Retinal Lasers in the Era of Anti-VEGF

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PRP
- Diabetic Retinopathy Study
  - 1970’s
  - National Eye Institute Study
  - Proved panretinal photocoagulation works in PDR
- Early treatment of Diabetic Retinopathy Study
  - 1980’s
  - National Eye Institute Study
  - Recommended close follow up without PRP for:
    - Mild/moderate NPDR

Early treatment of Diabetic Retinopathy Study
- National Eye Institute Study
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PRP vs Anti-VEGF for PDR
- Avastin shown to be non-inferior to PRP in terms of vision gain
- Anti-VEGF lessens the risk of worsening diabetic retinopathy when used to treat DME
- Avastin shown to be more expensive compared to PRP alone over a two year time frame
- PRP is a permanent treatment and anti-VEGF requires chronic therapy
- Decision on what to do for primary treatment of PDR is highly patient dependent...


When to Use PRP Now?
- Good clinical indicators:
  - Any degree of neovascularization
  - High-risk NPDR
  - Poor outcome in fellow eye (NVG/TRD)
  - Poor expected compliance
- Anti-VEGF agents (Avastin/Eylea/Lucentis)
  - Treat neovascularization and may delay need for PRP
  - A series of anti-VEGF injections will cause retinopathy regression
  - Highly dependent on patient adhering to monthly follow up
- Main determiner of PRP timing is predicted patient compliance
- PRP still has a significant role in treating diabetic eye disease

High Risk NPDR 4-2-1 Rule
- Diffuse intraretinal heme in 4 quadrants
- Venous beading in 2 quadrants
- Intraretinal microvascular abnormalities in 1 quadrant
**Why does PRP work?**

- Retinal vascular disease (Diabetes, Eales, sickle cell)
  - Create ischemic retina
  - Leads to oxygen demand/availability imbalance
  - Oxygen deficient tissue then secretes:
    - VEGF
    - Various other cytokines
    - Causes neovascularization and vascular leakage
  - Permanent vision loss

- PRP rebalances oxygen demand/availability by
  - Coagulating RPE cells \(\rightarrow\) kills photoreceptors and reduces oxygen need
  - Allows choroidal oxygen to penetrate to the inner retina
  - Decreasing cytokine production
  - Reversing neovascularization and vascular leakage

**PRP**

- Conventional settings:
  - Wavelength: 514-532 nm
  - Duration: 100-200 ms
  - Spot size: 100-500 um
  - Power: 200-750 mW
  - Spots: 1300-1500

- CRI settings:
  - Wavelength: 532nm (green pascal)
  - Duration: 100 ms
  - Spot size: 200
  - # of Spots: Completely dependent on:
    - Disease severity
    - Projected patient compliance
    - Power: titrate to treatment, any power appropriate
    - Young diabetics may need less than 200 mW
    - Dense cataracts may require very high mW

**PRP for non perfused peripheral retina**

- Using wide field fluorescein angiography to detect ischemic areas for later ablative PRP
- Logically should work to reduce diabetic/CRVO macular edema by reducing VEGF load
- No consensus that it does work
- Dr. David Brown presented data at the 2016 Angiogenesis conference showing no improvement after peripheral total ablation to non perfused areas
- Dr. Wykoff also recently stated he has seen no improvement in CRVO and DME after targeted PRP using wide field IVFA
- Final data presented at AAO 2016 confirms lack of effect
- Better option: ratchet down disease with anti-VEGF and do non ablative PRP
- Wide field IVFA still essential for detecting peripheral disease

**Macular Focal Laser**

- Classic treatment for diabetic macular edema
- Use now greatly diminished with the advent of anti-VEGF therapy
- Anti-VEGF indicated in 95%+ of DME cases
  - Patients with poor compliance, limited medical access, or those unable to tolerate injections make up majority of focal laser cases for DME at CRI
- Focal treatment of non foveal choroidal neovascular membranes
- Treatment of macroaneurysms
- Focal treatment of CSR choroidal leakage (non foveal)

**Heavy Focal Examples**

- Chorioretinal scars, foveal atrophy
Heavy Focal Examples

After 360 foveal focal by outside doctor

After a series of Avastin injections

Large perifoveal micro A identified

One month after laser

Three months after laser

Focal Laser for Diabetic Macular Edema

- Focal laser should ONLY target micro aneurysms to treat diabetic macular edema
- Focal laser should NOT be used as grid treatment to reduce swelling
  - Destroys photoreceptors leading to:
    - Decreased contrast sensitivity
    - Decreased ability to fixate
    - Decreased reading speed
  - Destroying the macula to reduce swelling is a bad idea

Focal Laser

- Classic settings:
  - Small spot size: 50-100 um
  - Short pulse duration: 50-100 ms
  - Power titrated to whitening of retina
- Settings used at CRI:
  - Spot size: 100 um
  - Duration: 15-35 ms
  - Power titrated to occlusion of microaneurysm

Focal Laser for CNV, Macro Aneurysms, and CSR:

- Much longer duration
- Much higher power
- Bright white spot needed
- No set settings, high degree of customization needed

Sub threshold laser for DME

- Relatively new modality designed to counteract anti-VEGF effect on laser industry
- Focal laser pays about 5X the reimbursement of an anti-VEGF injection
- In theory creates an effect on RPE cells to reduce VEGF without killing overlying photoreceptors
  - Uses 10-25% of energy needed to create a visible effect
  - Invisible effect during treatment and after if done correctly
  - Very safe when done correctly, minimally effective in most cases
    - Strong push for adoption by industry and some retina specialists
- Conclusion: Only industry sponsored studies show effect; only industry sponsored doctors push it
Photodynamic Therapy
- Dying laser modality
- Very expensive IV medicine needed (verteporfin)
- Hard to get insurance to pay for it
- No new FDA approved lasers being made
- Still making lasers in Europe
- Hard to service and repair
- Vitreous Macular Consultants (Bailey Freund, Yannuzzi, Rick Spaide)
- Only functioning PDT in greater Manhattan
- CRI PDT laser still works
- Useful for:
  - Choroidal hemangiomas
  - Retinal Capillary hemangioblastomas (Von Hippel Lindau)
  - Central Serous Chorioretinopathy

Laser Indirect Ophthalmoscopy
- Retina Tears/holes
- Walling off chronic retinal detachments
- Walling off retinoschisis
- PRP in some clinics
- Ablative treatment in ROP and COATS
  - Intravitreal Avastin now replacing most ROP laser, and used in Coats as well

Can be temporized with Avastin
permanent treatment usually needed: cryo, focal laser or PDT

Drainage site
CRYO for ROP

Laser for ROP

Anti-VEGF should be the new gold Standard for ROP
Fear of systemic side effects and liability Prevent complete adoption

Briefly: Retinal Imaging

- Classic:
  - Thorough macular exam with contact lens at slit lamp
  - Fluorescein imaging and indocyanine green
  - B scan if needed
- Modern:
  - Optical coherence tomography
  - Fundus autoflourescence
  - OCT angiography
  - Rarely Fluorescein or indocyanine green imaging

Optical Coherence Tomography

- The most important imaging modality in Ophthalmology today
- Non invasive and fast
- Uses light to create cross sections of the retina
  - Interprets back scattering of life as the tissue is penetrated
- Resolves down to 5 um
- Initially were false color images, all modern machines use gray scale which is more accurate
- Colorized images are misleading

OCT

- HEI, CRI, and the VA
  - All use Heidelberg Spectrals
  - Best OCT system available today
  - Expensive
- Zeiss (Cirrus); Bioplogen, Topcon, Optopol, Optovue (iVue), etc
- Need special modules for things like fundus autoflourescence, fluorescein angiography, ICG angiography

International Nomenclature for OCT Meeting

Consensus Normal OCT Terminology

Rick Spade
Fluorescein Angiography
- Developed 1961
- Past gold standard for retina imaging
- Displaced by high quality OCT scans
- Will be replaced by OCT angiography
- Only advantages over OCTA:
  - Shows leakage
  - Can be billed for

Fluorescein Angiography
- Complications:
  - Nausea
  - Intractable vomiting
  - Pruritus
  - Anaphylaxis
  - Bronchospasm
- Death
  - Ex fellow of Dr. Charles had a patient die in office 10 years ago
  - 7 figure settlement

OCT-Angiography
- Future of angiography
- Non invasive
- Fast
- Shows everything IFVA does except leakage
- However, unable to produce wide field images

Summary
- Anti-VEGF has replaced most indications for posterior pole laser
- PRP and focal still have a role for a number of retinal diseases
- Ablative laser still have widespread use in ROP despite anti-VEGF replacing it in many practices including CRI
- OCT angiography will be available at CRI shortly

Questions