1 Principles of Confocal Scanning Laser Ophthalmoscopy for the Clinician

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THE EVOLUTION OF THE OPTIC DISC EXAMINATION

The examination of the optic disc is unique in many respects in that it provides an opportunity to directly observe the effects of progressive neurodegenerative diseases such as glaucoma on a microscopic scale. Since the advent of the direct ophthalmoscope, methods to develop better quantitative parameters that describe optic disc structure have been sought. Subjective estimation of the cup/disc area ratio has long been used to quantify the degree of cupping in glaucoma in the clinical setting. However, detection of progressive glaucomatous change in the optic disc using this method is extremely difficult, if not impossible, due to poor reproducibility and high inter- and intra-observer variability. This certainly is not surprising given the complex architecture of the optic disc and the difficulties associated with clinical examination. Attempting to reduce the subtleties of optic disc contour to a single linear variable, such as cup/disc ratio, is clearly inadequate and ignores much of the three-dimensional shape of the neuroretinal rim and optic cup.

Photography of the optic disc by monocular and stereophotographic techniques has been the traditional method to document the appearance and demonstrate longitudinal changes in the disc. However, these nonquantitative methods require subjective physician interpretation and can be difficult and time-consuming in a busy clinical practice. Over the past 20 years, more objective ocular imaging techniques have been developed in an effort to provide accurate, reproducible quantitative measurements of the contour of the optic disc.

The goal of this evolving process has been to develop a technique capable of obtaining reproducible topographic information that can provide a more objective method to detect characteristics of the optic disc indicative of glaucomatous optic neuropathy, and detect the changes over time in the shape of the optic disc associated with progressive glaucomatous damage. The culmination of these efforts has resulted in the development of confocal scanning laser ophthalmoscopy, which provides rapid, noninvasive, noncontact imaging of the ocular fundus. Unlike conventional photography, which obtains two-dimensional imaging, scanning laser techniques utilize confocal imaging methods to obtain high-resolution images both perpendicular (x-axis, y-axis) to optic axis and along the optic axis (z-axis) (Figure 1.1). Confocal imaging procedures were initially developed over 30 years ago as a technique to provide optical sectioning of biologic and industrial specimens. These principles have been subsequently modified for a variety of uses in ophthalmology including in-vivo corneal, retinal, and optic disc imaging.

The Heidelberg Retina Tomograph II (HRT II) represents the latest iteration in the application of confocal scanning laser ophthalmoscopy to the examination of the optic disc. The HRT II is a scanning laser ophthalmoscope specifically designed to acquire three-dimensional images of the optic nerve head and posterior pole. This instrument provides rapid, reproducible topographic measurements of the optic disc including the size of the optic disc, the contour and shape of the optic disc, neuroretinal rim, and optic cup, along with measurements of the peripapillary retina and nerve fiber layer. In addition, the HRT II is much easier to use in a clinical setting than its predecessor, the original Heidelberg Retina Tomograph (HRT). This newer instrument is much more compact, provides greater automation of image acquisition, standardizes many of the important aspects of the imaging process, and includes software capable of providing clinically valuable automated analysis not seen in prior versions.

PRINCIPLES OF OPERATION

Confocal scanning laser ophthalmoscopy

Both the HRT and HRT II utilize a rapid scanning 670-nm diode laser to acquire images of the posterior segment. The emitted beam is redirected in the x-axis and y-axis along a plane of focus perpendicular to the optic axis (z-axis) using two oscillating mirrors to obtain a 15° x 15°, two-dimensional image reflected from the surface of the retina and optic disc. A luminance detector measures the light reflected from each point in the image after passing through a confocal imaging aperture. The confocal aperture limits the depth from which reflected light reaches the detector to a narrow range centered around the location of a set focal plane on the retinal or optic disc surface. Light that is deeper or shallower than this focal plane (i.e., not in the specific focal plane) is suppressed to provide an optical section of the posterior pole corresponding to this set focal plane (Figure 1.1). The depth of the focal plane is automatically adjusted by shifting the confocal aperture to acquire multiple optical sections through

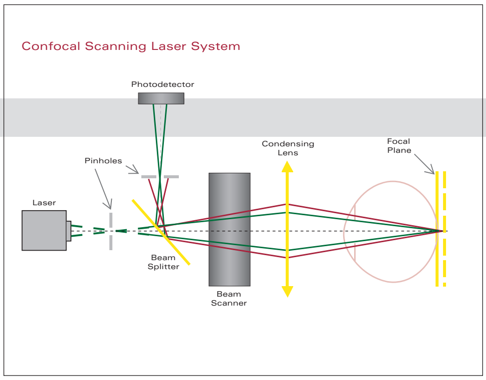

Figure 1.1

Schematic diagram of a confocal scanning laser system used in the HRT II.

the tissue of interest in order to create a layered three-dimensional image. Thus, the three-dimensional image contains information from multiple focal planes as the focal plane is shifted through the tissue — in this case, the optic disc.

The HRT II acquires reflectance images using 16 to 64 imaging planes to a depth of 4 mm. The number of optic sections increases at greater scan depth in order to image deeper optic cups. These optic sections are then combined to develop a three-dimensional contour map of the optic disc surface. The value of reflectance obtained from each focal plane at every point in the 15° image in the z-axis forms the z-profile for that point, from which a measurement of retinal height can be obtained from the distribution of the amount of reflected light along this z-axis. Thus, the z-profile of each point may be presented as a plot of reflectance intensity versus scan depth (Figure 1.2 A,B). The peak intensity from the z-profile plot is assumed to correspond to the location of internal limiting membrane that overlies the retina and optic disc (the internal limiting membrane of Elshnig). The final result produces a topographic map of 384 X 384 height measurements of retinal and/or optic disc surface topography.

THE HRT AND THE HRT II

The first commercially available instrument was the Heidelberg Retinal Tomograph (HRT), which was used primarily for clinical research. This confocal scanning laser has demonstrated excellent reproducibility, high sensitivity and specificity for the detection of glaucoma, and has provided very promising results with respect to the detection of progressive glaucomatous damage. In addition, this technology has been evaluated to a much greater extent than any existing optic disc or nerve fiber layer imaging system and is the device used in the confocal scanning laser ophthalmoscopy study performed as an ancillary project of the Ocular Hypertension Treatment Study (OHTS).[1,2] However, the HRT requires an experienced operator and fine-tuning of several manual settings in order to obtain high-quality images, which makes routine use of the

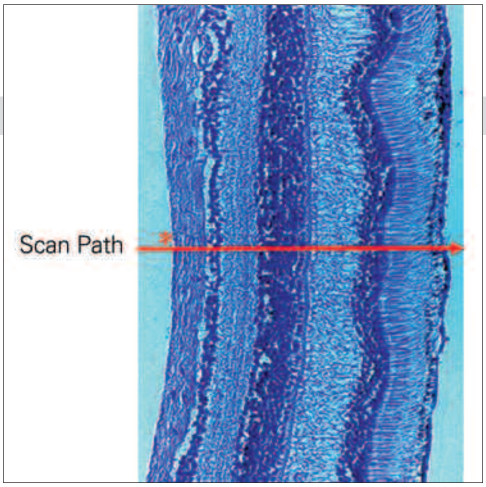

Figure 1.2A

The z-axis of the scan path (red arrow) of the scanning laser through the retina.

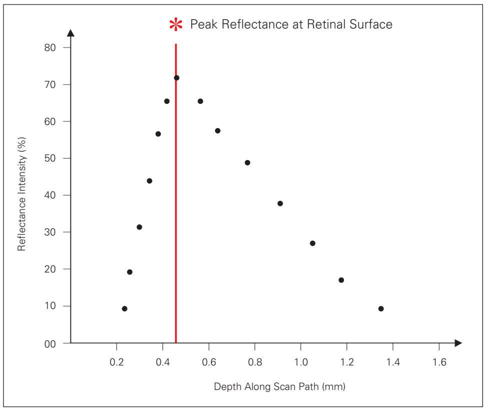

Figure 1.2B

Plot of reflectance intensity along this scan path for one point in the 384 X 384 pixel HRT II image. The peak reflectance along the z-axis is considered to correspond to the height of the retina surface (red asterisk) at that point.

HRT in the clinical setting difficult. The extensive experience gained from the development of the HRT along with ample clinical research using this instrument has provided the means to develop the more user-friendly HRT II.

The HRT II also utilizes a diode laser to acquire reflectance images. The theoretical resolution of both the HRT and the HRT II is similar and limited by the optics of the eye to 10 μm in transverse resolution and 300 μm in axial resolution (full width at half height). Peak-to-peak resolution in the axial plane is considerably less at approximately 50 to 60 μm. The much more compact HRT II has incorporated several automated scan procedures that have improved the ease of routine clinical use compared with prior versions of the HRT, which were considerably more cumbersome. These modifications include a higher resolution for the 15° image (the same as that used on the 10° scan of the HRT), a pre-scan planning mode, automatic selection of the fine focus and scan depth, automated serial scanning with built-in quality control measures, and automated averaging of serial scans.

The original HRT was able to obtain scans using three field size settings: 10° x 10°, 15° x 15°, or 20° x 20° centered on the optic disc. The resolution at any of these settings was 256 x 256 pixels. Thus, pixel size for the HRT varies from 10 to 26 μm per pixel depending on the scan area used. The HRT II in contrast is set to measure a 15° scan area. This change further automates the imaging process, provides a larger field of view to aid in centration of the optic disc and assessment of the nerve fiber layer, and minimizes vignetting of the optic disc at the edge of the scan field. In order to obtain a similar transverse resolution with the HRT II that is comparable to the maximal transverse resolution of the original HRT for a 10° image, the HRT II uses a higher resolution of 384 x 384 pixels. The higher number of pixels for the set 15° image maintains the highest resolution with the HRT II of 10 μm/pixel (the best resolution obtained using the 10° scanning field with the original HRT), making it possible to combine images from the two instruments for serial analysis (see Chapter 5).

With prior versions of the HRT, the fine focus and scan depth had to be adjusted manually. This process has been fully automated with the HRT II. Once the patient is positioned and the optic disc is in focus, the HRT II automatically performs a pre-scan through the optic disc when the unit is activated for imaging to determine the depth of the individual's optic nerve. This scan traverses through the optic disc. Using information from this pre-scan, the fine focus and scan depth are automatically adjusted to ensure that the entire optic disc is included on the imaging cross-sections.

Next, the HRT II uses this planning pre-scan to determine the number of imaging planes (planes of focus) to use that will incorporate the entire disc from the retinal surface to the base of the optic cup. The longitudinal field of view (the range of scan depth) of the current instrument ranges from 1 to 4 mm. Each successive scan plane is set to measure 0.0625 mm deeper as the scans are taken incrementally through the tissue. Thus, if the pre-scan determines that a 1 mm scan depth is required, 16 imaging planes will be used, whereas, if the depth is 4 mm, the imaging planes are increased to 64. Unlike the original HRT, in which the longitudinal resolution varies with scan depth, the HRT II maintains the axial resolution of the scan at 62 μm by varying the number of imaging planes. Thus, the HRT II maintains a constant digital resolution in both the transverse axis and longitudinal axis despite individual differences in the depth or size of the optic disc.

Finally, as mentioned previously, the HRT II automatically obtains three scans after the pre-scan for use in analysis. Automated quality control measures detect scans that are inadequate due to blinking and/or fixation shifts, and repeats the faulty scan to ensure that three adequate scans are obtained during each imaging session for analysis. The HRT II then automatically aligns and averages the scans to create the mean topography image for the scan session. This, more than any other feature of the HRT II, provides the foundation for its successful clinical application. It enables an individual assessment of the noise or variability of the images for a given eye at a given visit, therefore enabling the individually tailored analysis of progression. Many of these procedures had to be manually performed using the original HRT, adding to the difficulty in post-acquisition image processing.

PATIENT SAFETY

The 670-nm diode laser used in both the HRT and HRT II does not pose any safety hazard and is categorized as a Class 1 laser system. The intensity of the scanning diode laser is 100 times lower than the luminance of a digital fundus flash camera, making the imaging process much more comfortable to the patient than with conventional fundus photography. A time limit has been incorporated into the operative software of the HRT II that limits the duration that the laser beam can be switched on in order to further guarantee the safety to both the operator and the patient. After this time period, image acquisition will be transiently interrupted and the message “Laser Safety: laser timed out” is displayed. Imaging can continue after a set waiting period. However, this safety feature is not generally activated during normal clinical use of the instrument.

BASICS OF OPERATION

The advances incorporated in the HRT II have made clinical operation of the instrument considerably easier for the imaging technician. Each two-dimensional optical section takes about 0.025 second, and a single scan of 2 mm in depth can be performed in about 1 second. A typical imaging session with the HRT II including the pre-scan and three confocal scans can usually be obtained in under 7 seconds. The unit automatically repeats scans interrupted by blinks or large saccades so that three high-quality scans are obtained for each imaging session. The individual scans are then stored on the hard drive for later processing.

Once the three scans are stored, post-scan image processing may be carried out at any time. The software automatically aligns and averages the images to obtain a matrix of mean height measurements. The result produces the reflectance image and the topography image. After image processing is complete, the software displays both of these images with the reflectance image on the right and the topographic image on the left.

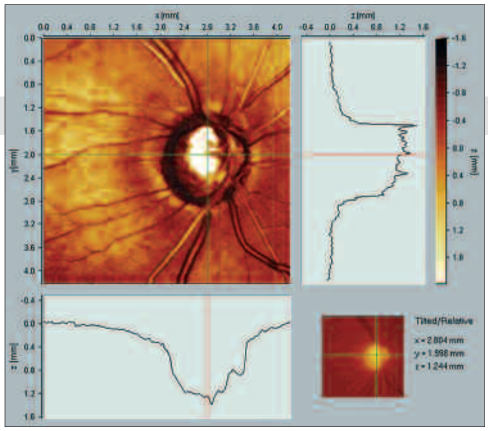

Figure 1.3

The reflectance image of the right eye of a patient with glaucoma. This false-color image has a similar appearance to an optic nerve photograph. Areas of highest reflectance, such as the base of the cup, appear brighter. In this view, the topographic image is displayed in the lower right and the cross-sectional height of the retinal surface in relation to the reflectance and topographic images are shown in the two graphs below (along the y-axis) and to the right (along the x-axis) of the reflectance image.

THE REFLECTANCE IMAGE

The reflectance image is a false-color image that appears similar to a photograph of the optic disc (Figure 1.3). If taken properly, the image should be clear and evenly illuminated, with sharp borders at the visible margins of the optic disc and retinal vessels. This image is the result of the summations of the two-dimensional reflectance images and is presented as a 384 x 384 pixel map illustrating the degree of reflectance from regions in the optic disc and peripapillary retina. Darker areas are regions of decreased overall reflectance, whereas lighter areas, such as the base of the cup, are areas of the greatest reflectance. This does not equate to height measurement and is purely related to the overall regional reflectance in the image. The reflectance image can be valuable in locating and drawing the contour line around the disc margin.

THE TOPOGRAPHIC IMAGE

The topographic image, in contrast to the reflectance image, relays information concerning the height of the surface contour of the optic disc and retina. This image is also false-color coded, but it is based upon the height measurement matrix constructed from the determination of the depth of maximal reflectance in the z-axis at each pixel (Figure 1.4). Pixels that appear bright in the topographic image are deeper, and dark pixels are elevated. Thus, the neuroretinal rim should appear darker than the surrounding retina and the base of the cup usually appears lightest. The topography of the optic disc may also be viewed in the 3-D view as a rotatable, three-dimensional model of the surface of the optic disc and the adjacent retina (Figure 1.5).

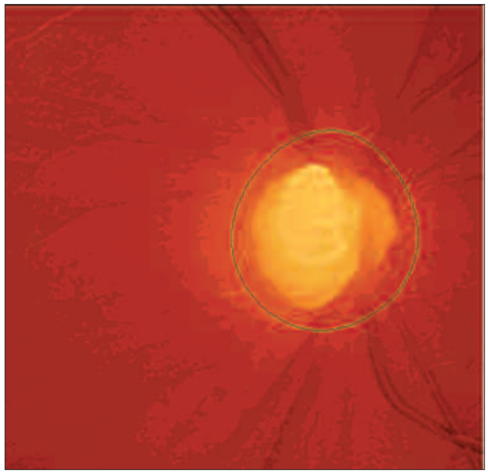

Figure 1.4

The topographic image of the same eye. This false-color image displays a 384 X 384 pixel map of the surface height. Lighter areas such as the base of the cup are deeper, while darker areas such as the surface along the retinal vessels appear darker. The contour line has been drawn around the disc margin in this image.

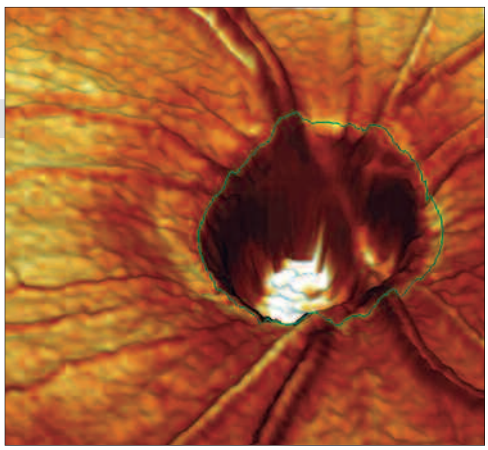

Figure 1.5

Pseudo-three-dimensional image of the optic disc. This view provides an alternative method to display contour information contained in the topographic plot. The surface characteristics of the retina and optic disc can be visualized in three dimensions by this display, which can be manually rotated.

THE REFERENCE PLANE

After the contour line is drawn around the border of the optic disc as described in Chapter 2, the HRT II software automatically places a reference plane parallel to the peripapillary retinal surface located 50 μm below the retinal surface as measured along the contour line in the papillomacular bundle (350° to 356°). The reference plane is the approximated location of the lower extent of the nerve fiber layer since the papillomacular bundle is assumed to show less change as glaucoma develops and progresses. The reference plane is used to calculate the thickness and cross-sectional area of the retinal nerve fiber layer along the contour line by subtracting retinal height as measured in the topographic image from the height of the reference plane. The height of the retina and location of the reference plane along the contour line can be viewed in the HRT II printout as a plot of the z-axis (mm) by the angle of location around the optic disc, beginning at the temporal horizontal midline of the disc and coursing clockwise in the right eye and counterclockwise in the left eye (Figure 1.6).

In addition, the parameters of area and volume of the neuroretinal rim and optic cup are also calculated based on the location of the reference plane. For both volumetric and planimetric calculations, the cup is considered to be the area of the image within the contour line that falls below the reference plane, whereas areas within the contour line that are of greater height than the reference plane are considered the neuroretinal rim (Figure 1.7). Optic disc parameters and their interpretation are reviewed in subsequent chapters.

REFERENCES

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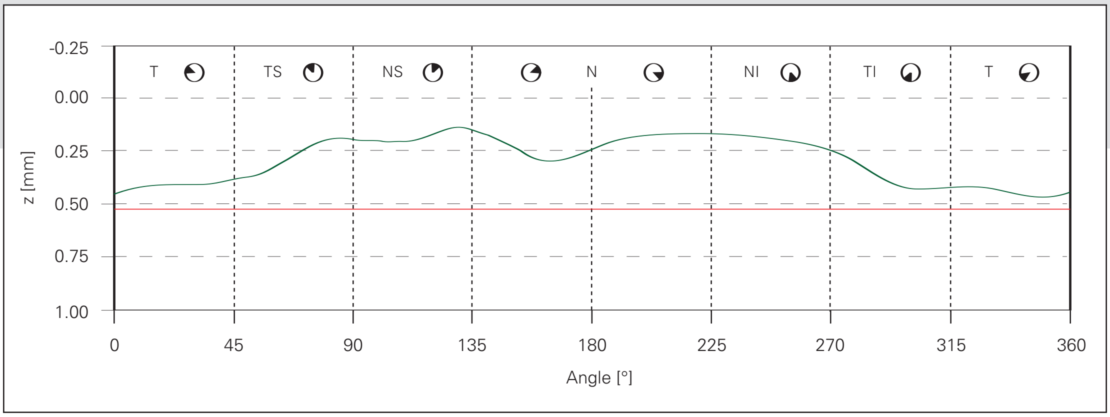

Figure 1.6

Plot of surface height around the contour line of the optic disc beginning in the temporal midline and coursing superiorly clockwise in the same eye. The green line illustrates retinal height and the red line represents the location of the reference plane place 50 μm deep to the retinal surface in the temporal peripapillary region. The thickness of the nerve fiber layer is assumed to be the differences between these two lines.

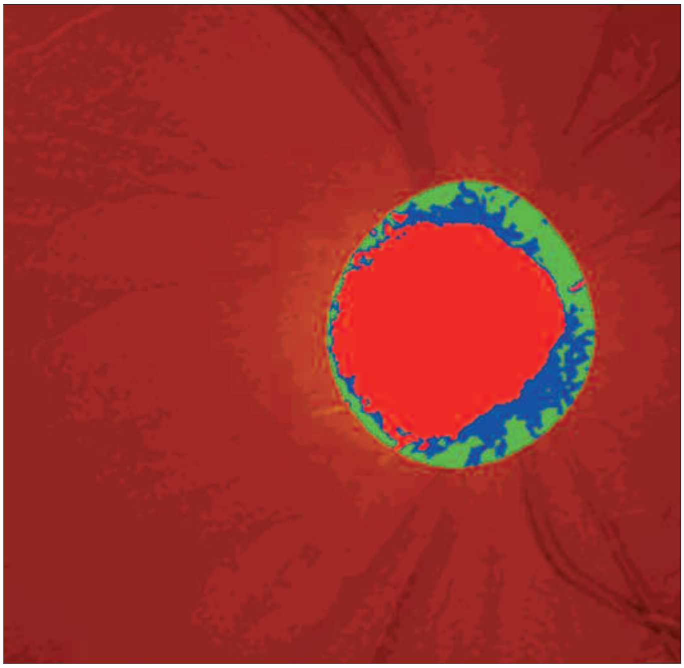

Figure 1.7

False-color coding of the area of the neuroretinal rim (blue and green) and the optic cup (red) overlaid on the topographic plot for the right eye of the same patient.