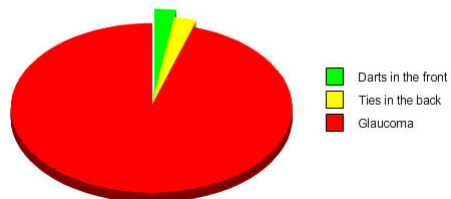Pressure Point – The Rationale and Utility of Target IOP in Glaucoma

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Silver Lining

Target IOP

Pros

- Clear objective makes management decisions easier

- Better patient buy-in with a defined target

Cons

- No one knows exactly what target IOP should be

- Could hinder needed personalization of treatment
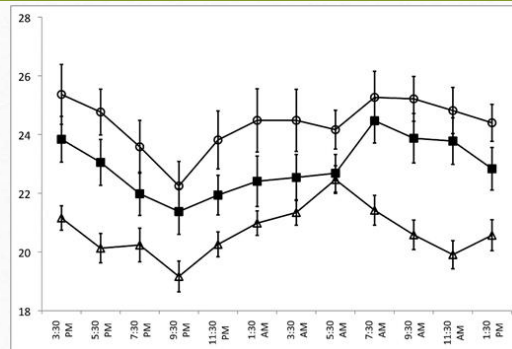
Target IOP

Too Aggressive

- Most importantly, may be unnecessary

- Increased cost to patient and to medical system

- Risk of associated complications

Too Lenient

- The obvious (nerve damage)

- More patients later requiring shunt surgery, which goes with the associated complications

IOP diurnal variation

IOP diurnal variation

- In healthy eyes, mean diurnal IOP variation is about 3-5 mmHg

- In eyes with POAG, mean diurnal variation is, on average, higher. Depending on the study, the mean variation in the untreated glaucoma patient is typically reported around 5-7mm Hg

- While some studies have shown no association, the majority of studies seem to be showing that a larger variation is an independent risk factor for glaucoma development and for VF progression in glaucoma. Jury is still out.

IOP range

- In light of knowing the large diurnal IOP variation, what does an individual IOP represent?
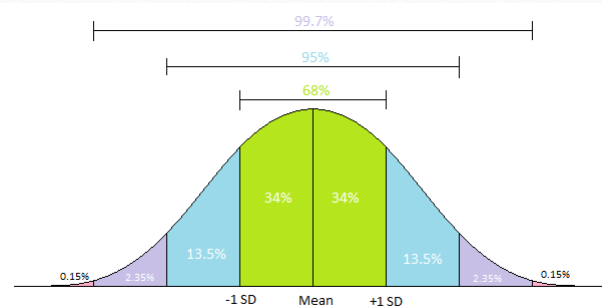
IOP range

- The two standard deviation range in an untreated glaucoma patient (mean being 5-7) is around 10-12 mmHg.

- So if a glaucoma patient's average IOP is 25, a single applanation measurement may conservatively range anywhere from 20 to 30. (IOP measurement will fall in this range 95% of the time)

- The variation is however suppressed in TREATED patients when IOP is in the normal range. Studies show the mean variation to be suppressed to about 5 (this value differs depending on the study. In general, the lower the IOP, the lower numerical variation)

So what do I make of an individual IOP?

- There's no way to know where the IOP we measure in a given day is falling in that 10mmHg range.
- However, we can know with strong certainty what the minimum average IOP is.
- For example, if we measure a pressure of 22, it's 95% probable that the patient's mean IOP is 17 or more.

Using individual IOPs

- Obviously the more measurements, the better, and even more so with checking IOP different times of day.
- Over time, this can allow for approximation of a mean. While useful, this takes several visits to establish with any reasonable reliability
- On the other hand, each IOP measured can define the minimum average IOP.
  - In other words, two measurements are taken, one 19 and one 23. While 21 could be the average, it's really quite unknown still. However we know with high certainty that the average IOP is 18 or greater (23-5).

Using individual IOPs

- One of the primary issues with setting a "target" IOP (meaning the goal for average IOP) is that it makes little sense to make a management decision based on any single IOP measurement. Additionally, around 40% of measurements will be above this number which for the patient can feel like failure.
  - For example, say you set a target IOP of 13 for a patient and initiate topical therapy. The next visit the IOP is 13, but the following visit the IOP is 15 (disappointed patient). Should you change therapy?
  - Again this is not to say that finding an average IOP over time isn't helpful. However, when setting a specific cutoff, it is easier to set a maximum IOP than an average IOP
  - So for example, a patient on treatment in the normal IOP range should have a variation of 5-6, and 2 standard deviations of variation should be no more than 8. So if you want the patient's average IOP to be 13, your maximum acceptable IOP would be 17. This gives a clearly defined decision point.

Using Max IOP

- Consider setting a "max" IOP (which you can still call a target IOP for the patient).
  - A patient with pre-perimetric open angle glaucoma comes in and you want the IOP to average 17 after starting treatment. Their P-max should then be set at 21.
  - At the subsequent visits, say the IOP is 16, 18, and 19. At each visit, the patient will be happy that they have met their goal on treatment = better patient buy-in. Even though you have two measurements above the average you are looking for, you know for now you can continue the same regimen.
  - You still have to use your brain. If over the year say the IOPs were measured at 18, 19, 19, 21 – you've learned that this particular patient has little variation and the average is probably higher than you would like. You would just revise down your maximum acceptable IOP.

Choosing a P-max

- A guideline only!
  - For primary open angle glaucoma:
    - Mild: Pre-perimetric or very early nasal step: 21 (average = 17)
    - Moderate: Field defect in one hemisphere, not involving central 20 degrees: 17 (average = 13)
    - Severe: Field defect in both hemispheres or in central 20 degrees: 14 (average = 11)
  - For NTG: Subtract 30% from initial IOP and add 3-4 = Pmax

Mild & Moderate glaucoma
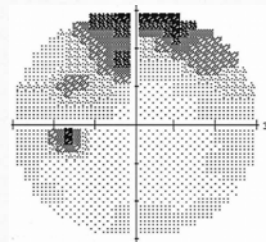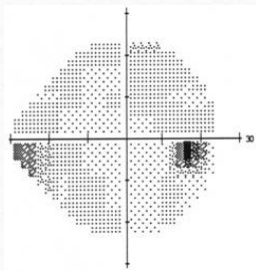
Advanced glaucoma
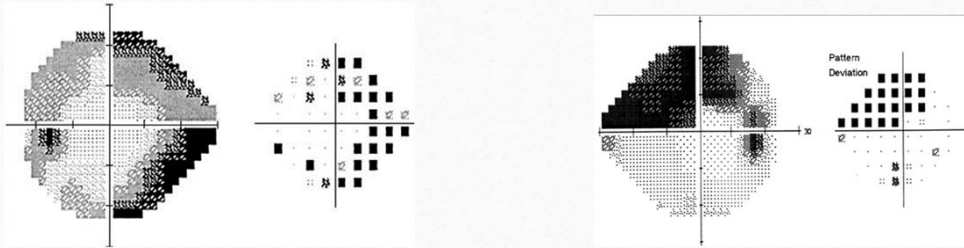
Why those numbers? – Mild glaucoma

- The CIGTS trial enrolled patients in general with more mild glaucoma, although there is some overlap with moderate/advanced. It is the best proxy of the major trials for mild glaucoma. This trial demonstrated that after 8 years on medication with an average IOP of 17-18, only 21% of patients had VF progression.

  - The surgery group achieved lower IOP but had similar VF progression. A difference in progression was only found in patients with more advanced disease

  - As VF progression in mild glaucoma patients achieving a mean IOP of 17-18 was similar to the lower IOP of 14-15, I can feel comfortable aiming for an average of 17 in mild glaucoma.

Why those numbers? - Moderate

- Less defined – no clear studies
- AGIS – In eyes that over 6 years had zero visits where IOP measured over 17, they had essentially zero visual field progression.
  - Although the average IOP of these eyes was slightly below 13 (12.3), these eyes represented on average a more advanced glaucoma population
  - While the evidence for a specific number is modest, targeting an average of 13 is highly probable to be sufficient for the vast majority of moderate glaucoma while not being unduly aggressive

Why those numbers? – Advanced glaucoma

- AGIS – as before, even in primarily advanced glaucoma maintaining an average IOP of 12.3 over 6 years resulted in essentially no VF progression.
  - Some patients included in this trial would also fit the "moderate" definition

- There is another study done in India with 245 patients (Sihota, et al) which followed patients over 10 years and demonstrated no VF progression in advanced glaucoma patients who maintained an average IOP between 10-12.

- This builds the case for a Pmax of 14 and mean of about 11 in true "advanced" glaucoma.

The "Art" of Glaucoma

Jackson Pollock Convergence Albright-Knox Art Gallery

The "Art" of Glaucoma

- Why these guidelines are just guidelines
  - In those with a short life expectancy, the RNFL will outlast the disease (and they probably don't want to spend their time in a glaucoma clinic)
  - Ticking time bombs (strong family history of blinding glaucoma and pachy of 470)
  - Studies tend to demonstrate that some patients will have VF progress despite good therapy and some people will retain VF despite no therapy
  - Still, guidelines provide an efficient starting point which will work for probably 80% of patients

Brief notes on treatment

- For drops, start with a PGA
  - If insurance covers it, bimatoprost has slightly higher efficacy
  - Branded PGAs tend to have better efficacy than generic if they're affordable
- Unless there is a contra-indication, typically go in order of efficacy: beta blocker, alpha agonist, carbonic anhydrase inhibitor.
  - Still learning where rho kinase inhibitors fit
  - Obviously use combinations to help with compliance

Brief notes on treatment

- When to use SLT?
  - I recommend as first treatment or second after PGA
    - This is what I'd choose for my own eye as first line
    - Improved chance of a good outcome when done 1st/2nd line -> builds patient trust
- When to refer for surgery eval?
  - Advanced glaucoma
  - Clear progression despite max topical therapy, regardless of IOP or level of VF loss
  - Obvious that topical therapy won't be sufficient or can't be administered long term
  - ?? Persistent need for several agents

Main takeaways

- Remember each IOP is somewhere along the 2 SD curve on either side of the mean. A single IOP only really tells you the patient's minimum average IOP

- Consider writing down a Pmax to use as a clear decision point and to help with patient buy-in (higher success rate)

- Consider the early, moderate and advanced Pmax of 21, 17, and 14 (with associated target means of 17, 13, and 11)

- Adjust your targets as you get more information points

Patient Scenario #1

- A new patient with no ocular history presents for comprehensive exam. IOP is measured at 19 OU, OCT ONH demonstrates ONH thinning and OD visual field is shown. Which of the following is the most appropriate next step?

  - Start latanoprost, see back in 1 month for IOP ck

  - Start latanoprost & combigan, 1 month for IOP ck

  - Recommend SLT in 1 month

  - Refer to glaucoma surgeon for possible shunt
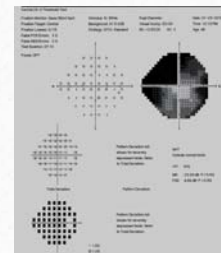
Patient Scenario #2

- You diagnosed a patient with glaucoma at their last visit and are seeing them back after starting bimatoprost. You previously set their goal for average IOP to be 13. Today, their IOP measures 15. The patient asks you if their treatment is not working. What can you tell them?
  - Their average IOP is too high and they need to start another medication
  - Their average IOP is too high, but we'll keep an eye on it
  - Their average IOP is 11 or higher, but we don't know yet if it's too high. Since the IOP is 17 or less we can continue to monitor for now
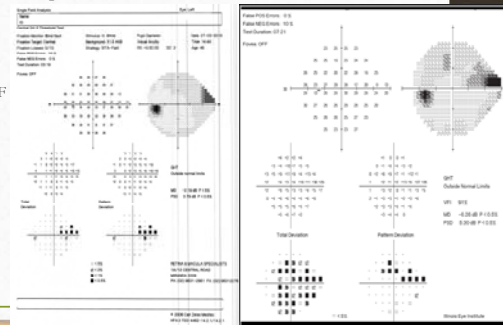
Patient Scenario #3

- A patient with no ocular history is referred for eval and you diagnose pre-perimetric glaucoma. Their IOP is 24 and you recommend achieving a mean IOP of 17 with a Pmax of 21. You start the patient on latanoprost and at the next appointment the IOP is 22. What is the most appropriate next step?
  - Monitor for now since the IOP is close to the Pmax
  - If not cost-prohibitive, switch the patient to bimatoprost
  - Start the patient on combigan and continue latanoprost

Patient scenario #4

- You diagnose a patient with mild glaucoma and set a target mean of 17 and Pmax of 21, then start the patient on bimatoprost. Over the next two years the IOP is always in target range with a mean IOP of 16. The visual field two years later is shown on the right. What is the most appropriate next step?

  - Continue to monitor, mean IOP has been achieved
  - Revise the target mean to 11, Pmax to 14, start Combigan, f/u 1 month for repeat VF
  - Refer emergently for possible shunting procedure

Patient Scenario #5

- A 50 yo patient who lives alone with severe rheumatoid arthritis (can barely shake your hand) is brought in for eval and you diagnose the patient with moderate glaucoma. IOP measures 33. What is the most appropriate next step?

  - Prescribe bimatoprost and combigan and see back in 1 month

  - Refer for SLT

  - Have the patient attempt to put in ATs while in clinic. When they are unable, refer the patient urgently for shunt eval and consider Diamox based on timeline