Intravitreal Injection - The Role of the Comprehensive Ophthalmologist

Michael Rauser, MD
Department Chairman
Associate Professor
Loma Linda University Eye Institute
Ophthalmologist Trends

Sources: DHHS Physician Supply and Demand Projections to 2020

Source: Kevin Corcoran - Used with permission
Medicare Utilization - 67028 - IV Injection


Used with permission - Source: Kevin Corcoran
<table>
<thead>
<tr>
<th>CPT</th>
<th>Procedure</th>
<th>λ</th>
<th>CPT</th>
<th>Procedure</th>
<th>λ</th>
</tr>
</thead>
<tbody>
<tr>
<td>67028</td>
<td>Intravitreal injection</td>
<td>11%</td>
<td>68761</td>
<td>Punctum plugs</td>
<td>1%</td>
</tr>
<tr>
<td>66984</td>
<td>Cataract &amp; IOL</td>
<td>8%</td>
<td>67228</td>
<td>Retina laser</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>67210</td>
<td></td>
<td></td>
</tr>
<tr>
<td>66821</td>
<td>YAG</td>
<td>3%</td>
<td>67820</td>
<td>Epilation</td>
<td>1%</td>
</tr>
<tr>
<td>66761</td>
<td>Glaucoma laser</td>
<td>1%</td>
<td>15823</td>
<td>Blepharoplasty</td>
<td>1%</td>
</tr>
<tr>
<td>65855</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Frequency is per 100 office visits (%) on Medicare beneficiaries

Source: CMS data (2012), 18 - Ophthalmology

Used with permission - Source: Kevin Corcoran
<table>
<thead>
<tr>
<th>Rank</th>
<th>CPT</th>
<th>Procedure</th>
<th>Rank</th>
<th>CPT</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67028</td>
<td>Intravitreal</td>
<td>6</td>
<td>66982</td>
<td>Complex Cataract</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>66984</td>
<td>Cataract w/IOL</td>
<td>7</td>
<td>65855</td>
<td>Lx Trabeculoplasty</td>
</tr>
<tr>
<td>3</td>
<td>66821</td>
<td>YAG capsulotomy</td>
<td>8</td>
<td>67210</td>
<td>Focal Laser</td>
</tr>
<tr>
<td>4</td>
<td>68761</td>
<td>Punctum plug</td>
<td>9</td>
<td>15823</td>
<td>Blepharoplasty</td>
</tr>
<tr>
<td>5</td>
<td>67820</td>
<td>Epilation</td>
<td>10</td>
<td>67228</td>
<td>PRP</td>
</tr>
</tbody>
</table>

Source: CMS data 2012, 18 - Ophthalmology

Used with permission - Source: Kevin Corcoran
Resident experience with IV injections
The Case for Comprehensive Ophthalmologists Performing IV Injections

- Technically an easy procedure to teach and perform
  - Current residents receive extensive experience
- Strong safety profile
- Injection volume is high and growing
  - Meets a community need
- Cost effective use of manpower within a managed care environment
- Patient convenience
  - Travel considerations
What to do 1st?

- Diagnosis - including testing
  - FA - assists with diagnosis confirmation
  - Color photos - baseline documentation
  - Spectral Domain (SD) Retina OCT -
    - Diagnosis confirmation
    - Quantitative and qualitative assessment
    - Response to treatment
Diseases Worth Treatment Consideration

- Pseudophakic CME
- Macular edema associated with Retinal Vein Occlusion
- Diabetic Macular Edema
- Exudative ARMD

Different “treatment model” could be used for each condition
IV Injection Treatment Plan Models

- Injector alone model
- Injector “plus” model
- “Do all you possibly can” model
Injector Alone model

- Initially assess patient - tentative diagnosis made clinically
- Refer to Retina for:
  - Diagnosis confirmation
  - Diagnostic testing
  - Initial treatment (gives 1\textsuperscript{st} injection)
  - Treatment plan (Avastin q 4 weeks x 3 then reassess one month later)
- Comp doc does 2\textsuperscript{nd} and 3\textsuperscript{rd} injection; performs all injections not done at Retina “Assessment” visits
Injector ‘Plus” model

- Initially assess patient and diagnosis made. Includes some or all of the diagnostic testing (includes Retina OCT)
- Refer to Retina for:
  - Diagnosis confirmation
  - Possibly some diagnostic testing (FA / Color photos)
  - Treatment plan (Avastin q 4 weeks x 3 then reassess one month later)
- Comp doc treats with OCT guided follow-up
- Periodic reassessment with Retina to tailor management
“Do All You Possibly Can” Model

• Initially assess patient and diagnosis made. Includes all of the necessary diagnostic testing
• Follows established protocols for treatment
• Refers to Retina for incomplete or non-responders
Pre-op Assessment

- No active inflammation / Infection
- Note pre-op IOP / Glaucoma history
- Consent for procedure
Instruments needed on Sterile Tray

- Alcaine
- 5% Betadine solution
- 10% Betadine swabs
- 2% lidocaine plain on 3 cc syringe
- Eyelid specula
- Caliper
- Marking pen
- Sterile Q-tips
- 1cc syringe with 19g & 30g needles
My Injection procedure

- Mark procedure eye
- 1 drop proparicaine
- 1 drop 5% Betadine
- Eyelid prep with 10% Betadine swabs
- 2% lidocaine drops to cornea
- Place eyelid specula
- Mark injection site 3.5 mm posterior to limbus with caliper / marking pen
- Optional: 1 drop of 5% Betadine to injection site (DRCR protocol requirement)
My Injection Procedure

- Hold 2% Lidocaine soaked Q-tip over injection site for 30 seconds
- Draw up medication - filtered 19g needle on TB syringe/ prepare for injection (30g needle)
- Hold 2% Lidocaine soaked Q-tip over injection site for another 30 seconds
- Inject into vitreous cavity - hub of syringe to the sclera, use Q-tip in non-dominant hand to slide conjunctiva over injection site with needle withdraw
- Remove eyelid specula
- Optional - check perfusion of optic nerve with BIO
- Optional - check IOP
- No postop antibiotics (Artificial tears PRN)
What to Treat With?

• Use 0.05 cc dosing:
  • Avastin 1.25mg
  • Lucentis 0.3mg ; 0.5mg
  • Eylea 2mg
  • Triescence 2 mg
Treatment Protocols

- PRN therapy
  - Treat only if active disease / edema is present

- Fixed interval
  - Ex: Monthly treatment x 1-2 years of Lucentis / Avastin as in the monthly CATT study arms

- Treat and extend
  - Treat at each clinic visit, extend treatment interval if no active disease/ dry macula
  - If/ when recurrence develops - tighten treatment interval then fixed interval “for a while”.
Diseases Worth Treating

- Pseudophakic CME
- Macular edema associated with Retinal Vein Occlusion
- Diabetic Macular Edema
- Exudative ARMD
Pseudophakic CME - Ideal 1st Treatment Case

- Occurs in 1-2% of cases
- All cataract surgeons encounter this condition
- Self limiting disease
- Avoids the trip to Retina
- Not all cases respond to 1st line topical NSAIDs / Steroid
  - compliance
  - inflammation not fully controlled
- Most cases respond to one dose of Avastin (2nd line Tx)
  - “combined” CME/ DME cases often require multiple treatments
- Intravitreal Steroid (2mg Triesence) - 3rd line therapy
Macular Edema Associated with RVO

- Treatment options
  - Avastin - works in almost all cases
  - FDA approved - Eylea, Lucentis 0.5mg
- Use for center-involved macular edema
- Almost all cases respond to any ANTI-VEGF agent
- Early treatment provides better final visual acuity outcome versus delayed treatment
  - Treat as soon as center is involved
- Treat every 4-6 weeks until dry, then PRN or treat and extend
  - Some cases resolve in several months
Case #1 Va (RG) – Va 20/100

CMT - 644um

Signature:

Physician: Michael Rausch, M.D.
LLUMC
RG – 7 months of Avastin Tx – Va
20/40

Pre-treatment

Post-treatment
CS - Pre-Treatment 20/50 (673um)
CS 3 months post tx 20/30
EM 3 months after Avastin x 2 – Va 20/60 (440 um Heidelberg OCT)
Diabetic Macular Edema

- Center-involved DME requires Treatment with Anti-VEGF therapy
- Tx options: Avastin or Lucentis 0.3mg (FDA approved)
- DRCR-I study results
  - Average 8 injections within the 1st year with monthly follow-up and treatment of foveal DME
  - Average 2-3 injections in the 2nd year
- Early, aggressive therapy is best
- Avastin or Lucentis 0.3mg every 4-6 weeks - treat until dry
DRCR-I (Diabetic Retinopathy Clinical Research Network) Study

Visual Acuity (Letters Gained)

- Sham+prompt laser
- Ranibizumab +prompt laser
- Ranibizumab +deferred laser
- Triamcinolone +prompt laser

Primary outcome time point
DRCR-I Patient – Pretreatment (March 2008)

20/160  20/100
Pre-Treatment Imaging: OCT

OD
773 um

OS
790 um
Post-Treatment Imaging: Fundus Photos 2 yrs later

Visual Acuity - 20/30
Ranibizumab + deferred laser

Visual Acuity 20/800
Laser alone
Post-Treatment Imaging: OCT
Central Diabetic Macular Edema Injection Burden

- DRCR-I data (using their treatment protocol)

- Monthly clinic visits - Lucentis + deferred laser group
  - 1\textsuperscript{st} year - 8 injections
  - 2\textsuperscript{nd} year - 2-3 injections
  - 3\textsuperscript{rd} year - 1-2 injections
Exudative Age-Related Macular Degeneration

- The most difficult to manage
- Diagnosis is usually straightforward
  - Mimic cases
    - Chronic CSR
    - Adult vitelliform disease
    - ERM with CME
- Treatment options:
  - Avastin, Lucentis 0.5mg; Eylea 2mg
Exudative Age-Related Macular Degeneration

- Complex OCT findings
  - Edema
    - Intraretinal Edema / Subretinal fluid
      - Fluid almost always improves but may not resolve
      - ? treatment endpoint
  - Pigment Epithelial Detachment
    - More likely to need chronic therapy
- Need to look at multiple Retina OCT image cuts to fully understand anatomy and make treat decisions
Anchor Study: Secondary Endpoint: Mean Change in Visual Acuity Over Time

** note: Vertical bars are ± one standard error of the mean.

** PDT (n=143)

- Ranibizumab 0.3 mg (n=140)
- Ranibizumab 0.5 mg (n=139)

<table>
<thead>
<tr>
<th>Month</th>
<th>PDT</th>
<th>Ranibizumab 0.3 mg</th>
<th>Ranibizumab 0.5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

-15 -10 -5 0 5 10 15
0 1 2 3 4 5 6 7 8 9 10 11 12

ETDRS letters

Note: Vertical bars are ± one standard error of the mean.

* P < 0.0001
CATT Study (Comparison of Age-Related Macular Degeneration Treatment Trial)

- Comparison of Avastin vs Lucentis (Ranubizimab) for wet AMD therapy
- Multicenter clinical trial sponsored by National Eye Institute (not Genentech!)
- Designed to study the comparative efficacy of Avastin vs Lucentis, and also evaluate the “current practice” of PRN therapy vs monthly treatment regimens
- 1107 patients; monthly follow-up
- 4 treatment groups
  - Monthly Lu x1 yr; re-randomization to monthly vs PRN dosing
  - Monthly Avastin x1 yr; re-randomization to monthly vs PRN dosing
  - Lu PRN dosing x 2 yrs; after initial tx monthly evaluation and treat based signs of lesion activity
  - Avastin PRN dosing x 2 yrs; after initial tx monthly evaluation and treat based signs of lesion activity
CATT Study Summary

- Lucentis 0.5mg vs Avastin 1.25mg were equivalent in final visual outcome at 1 and 2 years
- Lucentis was better than Avastin in achieving a “dry” macula
- Monthly dosing (Lucentis / Avastin) vs PRN therapy by 2 years
  - Achieved slightly better final visual outcome vs PRN
  - Higher rate of geographic atrophy development
  - Higher rate of endophthalmitis
    - 10/11 pts in monthly treatment arm
    - 0.06% endophthalmitis injection rate
View Study Results

- Eylea q 4 week or q 8 week dosing interval (after monthly losing dose x 3) non-inferior to monthly Lucentis 0.5mg

- Dry macula at 4 months:
  - Lucentis 0.5mg - 70%
  - Eylea - 80%

- Eylea “Persistent edema” patients - better VA outcome with q 4 week therapy vs q 8 week therapy
Exudative AMD Injection Burden

• Combining injection data from CATT, Horizon, Seven Up studies:
  • 21-28 injections over 7 years
    • 5-7 injections in years 1 and 2
    • 4 injections in years 3 and 4
    • 1.6 years 5-7

Information presented at the Hawaiian Eye Meeting - Jan 2014
Exudative Age-Related Macular Degeneration

- Given more complex decision making process and evolving treatment paradigm - Injector alone model with Retina co-management may be best option
Summary

- Intravitreal injection therapies have revolutionized the treatment of retinal disorders
- Frequent injections are needed to stabilize disorders - many patients need chronic therapy
- The number of annual injections performed per year remains on a significant growth curve
- Comprehensive ophthalmologists will play an important role in the co-management of these patients