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The Role of the Macula OCT Scan in Neuro-ophthalmology

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Abstract

Background—Recent improvements in OCT resolution and automated segmentation software has provided a means of relating visual pathway damage to structural changes in the RNFL and corresponding soma of the ganglion cells in the inner layers of the macula and also in the outer photoreceptor layer in the macula.

Evidence Acquisition—Studies correlating retinal structure with function are reviewed in the context of optical coherence tomography (OCT) in optic nerve and retinal disorders

Results—Recently published work provides evidence showing a strong relationship not only between the retinal nerve fiber layer and visual threshold in optic nerve disorders, but also between visual sensitivity and the inner layers of the retina in the macula where the cell bodies of ganglion cells reside. Acquired and genetic disorders affecting the outer retina show correlation between visual sensitivity and the thickness of the outer photoreceptors. These relationships helps localize unknown causes of visual field loss through segmentation of the retinal layers using spectral domain OCT.

Conclusion—Advances in relating the structure of the ganglion cell layer in the macula to the corresponding axons in the retinal nerve fiber layer and to visual function further our ability to differentiate and localize ambiguous causes of vision loss and visual field defects in neuro-ophthalmology. Ganglion cell layer analysis in volume OCT data may provide yet another piece of the puzzle to understanding structure-function relationships and its application to diagnosis and monitoring of optic nerve diseases, while similar structure-function relationships are also being elucidated in the outer retina for photoreceptor diseases.

Keywords

optical coherence tomography; macula; visual function; ganglion cell layer; retinal nerve fiber layer

Most clinicians, especially neuro-ophthalmlogists and glaucoma specialists have been trying to understand whether the information yielded by optical coherence tomography (OCT) is really helping them to improve upon the clinical care of their patients. Since its inception, OCT had provided new information about the status of the optic nerve, in terms of axon loss, providing information about the thickness of the retinal nerve fiber layer (RNFL). As neuro-ophthalmologists have attempted to incorporate the quantification of RNFL thickness

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into their decision-making, they have gained new insight into both its clinical usefulness and its limitations. Recently, the use of the macula OCT has helped to further expand the usefulness of OCT in neuro-ophthalmology patients, especially as spectral domain OCT (SD-OCT) has improved resolution and shortened the time for sampling of tissue volume. More advanced image analysis algorithms have improved the ability to segment the retinal layers in the macula, allowing improved detection and differentiation of the cause of visual loss.

The RNFL in neuro-ophthalmology – usefulness and limitations

In the past, the use of OCT in neuro-ophthalmlogic clinical decision-making has primarily focused on the status of the retinal nerve fiber layer (RNFL) thickness in relation to the threshold sensitivity of the corresponding area of visual field (1). Theoretically, it is expected that the degree of thinning of the RNFL will have a meaningful correlation with optic nerve function in a patient with loss of axons (2–4) and less correlation of structure with function in locations where axons are still intact, but not functioning. In the latter case, either a return of function may still be possible, as in the case with some eyes with compressive optic neuropathy (5), acute optic neuritis (6–9), or ischemic optic neuropathy. Alternatively, the axons may have undergone irreversible dysfunction but not enough time has elapsed to produce atrophy and thinning of the RNFL (1). While it has generally been accepted that acquired, post-geniculate damage to the visual pathway in adults usually does not result in transynaptic retrograde degeneration with optic atrophy. Recently, evidence has been published which has questioned this by showing evidence of thinning of the retinal nerve fiber layer in each eye of patients with homonymous field loss, corresponding to what would be expected if transynaptic degeneration had taken place (10). Such results need confirmation with detailed MRI evaluation to confirm that the acquired pathology is restricted to the post-geniculate visual pathway and does not involve the optic tract.

The clinical interpretation of axon loss becomes even more difficult in the setting of optic disc edema associated with visual field loss, since there may be swelling of some axons with atrophy of neighboring axons, confounding the relationship between RNFL thickness and corresponding visual field sensitivity. This is where evaluation of the thickness of the retina in the macula or its inner layer may be helpful, since the retinal nerve fiber layer contributes very little to macular thickness. Loss of neurons in the setting of optic disc edema would be likely to be detected in the macula, where the ganglion cell layer would become thinner over time as atrophy takes place. This situation is most common in conditions where the optic disc edema lasts more than a few weeks, such as in anterior ischemic optic neuropathy (AION), papilledema from raised intracranial pressure, orbital optic nerve sheath meningioma with associated disc edema from venous stasis retinopathy, and in some cases of compressive optic neuropathy in the orbit, such as occurs in Graves orbitopathy.

Another potential confounding variable is the status of other components that make up the thickness of the RNFL, besides axons, such as blood vessels and glial elements, which may influence the measured thickness of the RNFL (1,11,12).

Attempts to quantify the relationship between structure and function between RNFL thickness and visual threshold at corresponding locations have revealed that there is a correlation (primarily studied in glaucoma and anterior ischemic optic neuropathy), but not as great as one would expect (1–4). Factors such as measurement variability in both visual threshold and in RNFL thickness, the influence of non-neuronal elements on the RNFL thickness such as blood vessels and glial elements, and the inter-individual variation in mapping of RNFL bundles to their corresponding area of the visual field all confound the correlation in an individual patient. We have recently reviewed this topic (1) and have

provided evidence for a linear model relating visual threshold (unlogged) and RNFL thickness in glaucoma and AION (2–4). This is depicted in Figure 1 in semi-log plots. If the data in Figure 1 were re-plotted with both axes on a linear scale, the relationship would be a straight line. The significance of the linear relationship provides evidence against a critical tipping point where loss of structure precedes loss of function. Rather, the fit of data to a linear model implies they are both proportionate to one another across all levels of disease severity.

While the relationship between RNFL thickness and visual field sensitivity appears to correspond to a linear model, there are still components of measurement variability (such as the variability between and within subjects) that impose limitations on this framework and its application to individual patients (Fig 2). In addition, the dynamic range of both the RNFL and visual threshold sensitivity and their associated measurement variability limit meaningful relationships to be explored once 10 decibels of threshold loss have been exceeded or if the RNFL thickness drops below 60 microns for arcuate field loss (as shown in the flat portion of the curve in Figure 2).

In glaucoma studies, the RNFL thickness has been shown to have a very good sensitivity and specificity for diagnosing glaucoma, using Receiver-Operator Characteristic curve analysis (ROC). It is important to keep in mind that such analyses are always influenced by the criteria that are chosen as the gold standard for the presence or absence of the disease. Such criteria include the characteristics of the population being studied, in terms of the distribution of severity of damage in the population included, and whether structure (disc appearance) or function (visual field sensitivity and the pattern of loss) is used as the criteria for the presence of glaucomatous or optic nerve disease.

A great deal of research has also been directed towards using the RNFL thickness to detect progression of glaucomatous damage over time. Most of these studies have applied techniques that have also been used to study progression of visual field loss, namely a) significant change in RNFL status at a given time point from a prior baseline measurement or b) linear regression analysis of RNFL thickness over time. The main problems encountered in detecting progression using these approaches are measurement variability and using population statistics to determine what constitutes a significant change over time. Individuals appear to vary considerably in the measurement variability of the RNFL, so applying population statistics (defining the variability of a given patient by applying the variability from a population of patients) to a given patient may not be optimal for individualizing the analysis of progression for a given patient. In addition, defining a statistically significant change over time may not always equate with what is a *clinically* significant change – one that would warrant a deviation in treatment. This is where monitoring progression by making use of the structure-function relationship has distinct advantages. True progression would be expected to result in a proportional change in both structure (RNFL thickness) and function (visual field sensitivity), based on the linear model relating the two, as described previously. Such an approach also helps to relate changes in structure to the corresponding function which could be more meaningfully related to quality of life measures. Because the rate of visual field progression in optic neuropathies such as glaucoma varies considerably among treated and untreated patients and the rate is, in general, slow, the challenge in the future will be to identify as early as possible which patients are at the most risk for progression and focus aggressive treatment on those patients while not applying the same treatment to patients who are at low risk for significant progression over their remaining life expectancy.

The macular OCT in neuro-ophthalmology – added value

For neuro-ophthalmology, the use of the OCT for diagnosis and monitoring of optic nerve disorders pose similar problems as those for glaucomatous optic neuropathy. Further challenges are provided by disorders where optic nerve edema and associated thickening of the RNFL prevent accurate assessment of simultaneous neuronal loss (see previous discussion, above). In addition, patients with visual field loss but no associated thinning of the RNFL pose a dilemma for the neuro-ophthalmologist because outer retinal disease (e.g. AZOOR) can masquerade as vision loss from optic neuropathy or in some patients with optic neuropathy insufficient time has elapsed to cause structural loss of neurons in the RNFL or the ganglion cell layer. The following disorders put these issues into perspective and highlight how the macula OCT scan can be used to compliment the RNFL scan and the pattern of visual field loss to arrive at the correct diagnosis and monitoring of their treatment over time:

1. **Multiple Sclerosis/Optic Neuritis**: In this setting OCT-based evidence for structural loss (although non-specific in itself) is being used to help substantiate the clinical diagnosis of multiple sclerosis in the setting of other neurologic or MRI abnormalities. More recently it has been proposed that OCT might be used as a quantitative tool to monitor the course and treatment of demyelinating disease and predict which patients are likely to progress at a faster rate, requiring a more tailored treatment approach (6–9). There is also evidence that total macular thickness may also reflect neuronal loss in multiple sclerosis (13). In the near future, probability plots relating the pattern of ganglion cell layer thinning with that of the corresponding axon bundles in the RNFL scan and relating this to the pattern of visual field loss will help to better determine areas of significant pathologic loss of neurons. A recent review has summarized the available evidence relating the loss of retinal structure to the status of demyelinating disease, including evidence for the use of OCT for monitoring progression of demyelinating disease (14).

   One of the main interest areas at present is whether acute optic neuritis represents a good model for evaluating the efficacy of new central nervous system treatment strategies for multiple sclerosis, such as the use of neuro-protectants and whether the use of OCT is a valid surrogate for modeling the status of multiple sclerosis and treatment strategy. Since thickening of the peripapillary RNFL is commonly observed by traditional OCT during the acute stage of optic neuritis where small amount of optic disc edema can be present, the RNFL scan can be misleading when attempting to ascertain whether thinning is due to reduction in edema or due to axon loss over time compared to the acute, baseline state. The macula thickness or that of the ganglion cell layer complex may provide a more accurate quantification of the change in ganglion cell number and associated axons over time, relative to the baseline OCT obtained acutely, since it is relatively unaffected by acute axon swelling. In this setting, the macula OCT scan (total thickness and inner ganglion cell layer) has the potential to provide an important adjunct to the RNFL as a structural indicator of therapeutic interventions during the acute stage aimed at preserving neurons.

2. Non-arteritic anterior ischemic optic neuropathy (NAION): Similar to optic neuritis, it would be desirable to use OCT to identify treatments aimed at preserving axons, such as steroids, agents that further reduce edema, neuro-protective agents or treatments aimed at improving oxygenation of the optic nerve during the ischemic state. However, similar to the problems outlined above with acute optic neuritis, the acute edema and associated thickening of the peripapillary RNFL measured with traditional OCT confound the assessment of axon loss during

the first 8 weeks, when optic disc edema is still present. The thickness of the macula OCT and ganglion cell layer complex would be expected to provide a better structural indicator of axon preservation or loss compared to the peripapillary RNFL scan. This is because the ganglion cell-inner plexiform layer complex does not become thickened during optic disc edema, as does the peripapillary RNFL. Furthermore, relating the geographic pattern of ganglion cell loss to that of the RNFL and corresponding visual field loss would provide a more powerful means of assessing clinically significant loss of structure and function, than just use of either the RNFL or ganglion cell layer thickness alone. In this regard, it will be important in the future to determine how long it takes for the ganglion cell complex to become thinner after irreversible damage to the RNFL, so that clinical assessment and treatment decisions can be made.

3. **Differentiation between NAION and arteritic AION**: A common problem facing the neuro-ophthalmologist is whether acute visual loss associated with optic disc edema in an elderly patient is due to giant cell arteritis or non-arteritic AION. Most clinical investigations focus on the presence or absence of systemic symptoms of giant cell arteritis, the presence of pallid optic nerve edema, the profoundness of the visual field loss and the presence of acute phase reactants to inflammation in the serum. Fluorescein angiography may also be beneficial in identifying outer retinal ischemia due to occlusion of one or more posterior ciliary arteries if obtained within the first 10 days of vision loss. In this setting, the macula OCT may also be useful for identifying acute loss of photoreceptor structure, particularly whether there is disruption of the inner-outer photoreceptor segment line of increased intensity seen with spectral domain OCT (15,16,17). The presence of OCT evidence of outer retinal layer disruption in the context of profound visual loss and optic disc edema would help point towards arteritic AION as the diagnosis, differentiating it from NAION.

4. **Compressive optic neuropathy**: The presumption in compressive optic neuropathy is that the greater number of axons that are present at the time of diagnosis, the higher potential for visual recovery if decompression is successful (5). Here the confounding variables related to the interpretation of OCT in compressive optic neuropathy lead to the following questions: 1) how much time must elapse before axonal degeneration is detectable on OCT performed at the time of diagnosis and 2) how many neurons/axons are required to support adequate visual function, which may influence treatment decisions? Since the central visual field is commonly affected in compressive optic neuropathy and treatment decisions are weighted more heavily towards the status of the central visual field and corresponding retinal ganglion cells, it would seem logical to monitor the thickness of the ganglion cell layer complex in the macula rather than the thickness of the maculo-papillary bundle of the RNFL scan. This is because the maculo-papillary bundle is relatively thin in normal eyes and varies between individuals, resulting in less dynamic range from which significant axon loss can be measured. Since the ganglion cell layer is thickest in the macula and perifoveal area, it should provide a better structural target upon which to make treatment decisions related to the chance of visual recovery after decompression.

5. **Papilledema**: When the optic nerve appears swollen, the main questions applicable to OCT are 1) whether true papilledema is present vs. pseudopapilledema (18), 2) whether the change in optic disc edema over time can be better quantified using thickening of the RNFL with OCT compared to the fundus appearance of the optic nerve, 3) whether subretinal fluid under the fovea is contributing to vision and visual field loss and 4) whether axon loss can be detected while the disc is still

swollen and differentiated from a reduction in RNFL thickness due to lowering of intracranial pressure. In this respect, the peripapillary RNFL measured with traditional OCT scan poses limitations on the assessment of whether disc edema is becoming less due to reduction of intracranial pressure or whether ongoing axon loss is responsible for the decrease in disc edema. The macula OCT scan and thickness of the retinal ganglion cell layer complex may add much needed clinical information in the setting of chronic papilledema undergoing treatment; if axons are indeed dying off, then the inner layers of the macula will show thinning, but if disc edema is less due to lowering of intracranial pressure and neurons are being preserved, then the macula inner layers should not become thinner.

6. **Differentiation of optic neuropathy from retinopathy and identifying disorders in which both are present**: OCT scans of other portions of the posterior pole besides the RNFL can be very revealing. For example, acute or subacute visual field loss with a thickened macula on OCT but without obvious evidence of retinal edema on fundus exam may help point the diagnosis more correctly toward a recent branch or central retinal artery occlusion (CRAO), and shift the diagnostic probability away from anterior or posterior ischemic optic neuropathy, inflammatory, or compressive optic neuropathy. In the chronic state, an abnormally reduced total macular thickness keeping company with a thinned RNFL and pale nerve may also help make the diagnosis of a previous retinal artery occlusion (causing thinning of both the ganglion cell layer, inner plexiform layer and the bipolar cell layer). In such cases the thinning of the macula is much greater than with optic neuropathy, since the bipolar cell layer usually becomes thinned in addition to the ganglion cell layer and inner plexiform layer. Segmentation of the retinal layers within the macula would help to further differentiate a past retinal artery occlusion from an optic neuropathy without requiring a Ganzfeld or multi-focal electroretinogram (ERG) or neuro-imaging. Another example would be a patient with possible neuroretinitis and persistent visual field loss; the combination of an OCT scan of the peripapillary RNFL and macula scan may help reveal the layers of the retina which are most likely to be the source of pathology explaining the visual field loss. Neuroretinitis usually affects both the RNFL, ganglion cell layer and other layers of the retina, along with the presence of highly reflective exudates seen in the outer plexiform layer in OCT scans of the macula.

   Most ophthalmologists use the macula OCT to diagnose disorders causing pathology in the inner or outer retina, which cause 1) fluid accumulation in the retina (e.g. cystoid macular edema, diabetic macular edema, vitreal traction, perifoveal telangiectasia, choroidal neovascular membrane), 2) disruption of the outer layer (e.g. trauma, neovascular membranes or inflammatory disorders), or 3) macular holes. Such patients often make their way into a neuro-ophthalmology clinic without a certain diagnosis and a macular OCT may be an important imaging tool for narrowing the differential diagnosis and reducing the cost of an extensive work-up for an unknown cause of visual loss. A common presentation might be a patient referred with a diagnosis of optic neuritis, but showing an enlarged blind spot or geographic visual field loss not corresponding to a retinal nerve fiber distribution. Such patients may have acute zonal occult outer retinopathy (AZOOR), the big blind spot syndrome, or multiple evanescent white dot syndrome (MEWDS) and can be diagnosed with greater certainty if the outer photoreceptor layer shows a disruption of the inner-outer segment line of brightness on spectral domain OCT. The retinal area of disruption usually corresponds to the location of visual field loss and may be reversible in some cases (15). Other pathologies encountered by a neuro-ophthalmologist which may result in thinning of the macula OCT or disruption of the photoreceptor structure include

hydroxychloroquine (Plaquenil) toxicity (19), and other retinopathies disrupting the photoreceptor layer, including retinitis pigmentosa (16, 17).

As discussed above, there are a number of clinical situations that limit the uses of the RNFL OCT scan by itself in aiding the diagnosis of visual loss, and assessing change over time. The incorporation of the macula scan acquired by spectral domain OCT may provide additional information to arrive at the correct diagnosis and in making treatment decisions over time. Although the average total retinal thickness of macula scans can be helpful, the spatial distribution of the thickness into sectors provides even greater information. Many of the newest report printouts from spectral domain OCT machines show the sector thickness and its relation to age matched normal scans as a probability plot, similar to an automated visual field. More recently, a posterior pole scan has been introduced in the Spectralis OCT (Heidelberg, GE), which encompasses approximately 17 degree radius of retina and which relates the asymmetry between the thickness of small square areas of the superior and inferior retina and also the inter-ocular asymmetry of square areas between the right and left eyes. In addition to the spatial distribution of thickness, the qualitative assessment of its structure in different the retinal layers can be very helpful, and additional quantification of the thickness of individual layers would be even more useful to localize which retinal layer is affected by a certain disorder, as shown in Figures 3–5. This has prompted an interest in imaging the source of the axons – the soma of retinal ganglion cells, which predominate in the macula. Accurate quantification of the thickness of each retinal layer would not only provide much needed information on the inner retinal layers but would also provide similar information on the outer retinal layers as a built in control to provide assurance of the location of the pathology. Here the question is how to best take advantage of the added resolution and spatial sampling offered by spectral domain OCT so that the ganglion cell layer can be accurately quantified to reflect the number of neurons present. This also presupposes that imaging of the ganglion cell layer in the macula region provides adequate spatial sampling to reflect the status of disease affecting not only the macula but also regions peripheral to it.

Segmentation of the ganglion cell layer within the central macula with spectral domain OCT and its potential advantages

1. The retinal ganglion cells are densest in the macula and form a stratified multi-cellular layer within the central 6 degrees of visual field. Therefore, loss of axons and the corresponding soma in this location is likely to cause a thinning of the retinal ganglion cell layer.
2. The lack of large retinal vessels in this location makes their confounding contribution to the thickness of the ganglion cell layer very minimal, compared to the peripapillary retina, where they do influence the RNFL measurement.
3. The mapping of visual field location to corresponding ganglion cell soma is less complicated than the situation with the RNFL bundles and may show less inter-individual developmental variability. Simplistically, a focal light in the macula activates the ganglion cells directly underlying it. In the foveal and perifoveal location this is not strictly the case and some modification has to be made in this area of the visual field due to displaced ganglion cells.
4. Recent advances in OCT image analysis using both manual (15) and automated analysis in three dimensions (19,16) have provided a potential solution for delineation of the different neuronal layers in the macula (Figs 3 and 4).
5. Preliminary attempts to quantify the correlation between visual threshold and retinal ganglion cell thickness in the macula appear to subjectively correlate with

the spatial pattern of visual field loss in the macula in patients with glaucoma (Fig 5) and anterior ischemic optic neuropathy. However, a quantitative correlation between ganglion cell thickness and corresponding overlying visual threshold has not yet been reported in detail.

Challenges associated with OCT analysis of the macula that need to be overcome before clinical monitoring of optic nerve function is useful

1. Current commercially available OCT and associated software are not capable of segmenting the ganglion cell layer in three dimensions. At best, some manufacturers segment the inner layers of the retina of the macula as a neural complex layer (RNFL, ganglion cell layer and inner plexiform layers), but this software analysis has not yet been rigorously validated. Recently Hood and colleagues reported to have manually segmented two dimensional line scans through the macula and have shown correlation of thinning of the ganglion cell +inner plexiform layer with corresponding loss of visual threshold in glaucoma, so this approach does have promise (20). Our group has reported automated segmentation of retinal layers using a 3D graph search approach applied to volume OCT scans, as shown in Figures 3–5 (21, 22).
2. Outside of the central 6 degrees of the macula, the ganglion cell layer is less of a multi-cellular layer. In areas where there is only a single layer of ganglion cells it is not known if loss of soma will cause a measurable, significant thinning of the cellular layer or whether it will just be replaced by glial and Mueller cells, making structural thinning of the ganglion cell layer of the inner retina difficult to measure (23).
3. Focal peripheral visual field damage would be unlikely to affect the retinal ganglion cell layer in the macula, making it theoretically less sensitive to detection and monitoring of peripheral field pathology. On the other hand, most optic nerve diseases do show some degree of diffuse loss and although significant abnormalities in visual threshold may not be detected, there still may be a measurable decrease in retinal ganglion cell thickness in the macula, even though a visual field test may appear to show mainly extra-macular loss of sensitivity.
4. It is currently not known how much time it takes for a decrease in the thickness of the ganglion cell layer to occur after damage to the optic nerve at different distances from the globe. The time delay between permanent damage and atrophy of the ganglion cell layer would provide a framework for dating the time of injury.

In summary, recent improvements in OCT resolution and automated segmentation software has provided a means of relating visual pathway damage to structural changes in the RNFL and corresponding soma of the ganglion cells in the inner layers of the macula and in the outer photoreceptor layer in the macula. These advances further our ability to differentiate and localize ambiguous causes of vision loss and visual field defects in neuro-ophthalmology. Ganglion cell layer analysis in volume OCT data may provide yet another piece of the puzzle to understanding structure-function relationships and its application to diagnosis and monitoring of optic nerve diseases, while similar structure-function relationships are also being elucidated in the outer retina for photoreceptor diseases.

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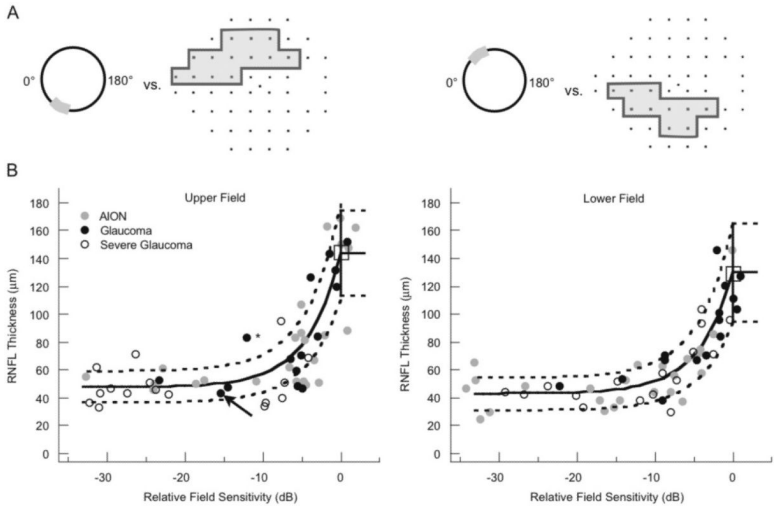

Figure. 1.

Relationship of the retinal nerve fiber layer (RNFL) thickness to visual field loss in patients with glaucoma and AION. (A) A schematic illustrating the location of the corresponding disc sectors and field regions for the superior arcuate field (left panel) and inferior arcuate field (right panel). (B) RNFL thickness as a function of field loss for the upper field/inferior disc (left panel) and the lower field/superior disc (right panel). Data are shown for patients with AION (n = 24; filled gray), asymmetric glaucoma (n =15; filled black), and severe glaucoma (n =16; open symbols), and for the mean of a group of 60 age-similar controls (open square). The theoretical structure-function curves are fitted to a linear function, but plotted here on a semi-log plot. For the upper and lower visual field regions, three theoretical curves are shown (50th percentile=solid line, 95th percentile, and 5th percentile = dashed lines). Reproduced with permission from reference 1.

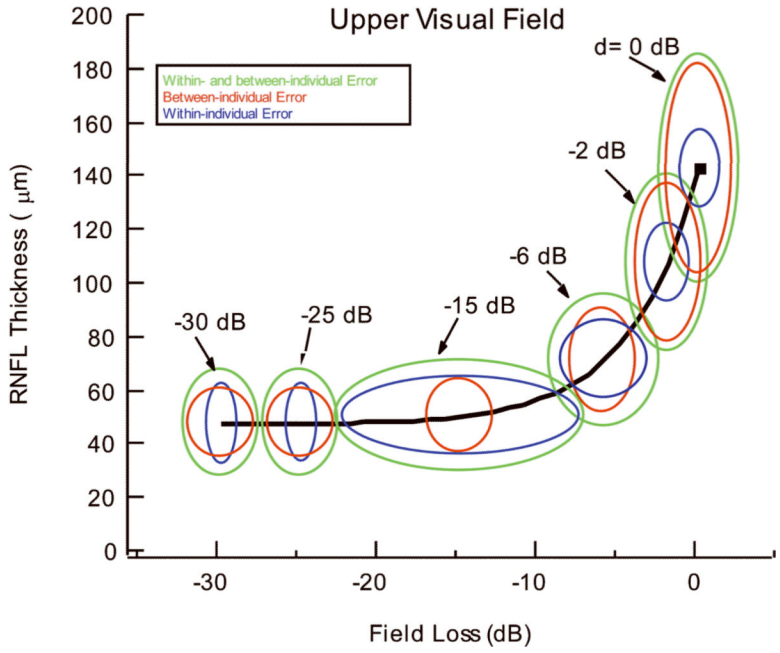

FIGURE 2.

This figure depicts the sources of measurement variability between subjects (red elipses) and within subjects (blue elipses) and combined variability (green elipses) in both function (visual field loss, x-axis) and structure (OCT RNFL thickness, y axis). The ellipses are the 95% confidence boundaries of the linear model of structure vs function with variability component shown for different levels of glaucoma disease severity, d, expressed in decibels of field loss. Note that for OCT, the within subject repeat measurement variability is fairly constant over the entire range of disease severity, but the repeat within subject variability increases dramatically for visual field sensitivity in the mid-range of severity. The inter-individual variation in visual field sensitivity is fairly constant, but for OCT it is highest between subjects that have normal visual field sensitivity. Reproduced with permission from reference 4.

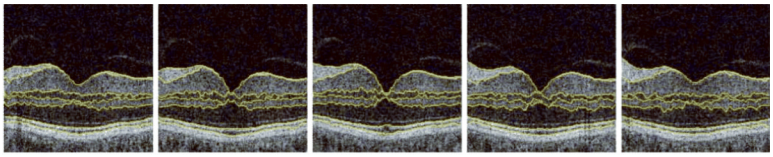

FIGURE 3.
Automated software 3D segmentation of the retinal layers of the normal macula using spectral domain SDOCT. Segmenation is shown for 5 successive slices of the volume macula scan (courtesy of Michael Abramoff M.D. Ph.D. and Mona Garvin Ph.D.)

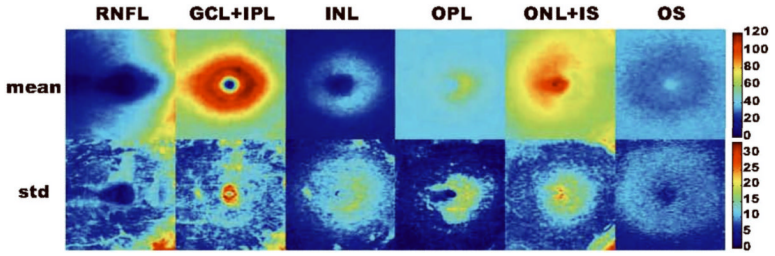

FIGURE 4.

Thickness (top row) and thickness variability (standard deviation, bottom row) maps of six macular intraretinal layers from the right eye of 15 normal subjects. The micron thickness of the different macula layers is color coded (red=thickest, blue=thinnest). Figure (courtesy of Michael Abramoff M.D. Ph.D. and Mona Garvin Ph.D.)

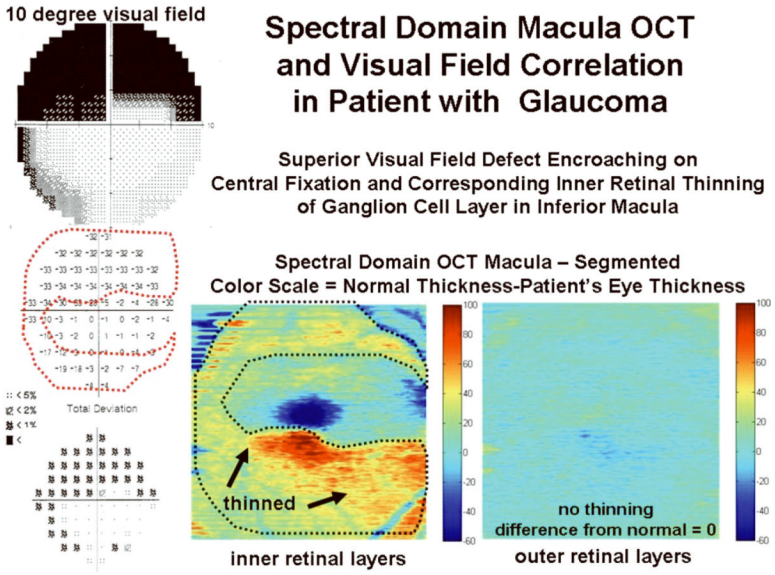

FIGURE 5.

Example of a glaucoma patient whose visual field defect came close to the center of their visual field and was tested with a denser visual field testing program covering only 10 degrees of radius and which corresponds to the area of retina covered by the macula scan on the corresponding spectral domain OCT. The gray scale map shows visual sensitivity loss that was worst in the top part of the visual field (dark areas), but also shows some loss in the inferior field. The visual field sensitivity difference from normal plot is also shown below the gray scale with the abnormal area with decrease in sensitivity surrounded by a red dotted line. The statistical probability plot of the same visual field data is shown in the lower left corner. 3D-OCT was obtained on this eye and segmented into the inner retinal layer (ganglion cells and axons, lower left color plot) and outer retinal layer containing the photoreceptors and bipolar cells (lower right color plot). The color plots show thickness as difference from normal, so in contrast to Figure 4, red signifies a greater difference from normal or a more thinned area. Note the high spatial correlation between the thinned layer containing the ganglion cells in the inferior macula (thinned areas are red and yellow and depicted as difference from normal) and the corresponding superior (and inferior) areas of visual field defect. However, there is no such thinning in the outer retina, which is known to be unaffected in most glaucomatous damage.