Introduction/Overview

1) Evaluation of the Optic Nerve requires descriptive quantitative and qualitative intrapapillary and parapapillary regions of the optic nerve head and the retinal nerve fiber layer (RNFL) variables including:
   a. Size and shape of the optic disc
   b. Size, shape and pallor of the neuroretinal rim
   c. Configuration and depth of the optic cup
   d. Cup-disc diameter ratio and cup-disc area ratio
   e. Position of the exit of the central retinal vessel trunk on the lamina cribrosa surface
   f. Presence and location of splinter-shaped hemorrhages
   g. Occurrence, size, configuration and location of parapapillary chorioretinal atrophy
   h. Diffuse and/or focal decrease of the diameter of the retinal arterioles
   i. Visibility of the retinal nerve fiber layer defects – local or diffuse

2) Unlike qualitative variables almost all quantitative variables have overlap between normal and glaucoma subjects...so qualitative variables are very important and have higher specificity in separating glaucoma eyes from normal eyes.

3) Despite technological advances, clinical identification of the optic nerve head characteristics remains the first step in diagnosis.
   a. Document with photographs and discograms

4) Goal: Differentiate between glaucomatous, nonglaucomatous, and normal optic nerves.

Optic Disk Size

1) Pearls
   a) Optic Disc size is of utmost importance since the optic disc size is correlated with the size of the optic cup and neuroretinal rim
      i) The larger the optic disc, the larger the cup and neuroretinal rim.
      ii) The disc size determines the CD ratio and the neuroretinal rim area.
      iii) Look for the thin white band encircling the disk to define the borders of the disk. This is the inner side of the peripapillary scleral ring
         (1) Most easily detected on the temporal sides
         (2) Compare the disc sizes of both eyes and look for asymmetry
            (a) Asymmetry possibly due to refractive status of the eye or the axial length.
            (b) Size asymmetry may account for CDR and NRR asymmetry.
b) A large cup in a large optic disc can be normal and an average cup in a small disc can suggest glaucomatous optic nerve damage.
   i) Size by itself does not determine glaucoma.

2) Variable Disk area with interindividual variability of .8mm2 to almost 6.0mm2 in a normal white population...i.e. Normal eyes with small optic disks and normal eyes with large optic discs
   a) Age: disk area independent of age beyond 10 years
   b) Gender: inconclusive with no variation to recent studies suggest 3.2% larger in men than women
   c) Body Length/weight: inconclusive with no variation to increased disc area of 0.02mm2 with each 10cm increase in body length (study excluded very tall and very small people)
   d) Refractive Error: within -5 to +5 D, statistically independent, new studies suggested disk area linearly increased by 1.2% +/-0.15% for each diopter toward myopia
      i) Higher Hyperopia (>+5): smaller disk than normal refractive error eyes
      ii) Higher Myopia(>-8): larger disk than normal refractive error eyes
   e) Race: AA>Asians>Mexicans>White (large-small) “one may infer that the disk size increases with ethnically determined pigmentation”

3) Microdisks: “smaller than the mean minus twofold SD”

4) Macrodisks: “larger than the mean plus twofold SD”
   a) Accounts for only 2.3% of population
   b) Primary Macrodisk:
      i) Independent of age after the first years of life
      ii) Independent of or only slightly dependent on refractive error
      iii) Marginally correlated with the size of the cornea (the larger the disk, the larger the cornea and the larger the anterior corneal curvature radius)
         (1) Asymptomatic Primary Macrodisk
            a) No morphologic or functional defects
         (2) Symptomatic Primary Macrodisk
            a) With morphologic and functional defects
               i) Optic disk pits
               ii) Morning glory syndrome
   c) Secondary Acquired Macrodisk:
      i) Increases in size after birth/with age
         (1) Usually in eyes with myopia, positively correlated

5) Morphogenetic Implications:
   a) Larger Optic Disks (as compared to smaller optic discs) have:
      i) A larger neuroretinal rim area
      ii) More optic nerve fibers
         (1) More lamina cribrosa pores/area
         (2) Therefore, small optic discs have a smaller anatomic reserve capacity
iii) Less nerve fiber crowding per square mm of disk area
iv) Higher count of cilioretinal arteries
v) Higher count of retinal photoreceptors and RPE cells with a larger retinal surface area and longer horizontal and vertical diameters of the globe.
vi) The larger the optic disc, the larger the optic cup and neuroretinal rim.
   (1) Therefore, a large cup in a large optic disc can be normal while a small avg optic cup in a very small optic disc suggests glaucomatous damage.

6) Pathogenetic Implications:
a) Small Discs: more commonly have optic disc drusen, pseudopapilledema, NAION
b) Larger Discs: more commonly have pits and the morning-glory syndrome
   i) Increased glaucoma susceptibility??: a few theories
      (1) Observed in AA
      (2) Larger in patients with NTG than POAG
         (a) Will usually also have a larger cup and therefore NTG patients will have a higher probability of detection and or referral/additional workup...
         (i) Patients with early NTG have a higher chance of detection if:
            1. Their disc is large
            2. Or if there is already sufficient glaucomatous cupping even if the nerve is avg size
      (3) Greater translaminar pressure difference
      (4) Increased risk of neuroretinal rim loss in regions with a long distance to the exit of the central retinal vessel trunk than in sectors with a short distance.
   ii) No increased glaucoma susceptibility:
      (1) Intraindividual bilateral comparison of non-highly myopic white patients with NTG or POAG showed that the larger nerve “showed neither a more marked nor a less pronounced glaucomatous optic nerve damage”
      c) Normal Discs: AION and retinal vessel occlusions, POAG (including juvenile-onset), age-related atrophy type of POAG, Secondary OAG (pigmentary>PXF)

7) Measurement of the Optic Disk Size:
a) Photos
b) Scanning Laser Tomography
c) Clinical Assessment
   i) Identify the optic disk limits as all of the area inside of the peripapillary scleral ring
      (1) Peripapillary scleral ring does not belong to the optic disc
      (2) Including the peripapillary scleral ring into the disc area will:
         (a) Increase the neuroretinal rim area
         (b) Decrease the cup-disc ratio
            (i) May cause us to underestimate the real damage and undertreat the patient!
   ii) Adjust beam length to the diameter of the optic disc, read on scale
   iii) Calculate disc area (Area = 3.14…r/4 x horizontal diameter x vertical diameter)
      (1) Modified formula of an ellipse
Optic Disk Shape

1) Slightly vertically oval
   a) Vertical diameter ~ 7-10% larger than the horizontal diameter
   b) Maximal disk diameter nearly equal to vertical diameter, horizontal diameter is almost equal to the minimal diameter
      i) Can also have round optic nerves
         (1) ISNT rule not always applicable in disks that are not vertically oval.
   c) Disk Form not correlated with age, sex, OD or OS, body weight, body height
      i) Correlated with increased corneal astigmatism and amblyopia
         (1) Corneal astigmatism was significantly highest in eyes with tilted disc and significantly smallest in eyes with an almost circular disk shape
            (a) The orientation of the longest disk diameter can indicate the axis of the corneal astigmatism
               (i) Consider K’s, retinoscopy in children if ONH is abnormal shape
            (b) Tilted disks (three-dimensional angulation of the anteroposterior optic cup axis) can have temporal hemianopsia – like VF defects that may be due to inferior nasal fundus hypopigmentation...careful to not diagnose as glaucomatous.
               (i) A torted optic disc is when the vertical axis of the optic dis is rotated >15 degrees.
         (2) Amblyopia significantly associated with an elongated optic disc shape and high corneal astigmatism

2) Glaucoma susceptibility is mostly independent of the shape of the optic disc
   a) As a single variable, Optic Disc Shape is not markedly important for diagnosis and pathogenesis of glaucoma in eyes with myopia < -8D
      i) But can be a factor because the optic disc shape influences the distance between the neuroretinal rim at the disc border and the central retinal vessel trunk.
   b) High Myopes (> -12D)
      i) Disc is more oval, elongated than any other group
      ii) More obliquely oriented than any other group
         (1) More myopic stretching does not exert a similar traction on the optic disc in all directions, some meridians are drawn stronger than others.
            (a) Does this irregular stretching increase glaucomatous susceptibility?

Neuroretinal Rim Size
1) Pearls
   a) The intrapapillary equivalent of the retinal nerve fibers and optic nerve fibers
   b) One of main targets of glaucoma eval
      i) ***Regarding morphologic glaucoma diagnosis, “the neuroretinal rim area is one of the
         most important quantitative variables”...but due to high interindividual variability in the
         normal population and early glaucoma there can be significant overlap
         (1) To have achieve higher diagnostic power, break up the disc into sectors
            (a) The Inferotemporal and superotemporal disc sector has a higher predictive power
                that the neuroretinal rim as a whole due to preferential loss of neuroretinal rim in
                the inferior and superior disc regions in the early to medium advanced stages of the
                disease.
   c) Similar to the optic disc size, high interindividual variability
      i) Correlate with the optic disk area...the larger the disc, the larger the rim
   d) Rim area is greatest with no disc cupping then less with temporal flat/sloping of the optic cup,
      and least in eyes with circular, steep disc cupping.
   e) Rim area and disc area corresponds with the positive correlation of optic disc size, optic fiber
      count, and total area of the lamina cribrosa pores.
   f) The nerve fibers within the neuroretinal rim are retinotopically arranged.
      i) Axons from ganglion cells close to the optic disc lie more centrally in the optic disc whereas
         axons from cells in the retinal periphery lie at the optic nerve head margins.

Neuroretinal Rim Shape

1) Neuroretinal Rim Shape Pearls
   a) Due to vertical oval shape of optic disc and the horizontal oval shape of the optic cup, usually
      follows ISNT rule (most broad to least broad)
      i) Helpful in diagnosing early glaucoma suspect in OHTN eyes prior to VF defects
      ii) Characteristic shape is so very important in the diagnosis of early glaucomatous optic nerve
          damage in OCHTN eyes prior to white-on-white VF defects
          (1) i.e., If “normal” HVF and (+) OCHTN, does the rim conform to the ISNT rule??
   b) The shape of the is associated with the following:
      i) The diameter of the retinal arterioles (wider in the IT arcade than in ST arcade)
      ii) The visibility of the RNFL bundles : significantly more often better detectable in the IT
          region than the ST region
      iii) The location of the foveola .53 +/- .34 mm inferior to the optic disc center
      iv) The morphology of the laminar cribrosa : the largest pores, and relatively the least amount
          of interpore connective tissue in the Inferior and Superior regions as compared with the
          temporal and nasal sectors
c) Glaucoma Damage:
   i) Regional preferences of neuroretinal rim loss depending on the stage of the disease...but can have diffuse loss too.
      (1) Early: rim loss is usually in the IT and ST disk regions; therefore LOOK very closely in these regions
      (2) Moderate: rim loss most relatively occurs in the temporal horizontal disk region
      (3) Advanced: inferior nasal then superior nasal rim loss
   ii) The sequence of disc sector rim loss (IT ->ST->Temporal Horizontal->Nasal Inferior->Nasal Superior) correlates with the progression of VF defects:
      (1) Early VF loss: nasal upper quadrant
      (2) Advanced VF loss: island of VA in the temporal inferior part of the VF
      (3) The larger the distance to the central retinal vessel trunk exit on the lamina cribrosa to the neuroretinal rim the more pronounced the loss of neuretinal rim and the perimetric defect in the corresponding visual field quadrant

d) Neuroretinal Rim Pallor
   i) A sign of optic nerve damage
      (1) More noticeable in eyes with nonglaucomatous optic neuropathy than in eyes with glaucoma...i.e. a pale rim is more likely due to nonglaucomatous optic neuropathy than glaucomatous optic neuropathy.
         (a) In glaucoma, if there is pallor, the overall pallor of the optic disc is mainly due to the enlargement of the pale optic cup
      (2) Non-glaucomatous optic nerve damage is usually not associated with neuroretinal rim loss, just pallor...pallor is one of the variables that is helpful to differentiate among glaucomatous and nonglaucomatous optic neuropathy

Optic Cup Size in Relation to the Optic Disc Size

1) General: The optic cup is the excavation in the optic nerve head, VERY important to consider when considering the cup size
   a) The size of the cup is determined by the size of the optic disk
      i) Positive correlation between the vertical diameter and the vertical CDR.
         (1) A large disk will have a large cup, an average disk will have an averaged size cup, and a small disk will usually have no cup.
         (a) Important principle to remember as early or even moderately advanced glaucoma may be missed is we judge only using the CDR
b) Border is determined by contour and NOT by pallor, therefore must examine stereoscopically
   i) Contour cup is more important than the color of the cup
      (1) The second kink in the blood vessel determines the cup margin.
         (a) The cup is horizontally oval
            (i) Mean horizontal CDR is 0.66 and mean vertical CDR is 0.56.

c) High interindividual variability (similar to the optic disk and neurretinal rim)
   i) Primary macrocups occur in primary macrodisks (pseudoglaucomatous/physiologic)
      (1) The Larger the optic disc, the larger the optic cup (pseudoglaucomatous – risk for over treatment)
      (2) Small optic discs normally have no optic cup (pseudonormal – risk for undertreatment!)
   ii) Constant in size after first years of life
   iii) In normal eyes, the areas of the optic disk and the optic cup are correlated...the larger the optic disc, the larger the optic cup (in contrast to glaucoma, the optic cup does not markedly enlarge and the neuroretinal rim will not decrease)
   iv) In small optic disks, cupping normally does not occur...small optic disks normally have no optic cup.
      (1) Early or moderately advanced glaucomatous optic nerve damage may erroneously be overlooked in small disks (“pseudonormal”)
         (a) Look carefully in the parapapillary region such as decreased visibility of the RNFL, diffusely diminished diameter of the retinal arterioles and/or focally reduced arteriole diameter, and parapapillary chorioretinal atrophy.
         (b) In contrast, a large optic cup in a large optic disk should not lead to the Dx of glaucoma if the other intrapapillary variables are normal, mainly the configuration of the neuroretinal rim.
   v) In addition to PPA, disk pallor, and depth of the optic cup, the increase in cup area is an important marker to differentiate between glaucomatous and nonglaucomatous optic nerve damage.
      (1) In other words, in contrast to glaucoma, the optic cup does not usually markedly enlarge in eyes with non-glaucomatous optic nerve damage. So therefore, the neuroretinal rim does not significantly decrease in eyes with non-glaucomatous optic nerve damage.

 Configuration and Depth of the Optic Cup

1) Normal Eyes
   a. The shape of the optic cup is horizontally oval...the horizontal diameter is about 8% longer than the vertical diameter.
   b. The shape of the optic disk is vertically oval, therefore the normal neuroretinal rim is broadest in the inferior and superior disk regions.
c. Optic Cup Depth
   i. Normal Eyes: Cup depth depends directly on the cup area and indirectly on the disk size...the larger the optic cup, the deeper it is.
   ii. Glaucoma Eyes
      1. Cup depth deepens depending on the type of glaucoma and level of IOP
         a. The deepest optic cups can be found in glaucomatous eyes with high minimal values of IOP (Juvenile-onset and Angle recession glaucoma)
         b. The optic cup is most shallow in eyes with the highly myopic type of POAG and eyes with the age-related atrophic type of POAG
         c. The depth of the cup is slightly associated with the degree of PPA...the deeper and steeper the cup, the smaller the PPA.

Cup/Disk Ratios

1) Pearls:
   a. Normal Eyes:
      i. Larger CDR horizontally than vertically (b/c of the vertically oval optic disk and the horizontally oval optic cup) except in less than 7% of normal eyes (therefore, for most of the eyes the quotient of the horizontal to vertical CDR is usually higher than 1.0
         1. In early to medium advanced stages, the vertical CDR increases faster than the horizontal CDR leading to an increase of the quotient of horizontal to vertical CDR to values lower than 1.0
         2. Independent of the size of the optic cup and disk
      ii. Dependent on the size of the optic disc and cup...therefore high variability and can be 0.0 to almost 0.9.
         1. Low CDR in smaller nerves with large CDR in larger nerves...both normal (physiologic)!
            a. Avoid overdiagnosing with large CDRs in large disks and underdiagnosing/misdiagnosing avg CDR in ocular hypertensive eyes with small nerves.
            b. May consider physiologic cupping as a diagnosis ONLY IF the nerve is larger to??-al
            c. Use an “optic disc grid”
      iii. Independent of the magnification, photos, etc
Position of the Exit of the Central Retinal Vessel Trunk on the Lamina Cribrosa Surface

1) Pearls:
   a. The local susceptibility for glaucomatous neuroretinal rim loss partially depends on the distance to the exit of the central retinal vessel trunk on the lamina cribrosa surface. (perhaps the retinal vessel trunk could act as a stabilizing element against glaucomatous changes in the lamina cribrosa. It could render more difficult a mechanical distortion and backward bowing of the lamina cribrosa in glaucoma AND/OR could speculate that the vascular supply to the adjacent tissue is better in closer vicinity of the retinal trunk than in the periphery...
      i. Former hypothesis supported by photographs of a W-shaped lamina cribrosa in glaucomatous eyes.
         1. The lamina cribrosa is more condensed and bowed more to the back in the inferior and superior disk regions than close to the center of the lamina cribrosa, where the retinal vessels emerge
         2. Superiornasal vessel trunk decentration -> leaves the inferiortemporal disk region without support by the vessel trunk ->more easily deformed IT sector compared to the SN sector
            a. May explain why we have increased frequency of IT neuroretinal rim notches than the ST sector in eyes with a normal disk shape and a normal position of the vessel trunk exit.
      ii. “The longer the distance to the central retinal vessel trunk exit from the neuroretinal rim, the more marked the glaucomatous loss of neuroretinal rim and the loss of visual field in the corresponding visual field quadrant...and the more enlarged the PPA in glaucomatous eyes compared with normal eyes.
         1. Consistent with glaucomatous neuroretinal rim loss inside of the optic disc and enlargement of PPA outside of the optic disc border.
         2. Spatially correlated PPA may be due to the backward bowing of the lamina cribrosa leading to backward draw of Bruch’s membrane leading to a compression of the PPA choriocapillaris with resulting damage of the RPE and deep retinal layers???
3. The longer the distance to the CRV trunk exit, the more enlarged was parapapillary atrophy in glaucomatous eyes compared with normal eyes.

iii. “The location of the central retinal vessel trunk exit can, therefore, be one of the several factors influencing local glaucoma susceptibility for NFL loss within the region of the optic disc.

iv. “Eyes with OAG and a temporal cilioretinal artery retained longer central visual field (and temporal neuroretinal rim) than OAG eyes without a temporal cilioretinal artery”

1. ??Better perfusion and/or supportive and stabilizing element

b. “In glaucomatous eyes with high IOP, deep and steep cupping, and relatively fast development of optic nerve damage, neuroretinal rim loss may occur earlier than parapapillary atrophy can develop…”

Optic Disk Hemorrhages

1) Prevalence and Incidence
   a. Normal population: 0-1.4% (so “…high specificity of about 99% points toward a helpful role in the early diagnosis of glaucoma…but not at all sufficient to separate normal eyes and eyes with early glaucoma”)
   b. OCHTN/Glaucoma: 2-33.4%
      i. Therefore high specificity because they rarely are “…found in normal eyes and they usually indicate the presence of glaucomatous optic nerve damage even if the visual field is unremarkable and they suggest progression of glaucoma.”
         1. But still has low sensitivity so not a useful tool in screening exams for glaucoma

2) Pearls:
   a. Splinter-shaped/flame-shaped hemorrhages at the border of the optic disk “hallmark of glaucomatous optic nerve atrophy”
      i. Usually thin in appearance and oriented perpendicular to the disk margin
         1. May be more flame or fan-shaped if abundant extravasation
         2. Shape due to orientation of the RNFL axons
         3. Can be on the optic disk tissue (laminar or prelaminar), on the neuroretinal rim, or in the peripapillary zone.
            a. If within the optic disc, then likely due to laminar pore tissue remodeling
               i. More common in myopic eyes
            b. Peripapillary disc hemes associated with RNFL defect
ii. Rarely (or very rarely) found in normal eyes
   1. May represent the extreme of disk hemorrhages in a possible spectrum of hemorrhages including also microscopical bleeding undetectable on ophthalmoscopy...so all figures related to frequencies of bleeding would relate to only a fraction of the total disk hemorrhages.

iii. Detected in 4-7% of eyes with glaucoma
   1. Associated with localized RNFL defects, neuroretinal rim notches, and circumscribed perimetrical loss
      a. Usually located more in the inferior temporal and/or superior temporal areas of the optic disc
   2. Duration
      a. Visible for 8 days – 12 weeks after the initial bleeding.
         i. Possible that higher IOP may stop bleeding relatively early -> smaller disk hemorrhage in high pressure glaucomatous eyes (therefore...must look closer in HPG than NPG??)
         ii. Possible that a lower IOP may stop bleeding relatively late -> larger disk hemorrhage in low pressure glaucomatous eyes
         iii. Therefore faster absorption of disk hemorrhages in eyes with HPG than NPG -> longer visibility of bleeding in NPG (larger hemes that last longer!) -> falsely higher incidence of hemorrhages in NPG than HPG??
   iv. Frequency increases from an early stage of glaucoma to medium-advanced glaucoma and then decreases again toward advanced glaucoma.
      1. About half of all initial hemorrhages were detected in the first year and about ¾ after 3 years. After 5 years of follow-up, however, few initial hemorrhages were found.
         a. “...disk hemorrhages are not found in disk regions or eyes without detectable neuroretinal rim”
      2. In early glaucoma, usually located in the IT or ST disk regions

3) Diagnostic Importance:
   a. High specificity of 99%
      i. Frequency of disk hemorrhages in nonglaucomatous eyes was about 1%
      ii. Usually indicates the presence of glaucomatous optic nerve damage (even if WNL HVF)
      iii. Suggests progression
   b. Low sensitivity:
      i. Other optic nerve diseases can have disc hemorrhages
         1. Posterior vitreous detachment, Optic disc drusen, vascular occlusive diseases of the retina, and systemic conditions (diabetes, hypertension, leukemia, systemic lupus erythematos)
a. Glaucomatous disk hemorrhages
   ii. Can’t be taken as a single variable to separate normal eyes from eyes with early glaucoma.
      1. Assume that disc hemorrhages do not develop in all patients with open-angle glaucoma or ocular hypertension.
   c. ~2 months after initial bleeding: may develop a localized defect of the RNFL and/or a broadening of a localized RNFL defect correlating with a circumscribed scotoma in the visual field
   d. Detection methods: Better detected with stereoscopic disk photography than by clinical examination
      i. OHTS: “80% of disk hemorrhages were only seen on disk photographs”
      ii. Detection can be more frequent and by more careful clinical examinations.
      iii. “Regarding the prognostic importance of disk hemorrhages, detection efforts should use both stereoscopic disc photography and clinical examination.”
4) Differences between the various glaucoma types
   a. Frequency of optic disk hemorrhages differs between the various types of OAG
      i. Disk hemorrhages were found most often in patients with focal NTG
         1. May be a falsely high frequency in NTG compared to patients with HTG because patients with NTG are more likely to be under care already because of how the optic nerve looked to begin with and they are more likely in a clinic based setting rather than a screening population based setting...possible bias?
         2. Disk hemorrhage is approximately 2-5 times more frequent in NTG than in HTG
            a. One study reported disc hemorrhages in 45.5% of eyes with NTG and 23.2% in eyes with HTG
            ii. Less frequent in patients with juvenile-onset POAG, age-related atrophic POAG, and highly myopic POAG
            iii. Disk hemorrhages can be found in all types of the chronic open angle glaucomas...suggesting that the pathomechanism associated with disk hemorrhages may be present in all these glaucoma types.
            iv. Primary angle-closure prevalence: 0.5%-5.7%
            v. http://content.time.com/time/video/player/0,32068,2603162825001_2149482,00.html
5) Pathogenetic Implications:
   a. Traumatic rather than ischemic...because no cotton wool spot?
   b. Due to four abnormal/imbalanced biomechanical forces on the lamina cribrosa and surrounding tissue:
      i. Intraocular Pressure
         1. Disc hemorrhages are not dependent on the IOP (higher prevalence of disc heme in NTG than HTG)?
a. Some “bleeders” (those who tend to develop disk hemorrhages) will continue to have hemorrhages despite IOP reduction, especially among NTG patients.

2. Disc hemorrhages are dependent on IOP?
   a. Trabeculectomy decreased incidence of disc hemorrhages in both NTG (42%-23%) and HTG (33%-6%) groups
   b. OHTS: IOP reduction decreased the risk of disk hemorrhages
   c. Disc hemorrhages develop more commonly in superior and inferior areas of the lamina cribrosa that contain large pores with less connective tissue—areas that are more susceptible to IOP related mechanical damage.

ii. Cerebrospinal Fluid Pressure:
   1. Translaminar pressure Gradient
      a. Lamina cribrosa: acts as a barrier (6-10 layers of connective tissue with 200-400 pores each) with a pressure gradient between CSP and IOP.
         i. One study suggested that the lamina cribrosa was significantly thinner in NTG patients with disc hemorrhages than in those without.
            1. Due to less supportive connective tissue to the axons -> steeper translaminar pressure gradients and high IOP-related stress on the optic nerve head.
   iii. Arterial Pressure: Systemic HTN may cause increased arterial pressure on the optic nerve
   iv. Venous Pressure: Increased venous pressure from Valsalva or head down posture may increase risk of disc hemorrhage by possibly increased episcleral venous pressure and choroidal expansion

Parapapillary Chorioretinal Atrophy

1) Overview
   a. “Halo glaucomatosus” - Elschnig (circa early 20\textsuperscript{th} century)
      i. Totally encircles eyes with end-stage glaucoma
      ii. Usually associated with marked fundus tessellation, shallow glaucomatous cupping, relatively low frequency of disk hemes and detectable localized RNFL defect, a mostly concentric loss of neuroretinal rim, and normal or almost normal IOP measurements.
b. (+) spatial correlation between the PPA and the location of the most marked visual field loss (– Heijl/Samander) and the neuroretinal rim loss in the intrapapillary region (larger in that sector with the more marked loss of neuroretinal rim AND in that quadrant that has the longest distance to the exit of the central retinal vessel trunk on the lamina cribrosa.)
   i. PPA is larger in that sector with the more marked loss of neuroretinal rim
   ii. The more neuroretinal rim loss, the greater the the area of PPA

c. Divided into a central beta zone and a peripheral alpha zone

d. “Presence or extend of a crescent correlated with the glauomatous disk damage” – Anderson

e. Progression of PPA, (especially beta zone) was described as an early glaucomatous finding in some patients with OCHTN
   i. Presence and size of parapapillary atrophy was related to the development of subsequent optic disc or visual field damage in patients with OCHTN
   ii. In patients with NTG, disc hemorrhages were closely associated with the size of parapapillary atrophy...so PPA is important in the morphologic diagnosis of glaucomatous optic neuropathy
      1. However, NON-glaucomatous optic nerve damage does not lead to an enlargement of parapapillary atrophy.
         a. One of few variables to distinguish between glaucomatous and non-glaucomatous optic nerve damage.

f. In normal eyes, both alpha and beta zone are largest and most frequently located in the temporal and horizontal sector followed by the inferior temporal and superior temporal region and smallest and most rarely found in the nasal parapapillary area.

g. Alpha and Beta PPA is different from myopic scleral crescents and/or tilted discs in that in the region of the myopic crescent, only the inner limiting membrane and underlying retinal NFL or its remnants cover the sclera while in the glaucoma Beta Zone, Bruch’s membrane and the choroid is interposed between the remnants of the retina an sclera.

h. Size, shape and frequency of alpha and beta zones do not differ significantly between normal eyes and eyes with non-glaucomatous optic nerve atrophy.
   i. Both zones however are significantly larger and beta zones occurs more often in eyes with glaucomatous optic nerve atrophy than in normal eyes.
      1. Size and frequency of beta zone significantly correlated with variables indicating the severity of the glaucomatous optic nerve damage such as neuroretinal rim loss, decrease of retina vessel diameter, reduced visibility of the RNFL bundles, and perimetric defects
   i. Frequently gets worse (enlarges) with glaucoma progression, nonglaucomatous optic nerve damage does not lead to enlargement of the PPA
      i. Therefore, PPA is one of the few factors that helps differentiate between glaucomatous and nonglaucomatous optic nerve damage.
         1. Very important morphologic finding of glaucomatous optic neuropathy
a. The depth of the cup is slightly associated with the degree of PPA...the deeper and steeper the cup, the smaller the PPA.

ii. “The longer the distance to the central retinal vessel trunk exit from the neuroretinal rim, the more marked the glaucomatous loss of neuroretinal rim and the loss of visual field in the corresponding visual field quadrant...and the more enlarged the PPA in glaucomatous eyes compared with normal eyes.

1. Consistent with glaucomatous neuroretinal rim loss inside of the optic disc and enlargement of PPA outside of the optic disc border.

2. Spatially correlated PPA may be due to the backward bowing of the lamina cribrosa leading to backward draw of Bruch’s membrane leading to a compression of the PPA choriocapillaris with resulting damage of the RPE and deep retinal layers?

3. The longer the distance to the CRV trunk exit, the more enlarged was parapapillary atrophy in glaucomatous eyes compared with normal eyes.

   a. The longer the distance to the CRV trunk, the larger is the beta zone.

2) Alpha Zone

   a. Peripheral zone, irregular hypopigmentation/hyperpigmentation and intimated thinning of the chorioretinal tissue layer

   b. Outer side is adjacent to the retina, inner side is adjacent either to the peripapillary scleral ring OR the beta zone (visible sclera and visible large choroidal vessels)

   c. Equivalent to pigmentary irregularities in the RPE

   d. Found in almost ALL normal eyes (15-20%), therefore more common than beta zone

   e. Relative scotoma

3) Beta Zone

   a. Adjacent to the peripapillary scleral ring, The Beta zone Borders the optic nerve

   b. Marked RPE atrophy and choriocapillaris, easily visible sclera and easily visible large choroidal vessels, thinning of the chorioretinal tissues, and smooth margins to the adjacent alpha zone on its peripheral side and to the peripapillary scleral ring on its central side

   c. If both zones are present, the beta zone is always closer to the optic disc than the alpha zone.

   d. Correlates with a complete loss of RPE, may allow the visualization of the circle of Zinn-haller

   e. Absolute scotoma

   f. Occurs more commonly in eyes with glaucomatous optic neuropathy than in normal eyes

      i. Size and frequency of Beta zone significantly associated with glaucomatous ONH damage, neuroretinal rim loss, decreased retinal vessel diameter, reduced RNFL visibility, VF defects
ii. Larger and occurred more often in monkey eyes after induced increase in IOP (after an ample period of time)
g. Can be considered an early sign of glaucoma in OHTN patients
h. Disc hemorrhages were closely associated with the size of the parapapillary atrophy
i. Focal arteriole narrowing was mostly independent of parapapillary atrophy.
4) Parapapillary Atrophy in the Various Types of OAG
a. Beta Zone (largest) High myopic POAG> Age-related atrophic POAG>Secondary OAG (PXF, PDS, and non-highly myopic POAG)>juvenile-onset POAG (smallest).
b. NTG: +/- PPA is larger in size in NTG than in POAG??

**Diameter of Retinal Arterioles**

1) Overview:
   a. Vessel diameter reduces with deceasing area of the neuroretinal rim, diminishing visibility of the RNFL and increasing VF defects.
      i. Studies show that it was actual stenosis of the vessel lumen...not an ophthalmoscopic artifact.
   b. Typical of optic nerve damage but not characteristic of glaucoma...low sensitivity?
      i. Also found in NAIONs, descending optic nerve atrophy (nonglaucomatous etiologies), advancing age.
         1. Severity of focal narrowing did not vary significantly between glaucomatous and nonglaucomatous optic nerve atrophy
         2. Perhaps slightly more narrow in eyes with NTG and eyes with NAIONs than other groups...(suggests NTG is a sort of slow NAION??-al)
      ii. Therefore, does NOT cause glaucoma but perhaps the vessel reduction is, at least partially, secondary to a reduced demand in the superficial layers of the retina.
   2) For glaucoma, the degree of focal narrowing of the retinal arterioles was significantly more pronounced if the optic nerve damage was more advanced.
   3) Focal arteriole narrowing was mostly independent of parapapillary atrophy.
   4) NOT specific for glaucoma and does not play a major specific role in the pathogenesis of glaucoma.
   5) Retinal arteriole diameters are widest at the temporal inferior disk borders, then temporal superior, then nasal superior area, and then nasal inferior disk region (corresponds to same order as NFL ease of visibility)
      a. Therefore, compare inferior vessels to the superior vessels to look for early glaucoma too?? - al
Evaluation of the Retinal Nerve Fiber Layer

1) Overview
   a. RNFL = the retinal ganglion cell axons that are covered by astrocytes and bundled by processes of Muller cells
      i. Easier to see with green light
      ii. More easily visible with clear media and deeply pigmented RPE
          1. Appears as bright, fine striations in the inner retinal layer fanning off of optic disk to the retinal periphery.
             a. Striations are actually tissue canals in which Muller cells process gather the axons into 20 micron diameter bundles
                i. Temporal and nasal: Finer striations with one fiber bundle per stripe only.
                ii. Temporal/Inferior and Temporal/Superior: Broader striations with several bundles per stripe
      iii. Minor defects better seen on RNFL photographs

2) Clinical findings in normal eyes
   a. Regionally unevenly distributed over 8 regions
      i. Most visible:
         Temporal/Inferior>Temporal/Superior>Nasal/Superior>Nasal/Inferior
      ii. Least visible: superior, inferior, temporal/horizontal, nasal/horizontal
   b. Visibility of the RNFL decreases with age.
      i. 1.4 million optic nerve fibers to start, loses about 4,000-5,000 fibers per year with normal aging changes

3) Clinical Findings in Glaucomatous Eyes: RNFL loss with decreased RNFL visibility (local or diffuse)
   a. Localized RNFL loss:
      i. Wedge defects: runs towards or touches the optic disc border, can be broad
         1. Often found 6-8 weeks after optic disc bleeding.
         2. Points to a localized type of optic nerve damage.
         3. Can be detected if more than 50% of the thickness of the RNFL is lost!
            a. Pseudo defects will not often extend to the optic disk border and do not have a broad base close to the temporal raphe of the fundus, slit-like or groove-like (“cleavage” of the RNFL common in high myopia)
      ii. Noted in about 20% of all glaucoma eyes
         1. Frequency increases significantly from “early” glaucoma to medium advanced glaucoma and then decreases with marked glaucomatous changes.
         2. More common in focal type NTG than in eyes with age-related atrophic OAG, highly myopic OAG, and the juvenile-onset of OAG.
3. Most often found in the temporal inferior sector followed by the temporal superior sector
   a. Rarely noted in nasal fundus region.
   iii. Also noted in ONH atrophy from optic disc drusen, toxo scars, ischemic retinopathies with retina CWS, post chronic papilledema, optic neuritis from MS... therefore not pathognomonic for glaucoma!
   1. Low sensitivity because of relatively low frequency in eyes with optic nerve damage
   iv. Localized defects NOT present in normal eyes...therefore must signify a pathologic abnormality
      1. Important application in OHTN patients who may have normal perimetric testing.
         a. Later testing shows correlating perimetric changes
   b. Diffuse RNFL loss: diffuse loss leads to decreased RNFL visibility
      i. More difficult to detect than localized loss. Look for:
         1. Less visible RNFL in the temporal inferior fundus region compared to the temporal superior fundus region (assuming no fundus irregularities)
         2. Increased retinal vessel clarity...occurs when there is diffuse RNFL loss...should not be clearly and sharply detectable
            a. “IMPORTANT variable in the diagnosis of optic nerve damage”
   c. Pearls:
      i. The RNFL should be examined during every routine ophthalmoscopy...especially for patients with early damage of the optic nerve and/or those with pseudonormal but glaucomatous minicups in minidisks and to classify an eye with a pseudoglaucomatous but normal large cup in a large disk.
      ii. Less helpful in advanced disease...better to use perimetry.
      iii. Nonglaucomatous Optic Atrophy: decreased visibility of RNFL, reduced retinal arteriole caliber, with increased optic disc pallor in context of unremarkable disk size/shape and no PPA?

Early or Preperimetric Diagnosis of Glaucomatous Optic Nerve Damage

1) Most important variables:
   a. Shape of neuroretinal rim
      i. Rim configuration depends on the distance to the exit of the central retinal vessel trunk on the lamina cribrosa surface
ii. Inferior and superior rims should be *markedly broader* as compared with the temporal disk region.

1. Consider glaucoma suspect IF the neuroretinal rim is more or less even in width in all disk sectors
   a. Size of the optic cup in relation to the size of the optic disc
   b. Diffusely or segmentally (localized) decreased visibility of the RNFL
   d. Occurrence of localized RNFL defects and disc hemorrhages.

### Differentiation of Glaucomatous Vs Nonglaucomatous Optic Neuropathy

1) Common features...both have:
   a. Decreased retinal arteriole diameter with focal arteriole narrowing
   b. Reduced RNFL visibility
   c. Localized RNFL defects (glaucoma, optic disc drusen, papilledema)
   d. Enlargement and deepening of optic cup
   e. Correlating neuroretinal rim decrease (AAION)

2) Nonglaucomatous Optic Neuropathy: usually does NOT have PPA

### References


