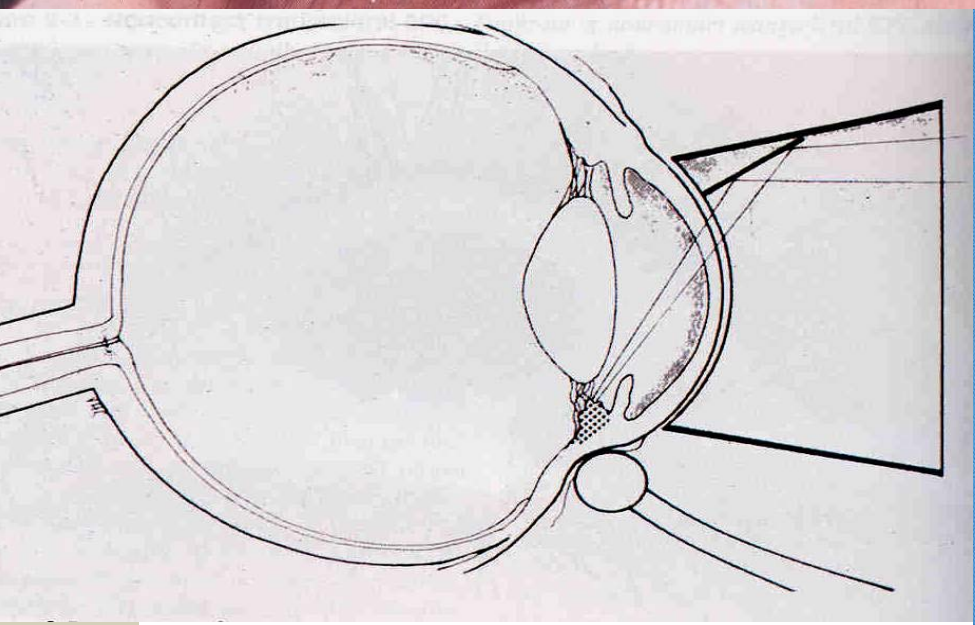
Photomydrisis

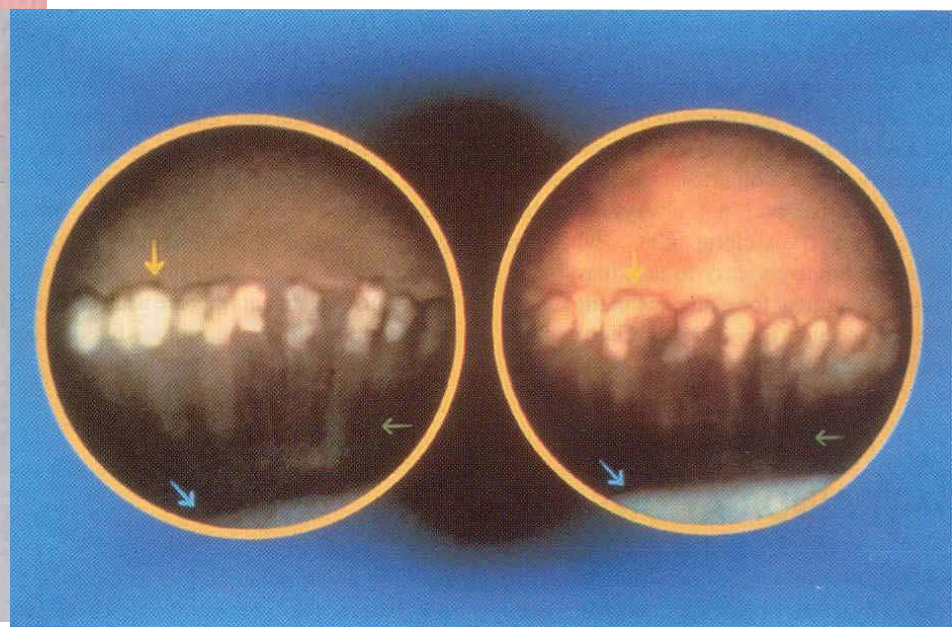
200 mW × 0.2 s ×200μm

200 mW × 0.5 s ×500μm



Transscleral cyclophotocoagulation

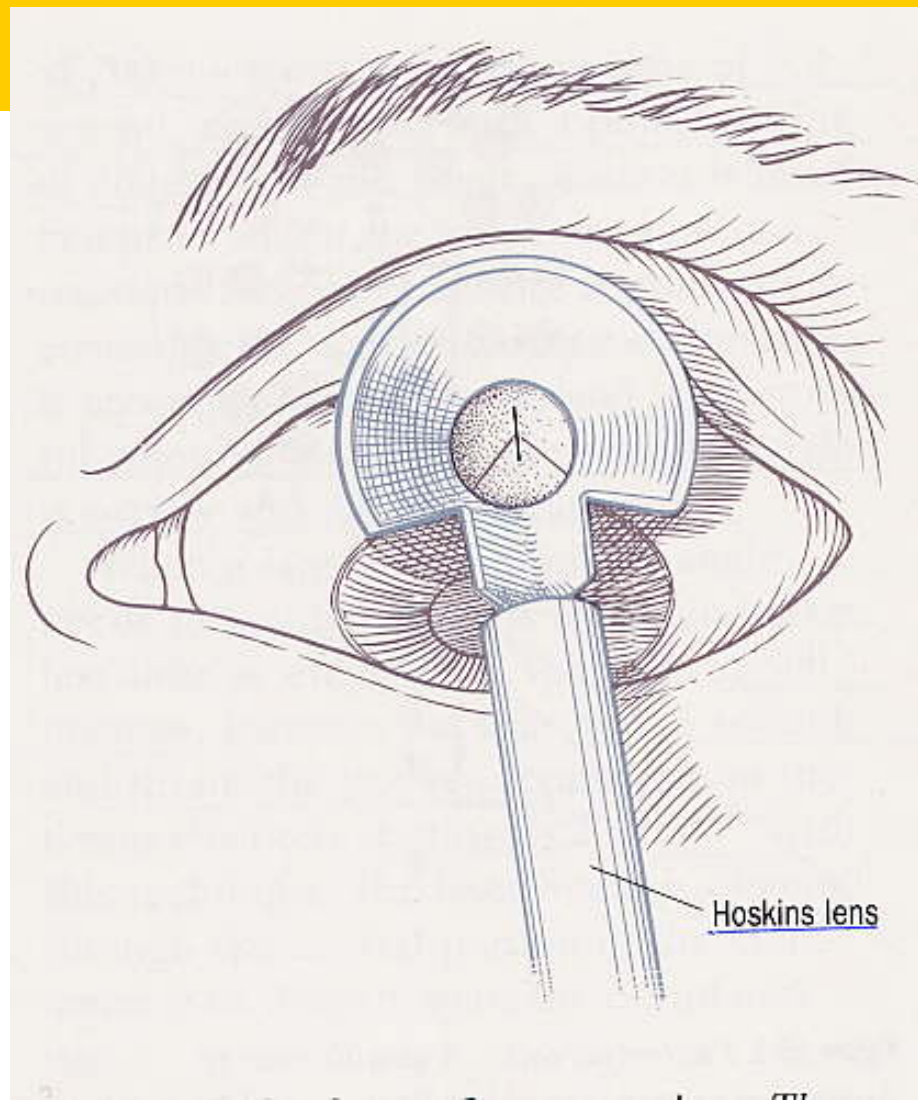




Suturelysis

Trabeculectomy flap suture

500-1000mW × 0.1 s ×100μm



Photodisruption

- 1962 Hellwarth: Q-switching ruby laser
- 1972 Kransnov: cold laser
- 1984 Frankhauser: Nd:YAG laser
  - Spot: <50 μm
  - 10^{10}-10^{11} w/cm^2
  - High local temperature exist briefly
  - Total heat energy is low

photodisruption

- High peak power ionizing laser pulse
- Optical breakdown
  - Plasma induced ablation
    - Thermoionic emission → free radical production → Cell ionization → plasma spark
    - 只瓦解雷射直接照射組織位置
  - Mechanical photodisruption
    - Cell ionization → shock wave, cavitation, jet formation, bubble formation
    - 會破壞週邊組織

Photodisruption

- Nd:YAG laser 1064 nm
  - Q switch : 30 mJ
  - Mode locked ~5mJ
  - Aiming beam: continuous wave He-Ne laser
  - Contact lens

- Clinical applications
  - Secondary cataract: posterior capsulotomy
  - Glaucoma: iridotomy
  - Post segment: vitreous membrane, floater

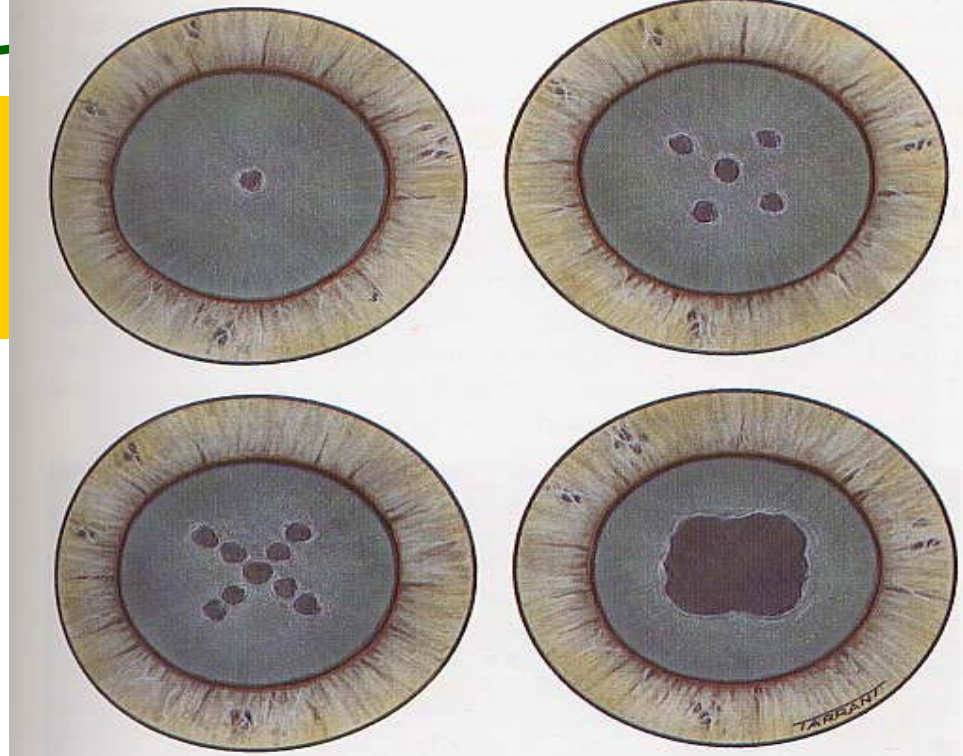
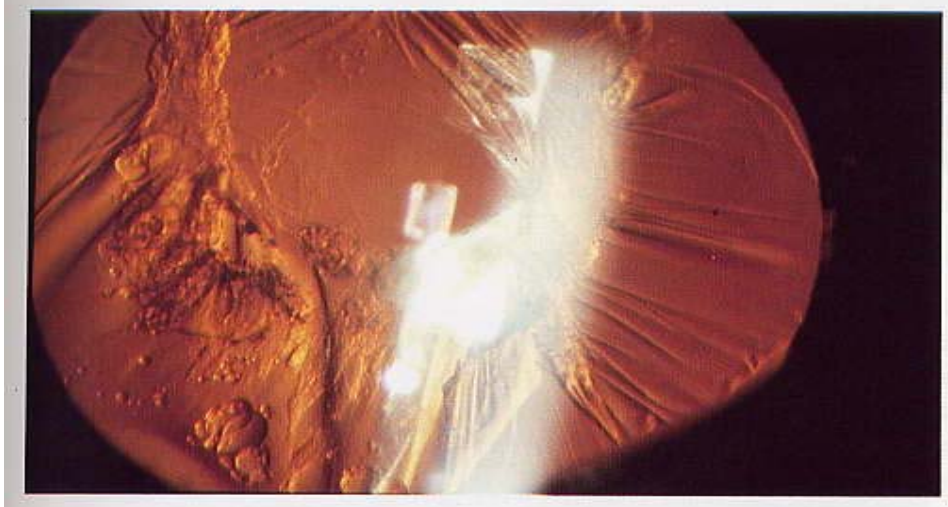
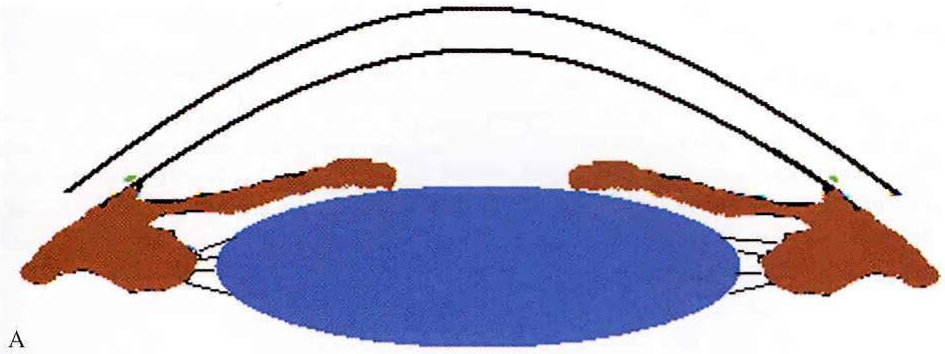


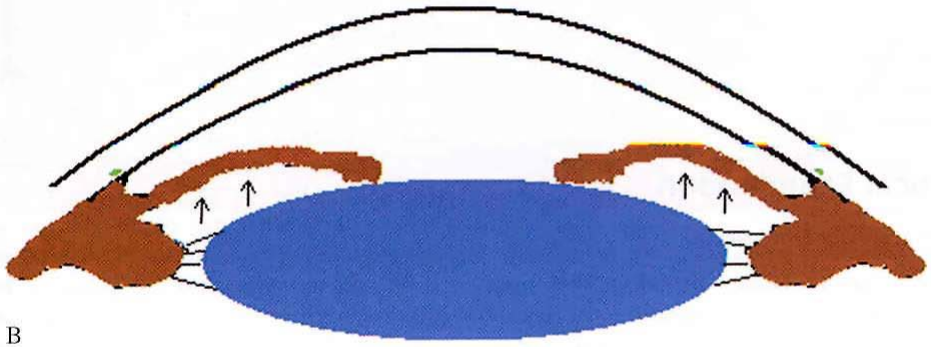
Figure 9.40 Technique of Nd:YAG laser capsulotomy (see text)



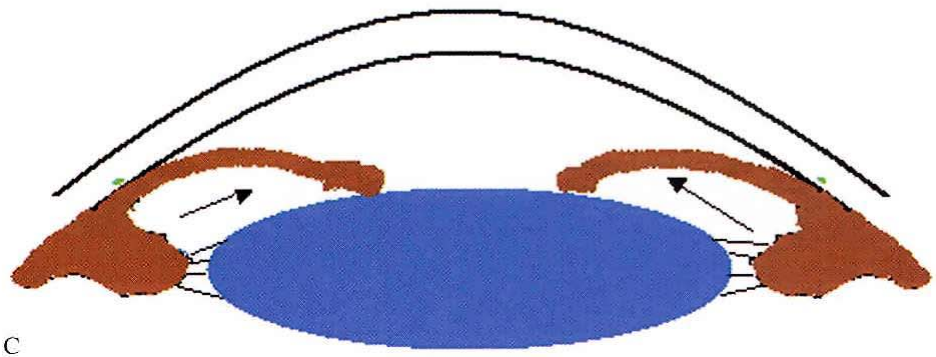
After cataract



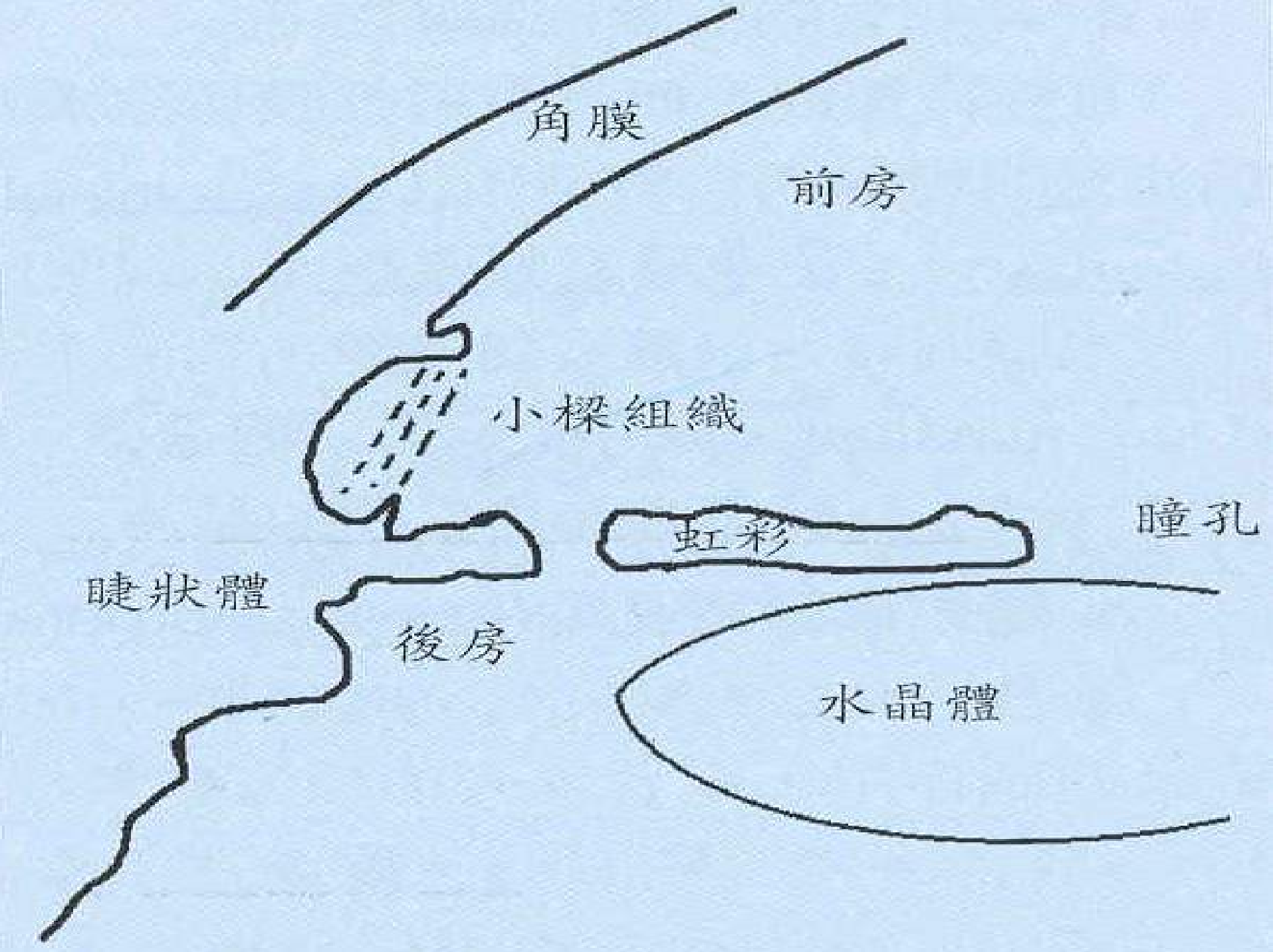
A



B



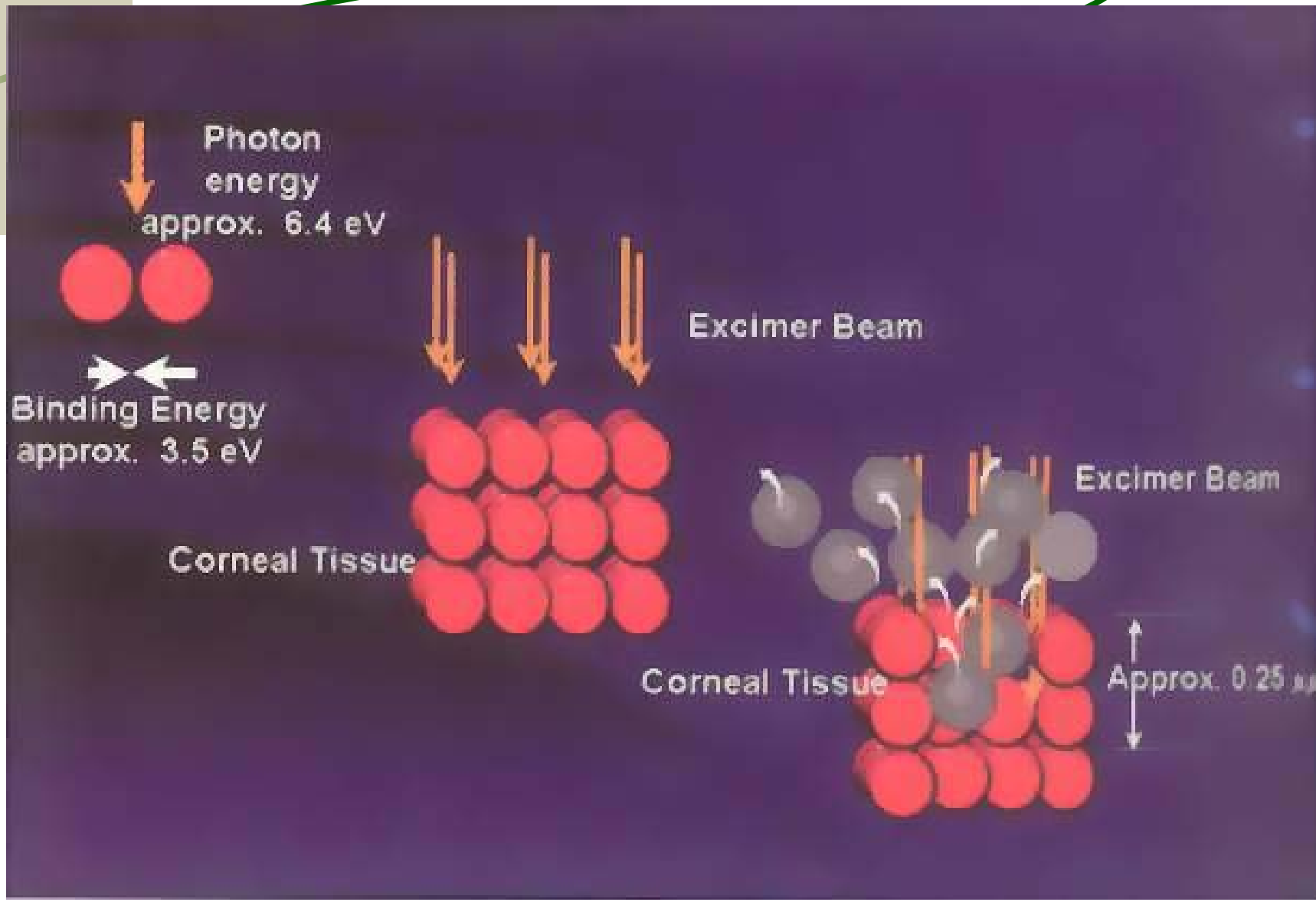
C


角膜
前房
小樑組織
虹彩
瞳孔
睫狀體
後房
水晶體

Photoablation

- 1982 Sriivasan & Mayne-Banton
- High intensity laser irradiation$\rightarrow\times$ molecular bond
- Ablation death < 1 μm
- Energy density: general 10^7~10^8 W/cm^2
- Eg: Excimer lasers

- Excimer lasers
  - Excited dimer
  - Argon fluroide (ArF) laser
    - 波長: 193 nm
    - 光子能量: 6.42 eV
    - Pulse duration: 12-15 ns
    - Ablation death/ pulse: 0.25 μm (cell diameter: 10 μm
    - Collateral damage: 極小

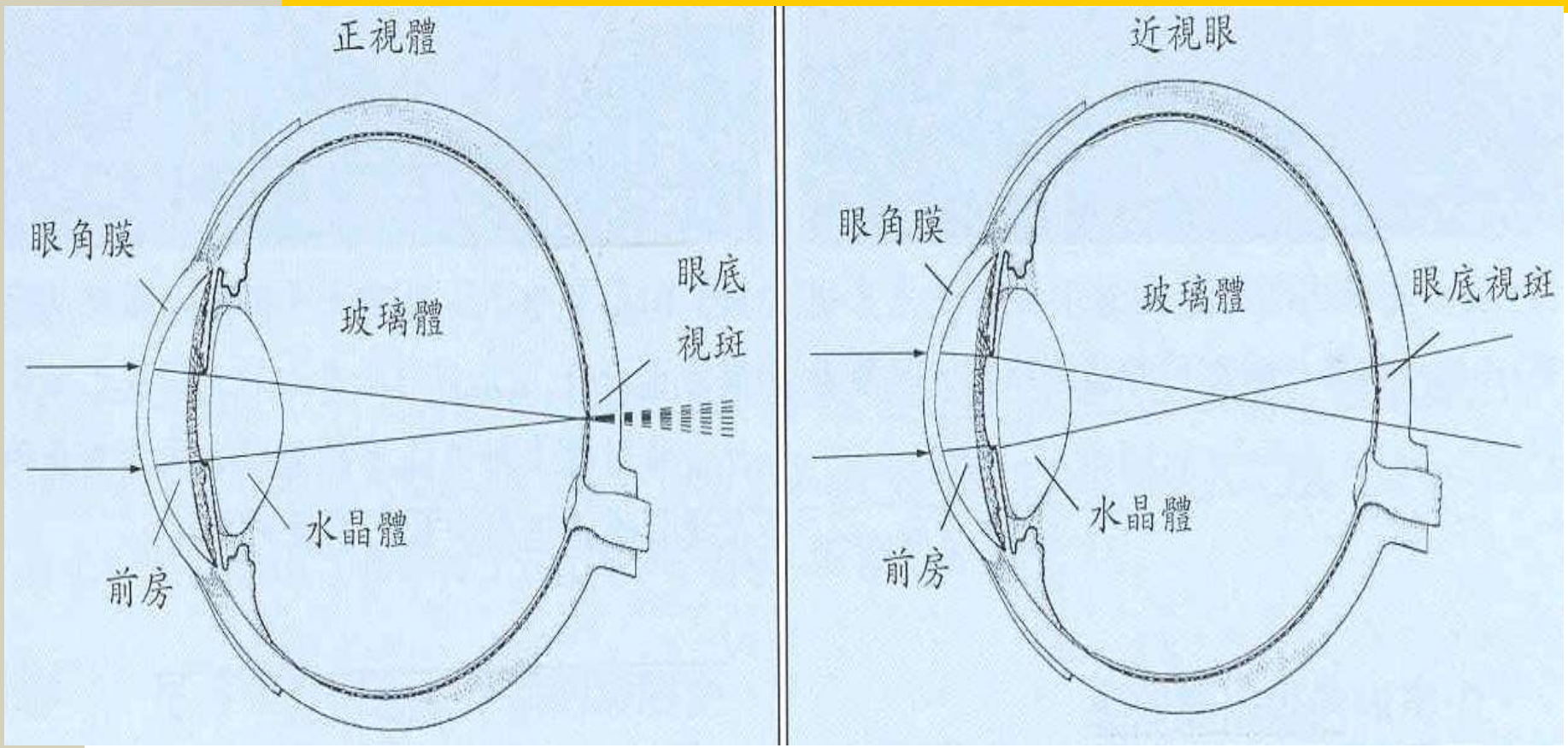

Photon
energy
approx. 6.4 eV
Binding Energy
approx. 3.5 eV
Excimer Beam
Corneal Tissue
Excimer Beam
Corneal Tissue
Approx. 0.25

High speed photo of wide-area excimer laser ablation of cornea

- Parameters of Excimers lasers
  - Fluence: 100-250mJ/cm^2
    - ↑ fluence → ↓ operation time, ↓ pulse variance
      → ↑ 熱效應, ↑ optical degradation,
      ↑ acoustic shock wave
  - Beam homogenecity
    - Homogeneous distribution: central island
    - Heterogeneous distribution:
      - Gaussian distribution
      - Anti-Gaussian distribution
  - Laser delivery system: 4種
  - Pulse repetition rate

Broad-beam laser	Scanning-slit laser	Scanning-spot laser	Flying spot laser
較不受手術中心偏移影響 手術時間短 雷射及發頻率低 無須eye tracking	Central island (+) 增進光速同一性 減少聲振波 沒有optical zone 限制 切割平整 中等能量輸出	Central island (-) 較不需要光速同質性 減少聲振波 治療遠視,散光 最小能量輸出	Central island (-) 較不需要光速同質性 減少聲振波 High repetition rate 治療遠視,散光 最小能量輸出
較高的能量 維持費高 Central island (+) 較大聲振波 無法矯正複雜的遠視,散光	eye tracking 手術時間長	eye tracking 手術時間長 需較高的雷射擊發頻率	eye tracking 手術時間長 需較高的雷射擊發頻率

- 相當安全
  - 穿透性 3-4 μm
- 危險性
  - Secondary fluorescence & cataractogenesis
  - 聲振波: central island
  - Toxic free radicals
  - mutagenesis


正視體
眼角膜
玻璃體
眼底
視斑
水晶體
前房
近視眼
眼角膜
玻璃體
眼底視斑
水晶體
前房

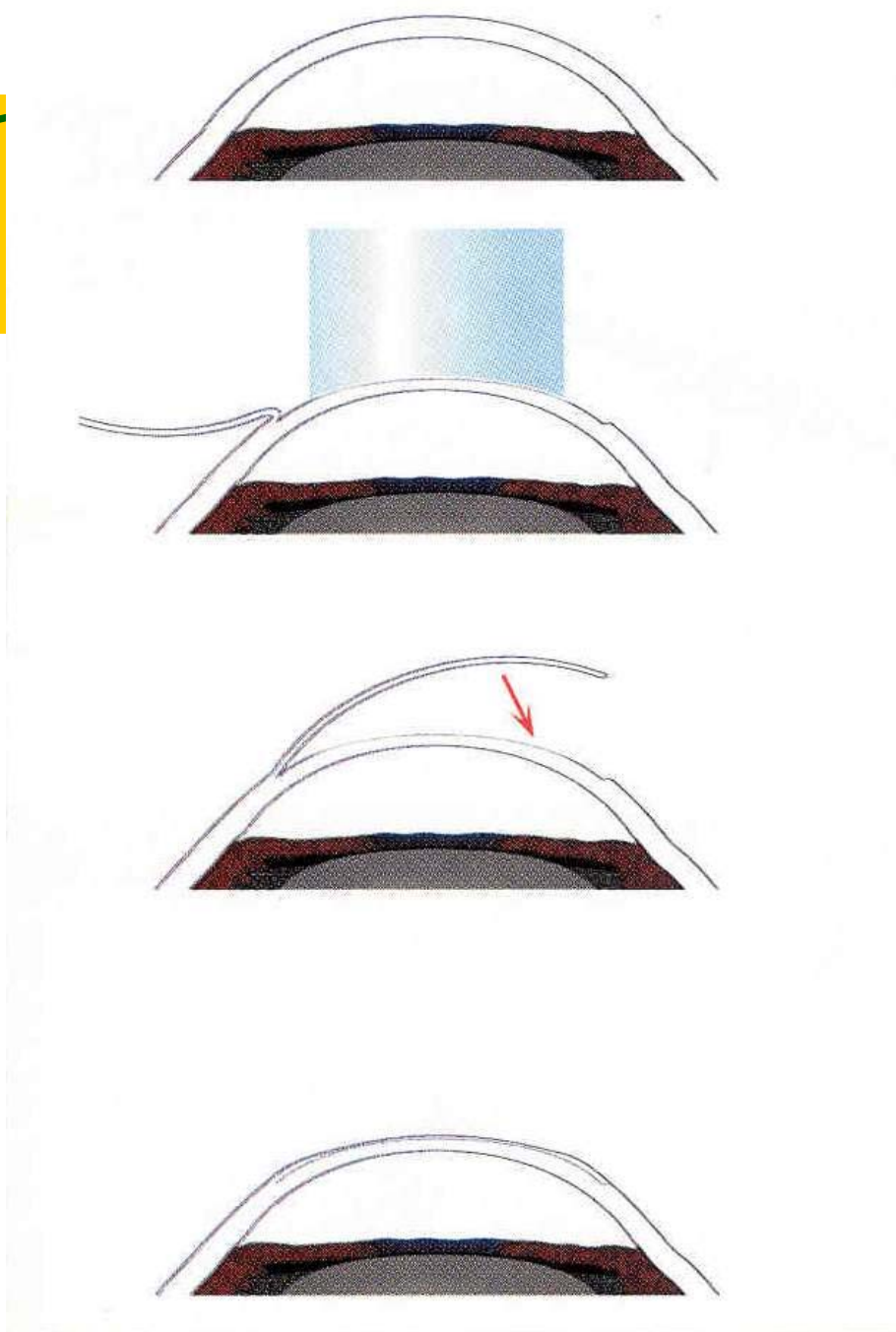


圖5-12：手術室中實際進行準分子雷射近視手術的狀況。

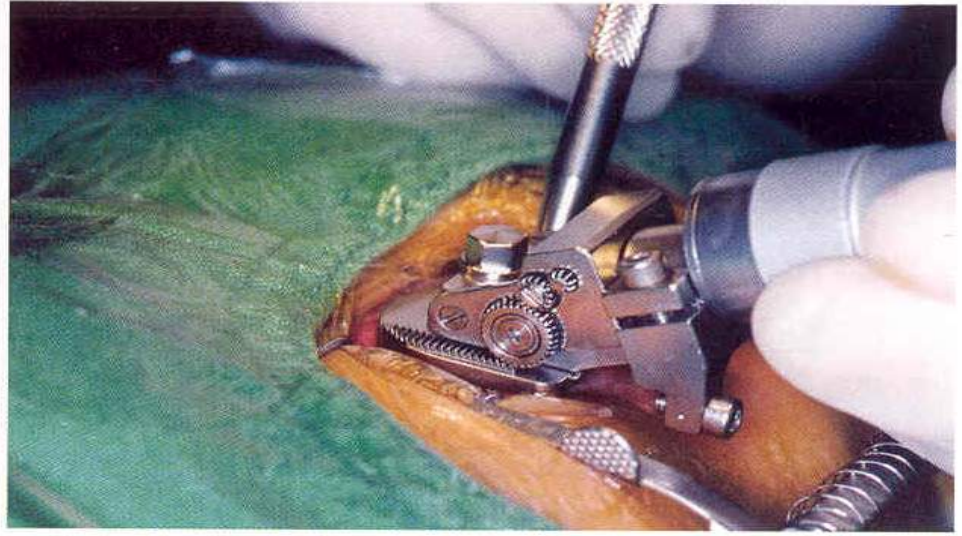


圖5-13：LASIK術中,以層狀角膜切割刀切開一個厚度約130μm至180μm，直徑約8-9mm的角膜瓣。

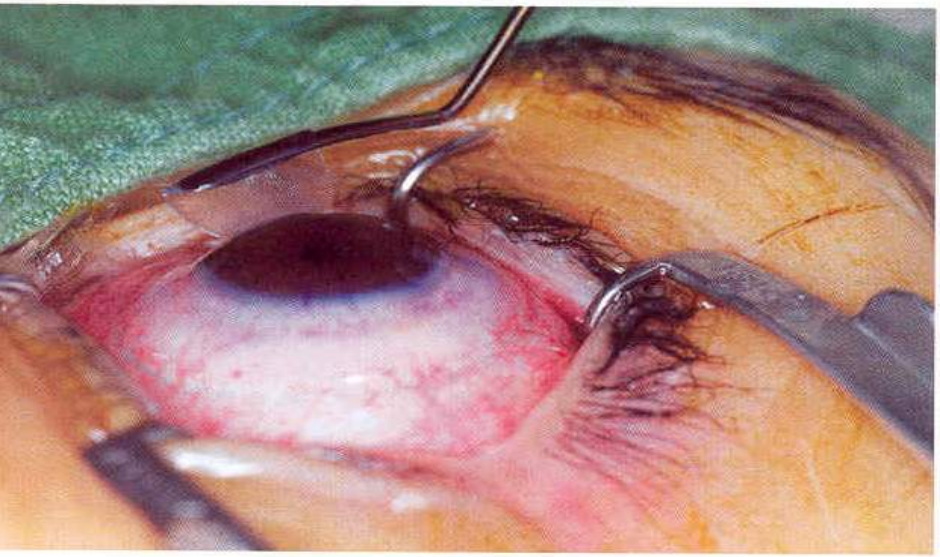


圖5-14：LASIK術中,掀起切割好的角膜瓣以施行雷射手術。

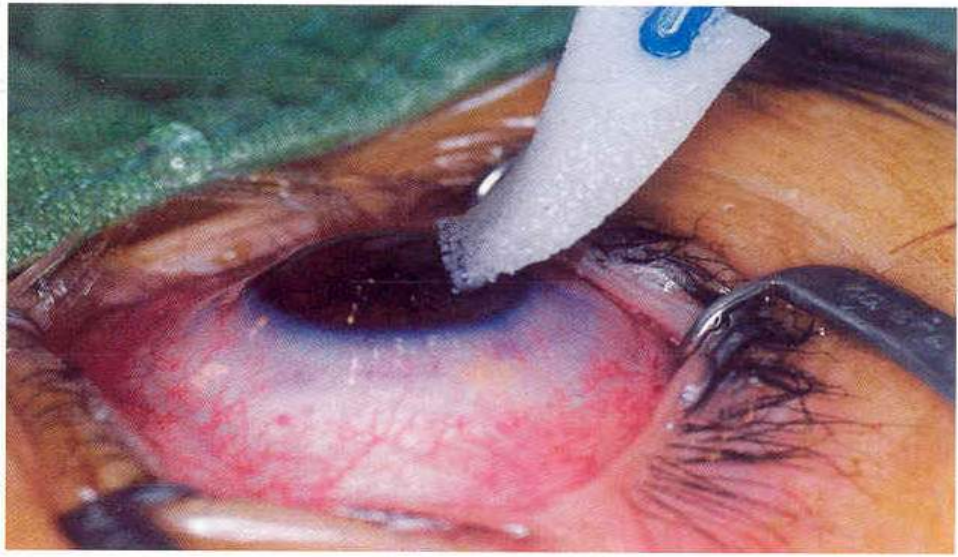
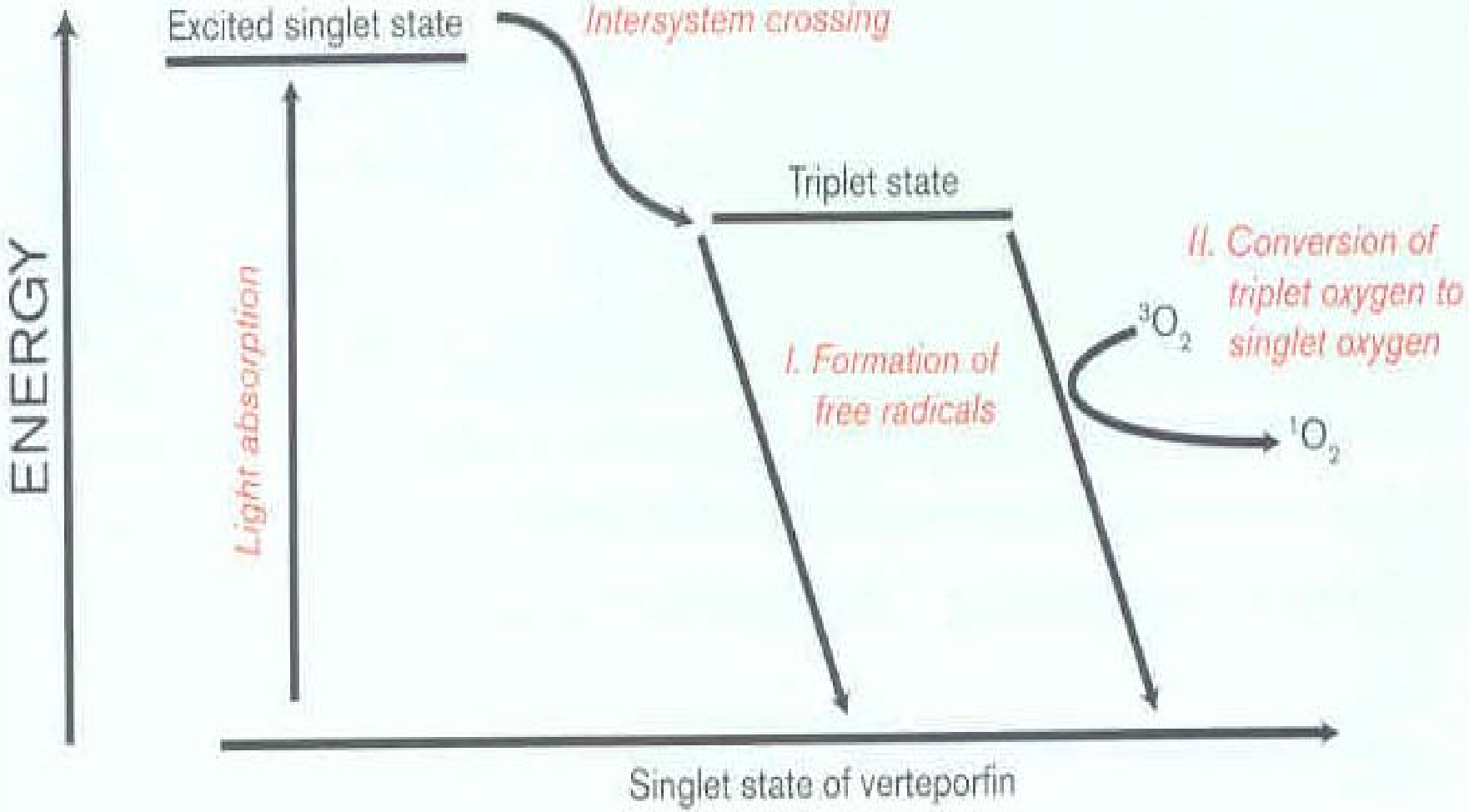


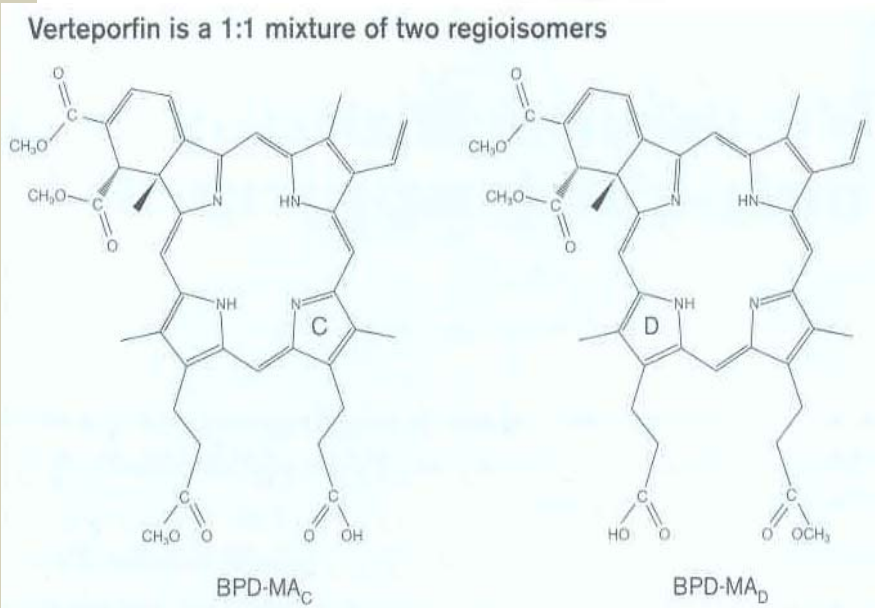
圖5-15：LASIK術中,在準分子雷射施行後,回復角膜瓣至原來位置。

Photochemical interaction

- PDT：Photodynamic therapy
  - Photosensitizer
  - Specific wavelength laser
  - Singlet oxygen or free radicals

Light-activated verteporfin generates reactive forms of oxygen





light-activated drug

generates reactive forms of oxygen

- 學名：Verteporfin **(C41H42N4O8)**
- **1:1 mixture of two regioisomers**
- 半衰期：5~6小時
- 代謝器官：肝臟

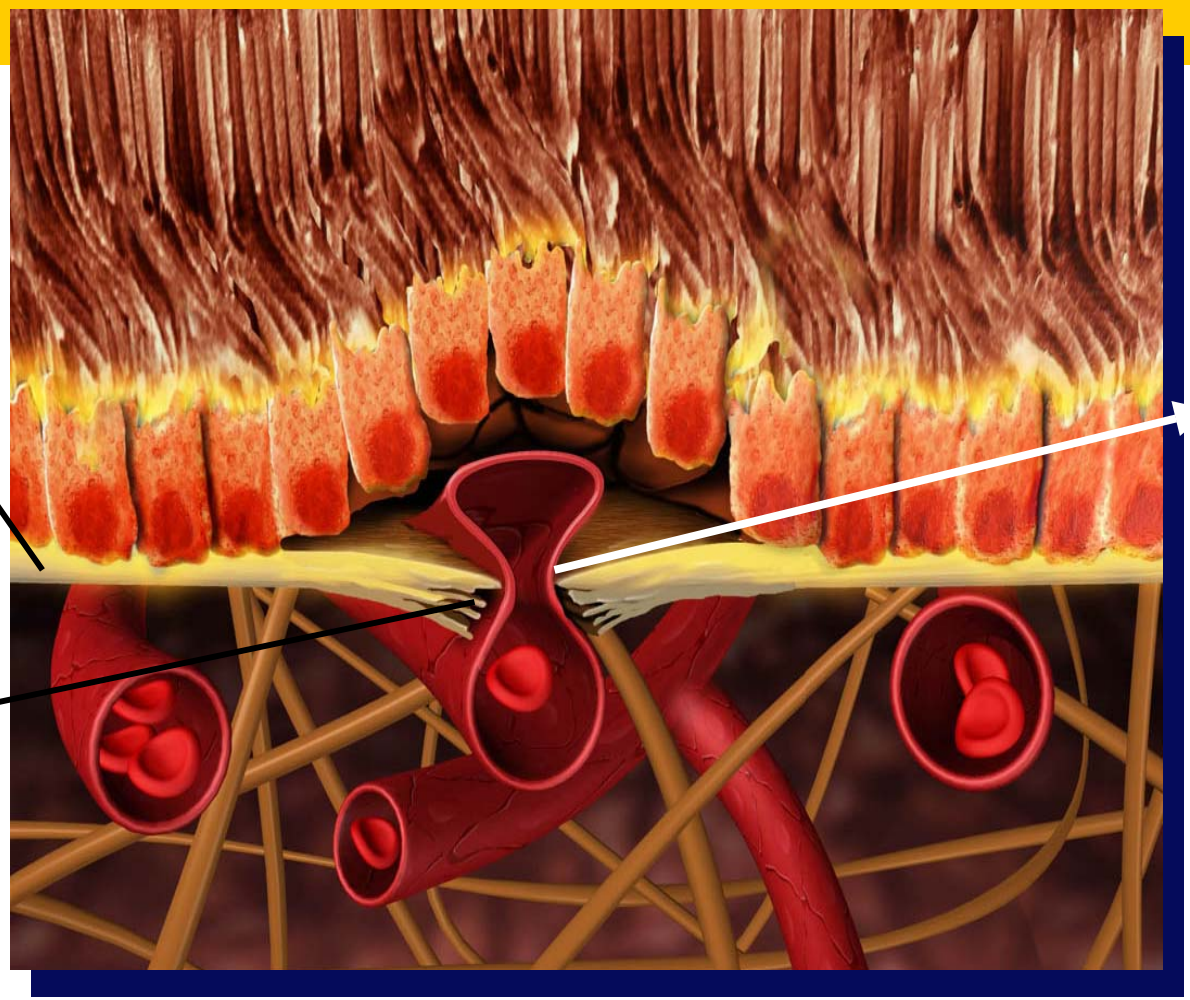
- 適應症：

  AMD：Age-relate macular degeneration

  PM：Pathologic myopia

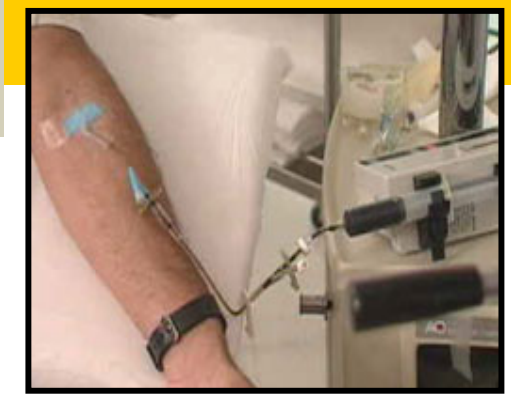
  OHS：Ocular histoplasmosis syndrome

所引起的 subfoveal CNV

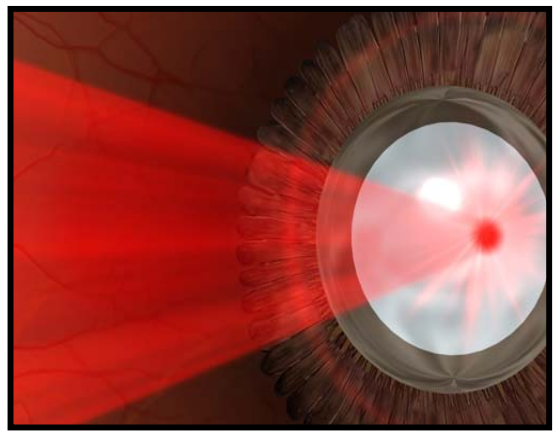

Retinal tissue
Bruch's membrane
CNV
Lacquer crack
Choroidal tissue

- 作用機轉：
- IV 注射 Visudyne：
  - Visudyne 與血液中的 LDL 結合，並將 LDL 當作載體，經血液循環到達 CNV 處；然後高 度選擇性吸附在 CNV 上的 LDL 接受體
  - （NV上之LDL接受體密度遠大於正常血管）
- 雷射照射：
  - 經波長 689nm 的雷射照射，而活化吸附在 CNV 上之 Visudyne 起作用，以 selective damage CNV tissue 而不會傷害到正常的 視網膜感光細胞

Step 1



Step 2



- Visudyne (6mg/㎡)：依照體表面積計算
- 雷射光：波長 689nm 紅光二極體雷射

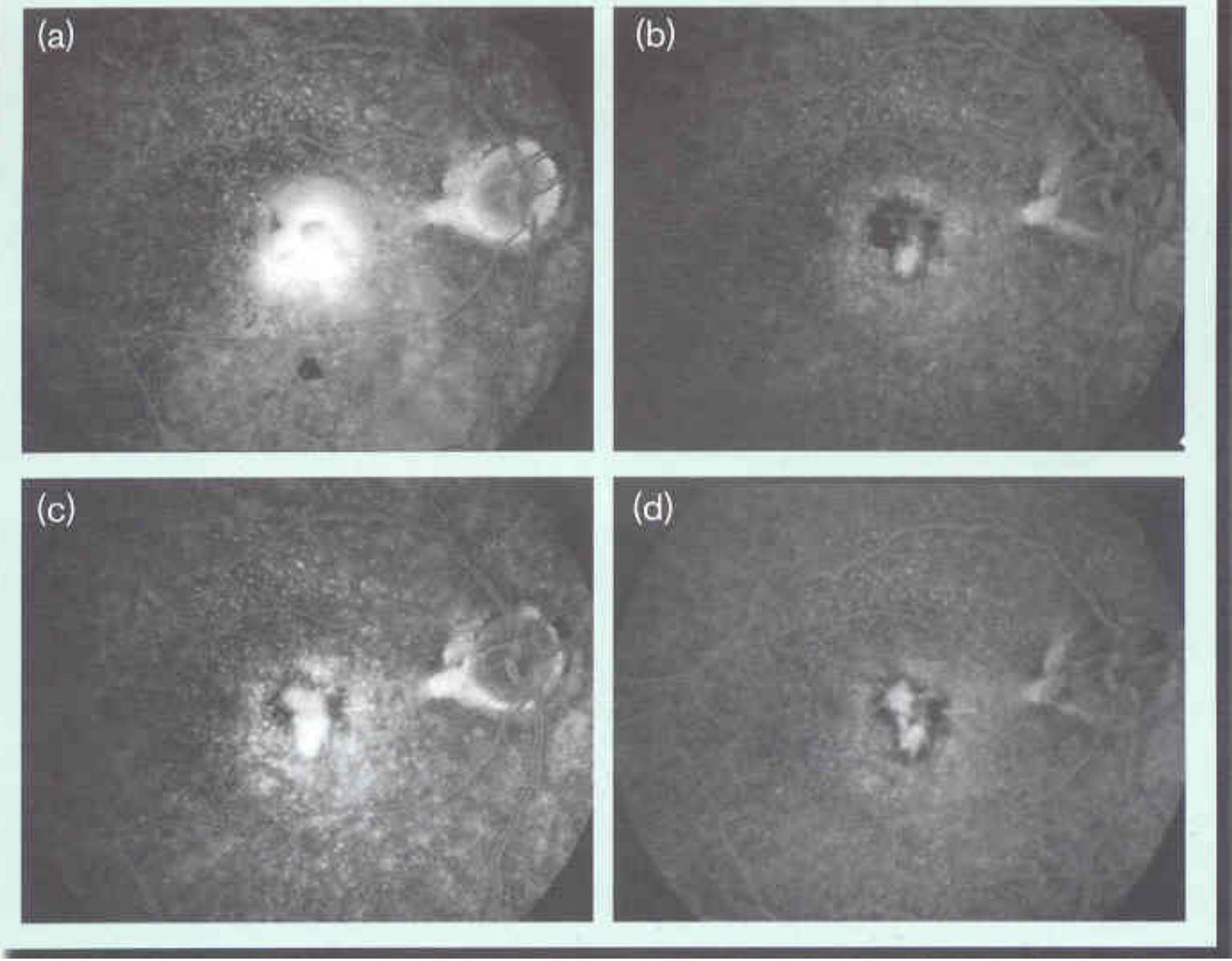
  雷射光劑量：50 J/c㎡

  雷射光強度：600 mW/c㎡

  照射時間：83 秒

★全世界病人所接受之治療 protocol 皆相同

Before and after Visudyne therapy



Diagnostic lasers

- Scanning laser ophthalmoscope
- Laser flare and cell meter
- Laser interferometer
- Optical coherence tomography
- Laser doppler velocimeter

RTA Posterior-Pole Report

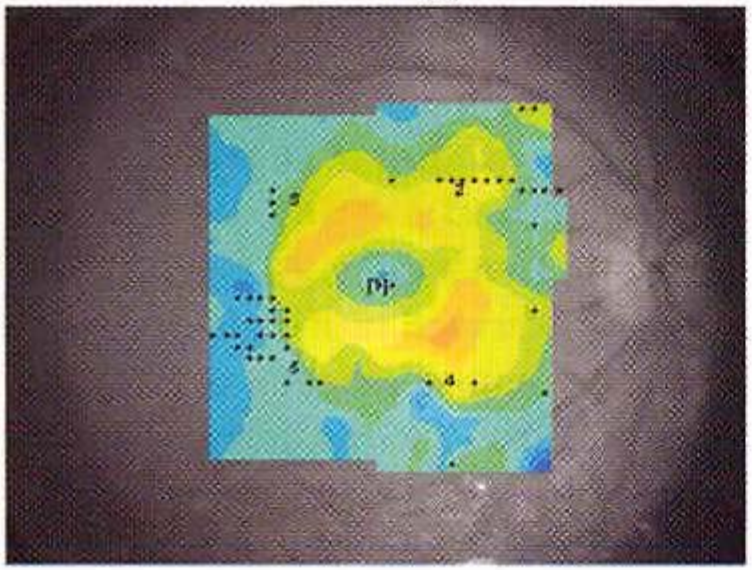
ID:
Name:
Session: 20010212
Eye: OD
Refractive Error: 0.00
Corneal Radius: 7.80
Patient Details:

Software Version: 4.05
Std. DB Version: 1.03
Validity Type1: 89%
Validity Type2: 93%
Registration Status:Registered
Printed On: 16:00, July 09, 2001

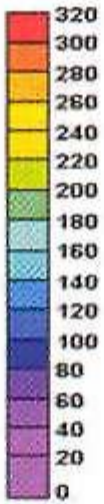
Session Details:

Thickness Maps

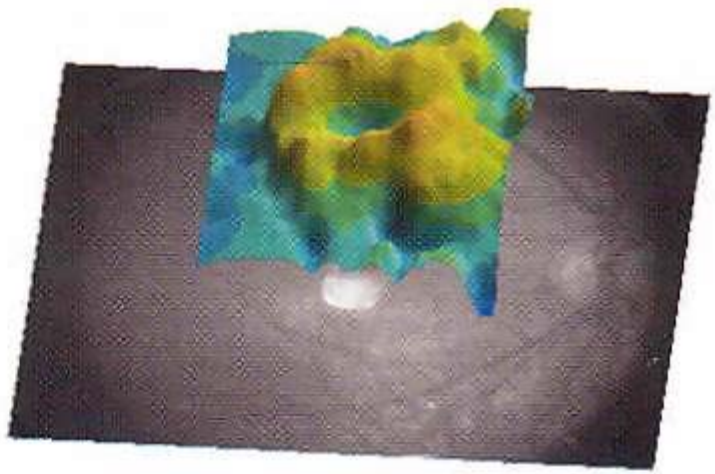
2D



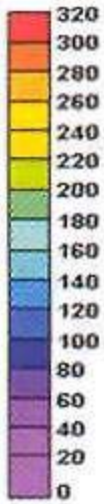
Microns



3D



Microns

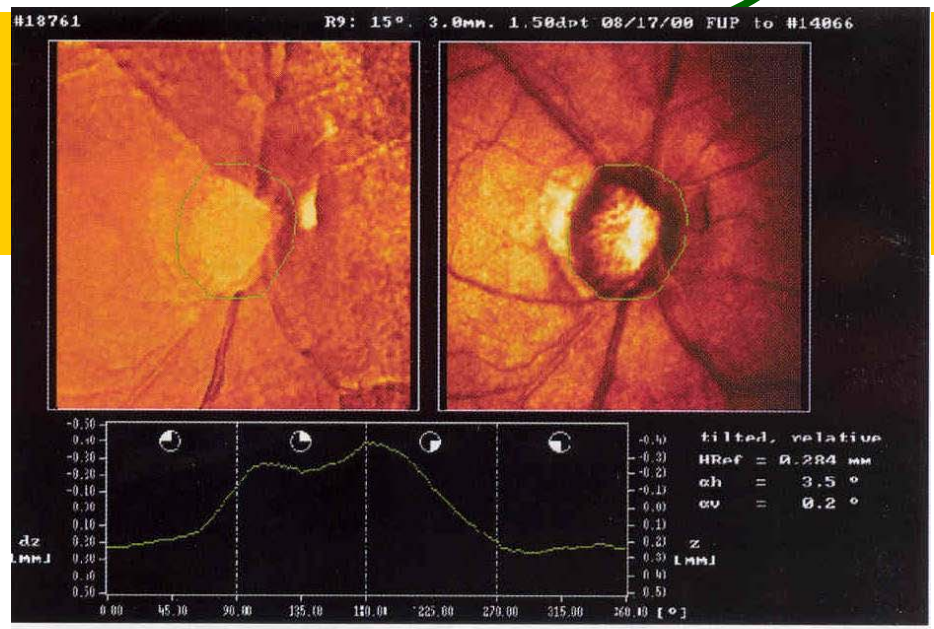


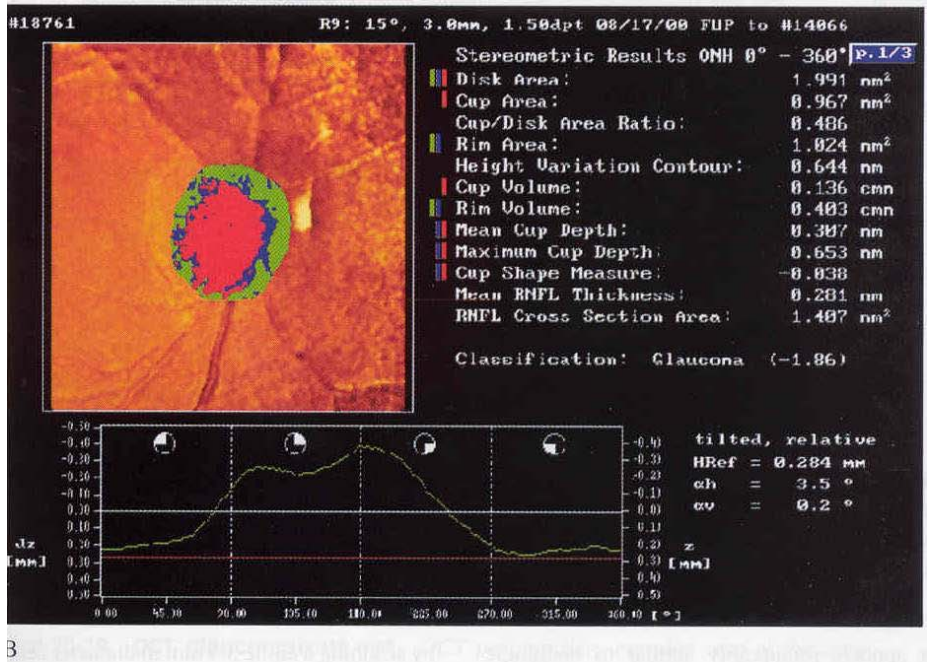
Legend: Black - Registered, Red - Unregistered, Blue - Manual, I - Fixation Error

Scanning Laser ophthalmoscope

eg: Heidelberg Retina tomography
diode laser: 830nm
3-dimensional images of optic nerve

glaucoma →



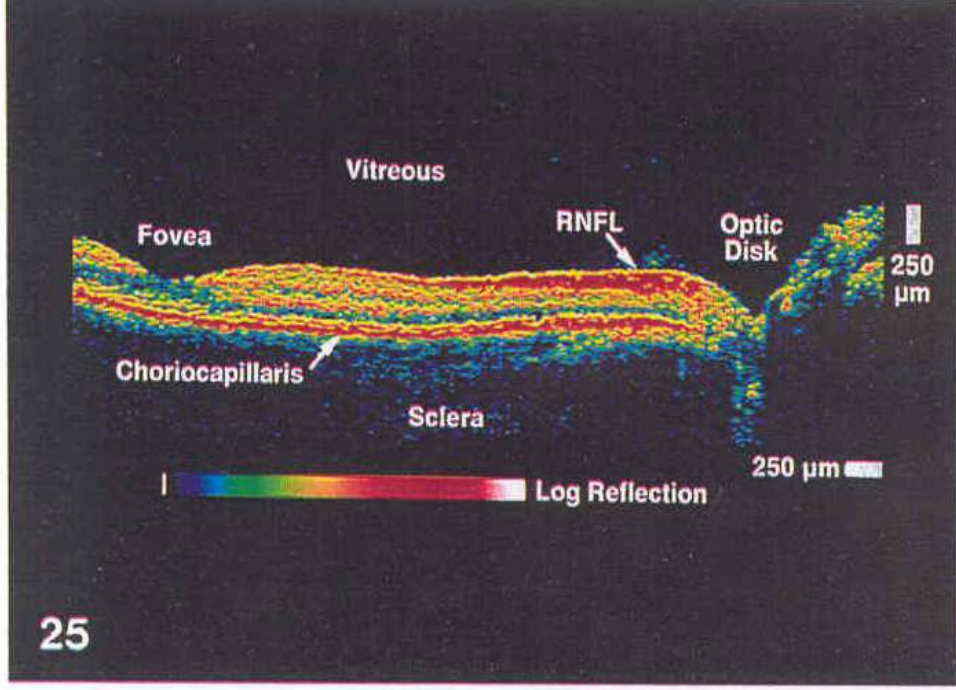


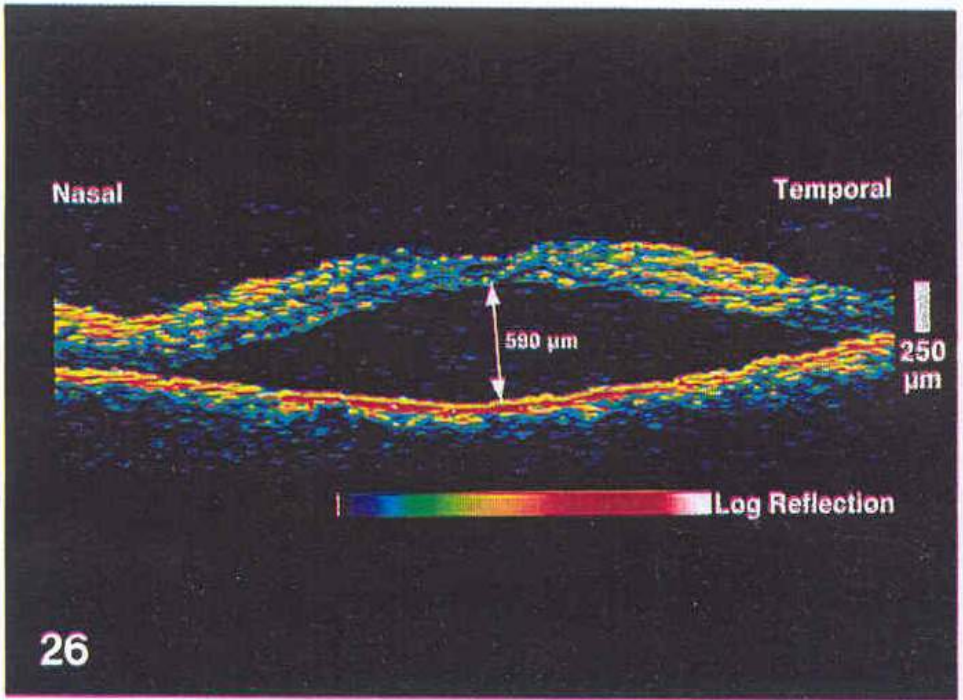
- Optical Coherence tomography
  - 2 dimensional laser interferometric ranging
  - High resolution
  - Similar ultrasound B mode

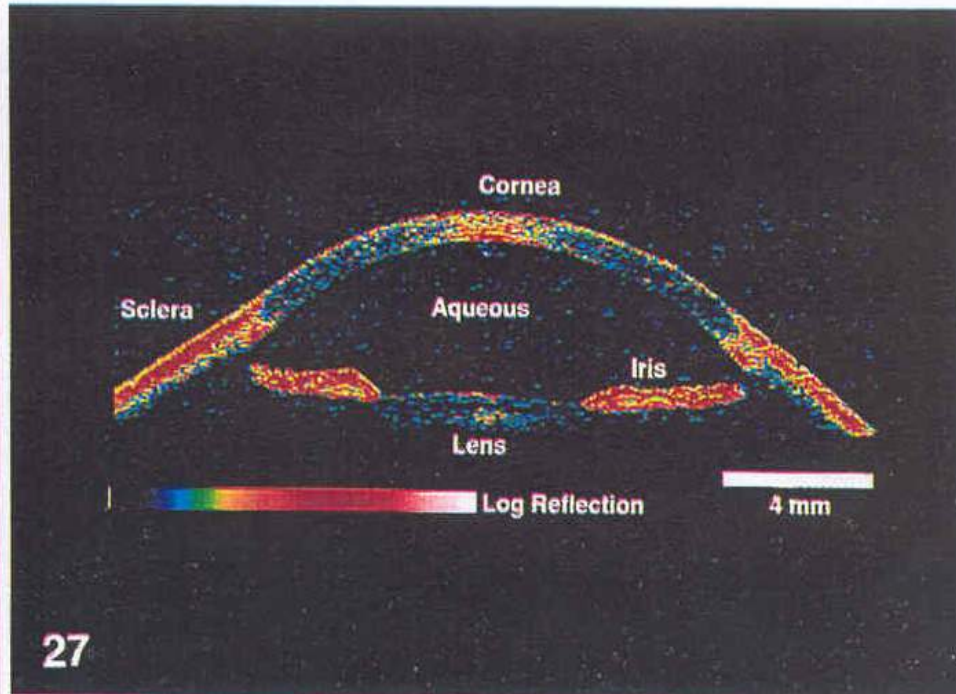
Fig. 25. False-color OCT tomograph obtained through the macula and optic disk of a human eye.

Fig. 26. OCT image of a neurosensory retinal detachment in a patient with a diagnosis of central serous chorioretinopathy.

Fig. 27. OCT image of the anterior human eye.








Thank You