Panretinal Navigated Laser Photocoagulation for PDR

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Proliferative diabetic retinopathy is a major cause of visual impairment and blindness among people with diabetes in developed nations.[1-4] The current standard of care is to perform panretinal photocoagulation (PRP), especially to eyes with high-risk characteristics as defined by the Diabetic Retinopathy Study (DRS).[5] The DRS and The Early Treatment Diabetic Retinopathy Study (ETDRS) demonstrated that, at 5 years, PRP reduced the risk of severe vision loss by more than 50% compared with observation.[5-7]

Slit-lamp delivery has been the standard method for performing PRP for decades. Green or yellow laser is typically used to produce 500-µm spots spaced 0.5- to 1-burn widths from each other with 0.1- to 0.2-second duration. Alternatively, laser delivery via indirect ophthalmoscopy offers better penetration through vitreous hemorrhage with better laser uptake.

PRP can be time- and labor-intensive, particularly with patient eye movement and fatigue. As such, PRP used to take several sessions to complete. The development of pattern scanning lasers attached to a slit lamp allows delivery of multiple laser spots in very rapid succession in a predefined pattern to cover a much bigger area in a fast sequence.[8-13] However, variations in laser burn effects and size on the retina are often seen even within 1 grid of laser pulses.[8] This effect becomes more noticeable as the treatment moves more peripherally. There, the angle of the incident laser beam varies more as the contact lens used by the physician reaches the limit of its tilt. As a greater part of the laser beam is directed through the edge of the lens, spherical aberration contributes to the variation in burn size, which is often seen in spot or pattern lasers applied with a slit lamp system.

The navigated laser system Navilas (OD-OS GmbH) is a new way of laser delivery with integrated imaging and navigation. It is designed to offer accurate treatment in the macular area and high-speed pattern laser spots placement in the periphery. It uses 50° field-of-view optics for imaging and treatment around the posterior pole while for the periphery larger areas of retina can be visualized through a special widefield contact lens, offering a field of view comparable to the TE Contact Lens (Volk Optics).

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In focal/grid laser applications, the Navilas image-guided system also provides a live fundus image overlaid with a fluorescein angiography (FA) image to optimize accuracy and speed. Physicians can determine the treatment area based on the FA and fundus photo prior to treatment. During treatment, prepositioning of the laser beam to targeted areas is algorithmically coupled and unaffected by eye movement. In peripheral treatment, the aiming beam together with the selected treatment pattern is positioned on the retina and stabilized to eye movements. This can potentially increase patient and physician comfort while ensuring that photocoagulation is delivered only to the intended areas within a potentially reduced treatment time.[14-17]

This article reports for the first time a technical description, the clinical use, comfort, and ease of use of navigated PRP in the treatment of proliferative diabetic retinopathy (PDR).

MATERIAL AND METHODS

In an interventional case series, 31 eyes of 24 patients with diabetic retinopathy were treated with the Navilas Laser System using panretinal optics. Patients were enrolled and treated at the Ophthalmology Clinic at the University of California, Irvine, Medical Center from September 2011 to December 2011. Institutional board review approval was obtained, and the study adhered to the tenets of the Declaration of Helsinski. Informed consent was obtained from all patients before enrollment in the study.

NAVILAS PANRETINAL LASER SYSTEM

The Navilas Laser System is a US Food and Drug Administration-approved ophthalmic scanning slit laser photocoagulator with an integrated delivery system coupled with a digital imaging device. The imaging principle is (like a slit lamp) based on a slit illumination projected through ophthalmoscope optics onto the retina. Either white light for color images, infrared light for more comfortable imaging, or blue light for FA imaging can be selected. With the Navilas, this slit is panned fast and automatically across the imaged area of the retina using a motorized mirror, unlike the slit lamp, where the slit is manually moved by the hand of the physician across the retina. The reflected light of the slit on the retina is imaged back through the ophthalmoscope optics directly onto a special 2-D digital imaging sensor. This setup is equivalent to the eyepiece and microscope optics of the slit lamp and the magnifying contact lens attached to the eye. The imaging sensor allows optoelectronic blocking of stray light and reflections from surfaces other than the retina while the slit moves over the retina. This is similar to the process the physician performs when moving the microscope to eliminate reflections of optical surfaces in the slit lamp depending on the position of the slit and area imaged on the retina, but again at a much faster speed. Because of the speed of the panning slit, 25 complete images of a large retinal area are captured every second, providing a better spatial perception and visual orientation on the retina for the physician compared with the limited static slit view that the surgeon has through the slit-lamp binoculars. The digital image acquired on the digital sensor is transferred to the digital display. The transfer of image data is monitored for data corruption and interruption to make sure that the physician always sees the real-time image of the retina. Only when image data displayed on the digital display are updated and current may the treatment laser application be enabled. The image overlay function provides a composite image, which combines previously captured FA, infrared, or color images with live color fundus images in an overlay process that aids the physician in identifying areas to be treated. With the Navilas, the image of the retina and the aiming beam is not observed through an eyepiece of a microscope, as in slit-lamp–coupled photocoagulators, but on a digital display that allows augmented viewing of the retina with multimodal image, planning, and documentation overlays. Computerized support of imaging and treating patients also improves documenting and teaching of those procedures.

Laser light from the 532-nm laser source is coupled into the imaging path of the Navilas laser system via an optical fiber. An optical zoom allows control of the application of laser spots with different diameters on the retina. A 2-D scanning system, controlled by the user via a trackball on a joystick in the slide base, a mouse, touch screen, or automatically by a control unit of the Navilas, is used for steering the aiming beam and the coaxially aligned treatment beam of the laser to the intended treatment position within the currently imaged field of view of the retina. The laser beam is coupled into the imaging beam path via a dichroic mirror deployed during treatment mode only.

Laser treatment is normally performed during visible light imaging of the retina to provide the clinician with a high-definition color image to assess the efficacy of the applied laser spots. Alternatively, infrared light imaging may be used during laser treatment. Under infrared illumination the patient will only see the aiming beam and experience the laser treatment pulses. The illumination needed for imaging will be invisible to the patient. Therefore the dazzling effect from white-light illumination usually experienced during conventional laser treatments will be eliminated, leading to more patient comfort and compliance during Navilas treatments. White-light snapshots may be taken at any time during the treatment in order to assess the laser effects in color.

Illumination and observation beams are transmitted through the dichroic laser mirror while the treatment radiation is reflected from the mirror onto on the retina. Similar to the delivery system of the PASCAL (pattern scanning laser, Topcon) photocoagulator, patterns are available with the Navilas laser system. User-selectable patterns include single-spot, rectangular, circular, and arcuate patterns.

For PRP, the Navilas laser system provides an exchangeable PRP objective to be used with a specifically designed PRP contact lens. For best optical performance, the patient's eye, the contact lens, and the Navilas optical head must be centered to each other, and their optical axes must be aligned. The Navilas rapid PRP contact lens forms a real aerial image of the retina up to the equator. To cover the retina up to the equator, no or minimal tilt of the lens is required, minimizing astigmatic changes of

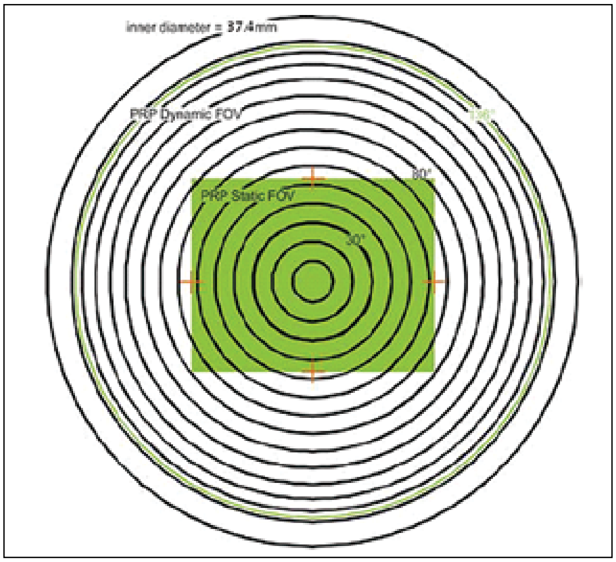

Figure 1. Field of view offered by the Navilas Rapid PRP contact lens. Black circles denote the field of view with spacing of 10° between circles. Particular circles are labeled for 30° (usual fundus camera), 80° (static field of view for Navilas PRP), and 136° (equator). The green rectangle marks the central static field of view that is covered by Navilas and fully displayed on the screen. By moving Navilas laterally the aerial image produced by the contact lens may be sampled. This aerial image diameter corresponds to more than the equator at 136°.

the image and of the projected laser spot. The image of the patient's retina is brought into focus by moving the optical head axially using a joystick on the slide base until a sharp and well-illuminated image appears. Unlike a slit-lamp microscope that allows viewing of only a slit of retina at a time, Navilas instantly images a static field of 63° x 50° (80° diagonal). By moving the optical head of the Navilas laterally or vertically using the slide base (similar to the slit lamp) the full equatorial field may be sampled.

PATIENT PREPARATION AND TREATMENT

The study was approved by the Institutional Review Board of the University of California, Irvine, and was performed at the UC Irvine Gavin Herbert Eye Institute. All patients were pharmacologically dilated with 1% tropicamide and 2.5% phenylephrine. All eyes were anesthetized with topical proparacaine drops. None of the patients received additional anesthesia. Thereafter, the Navilas rapid PRP contact lens was placed onto the cornea of the patient. Contact lens and Navilas optical head were lined up. The obtained image of the patient's retina was brought into focus by moving the optical head axially using a joystick until a sharp and well illuminated image appeared. Then

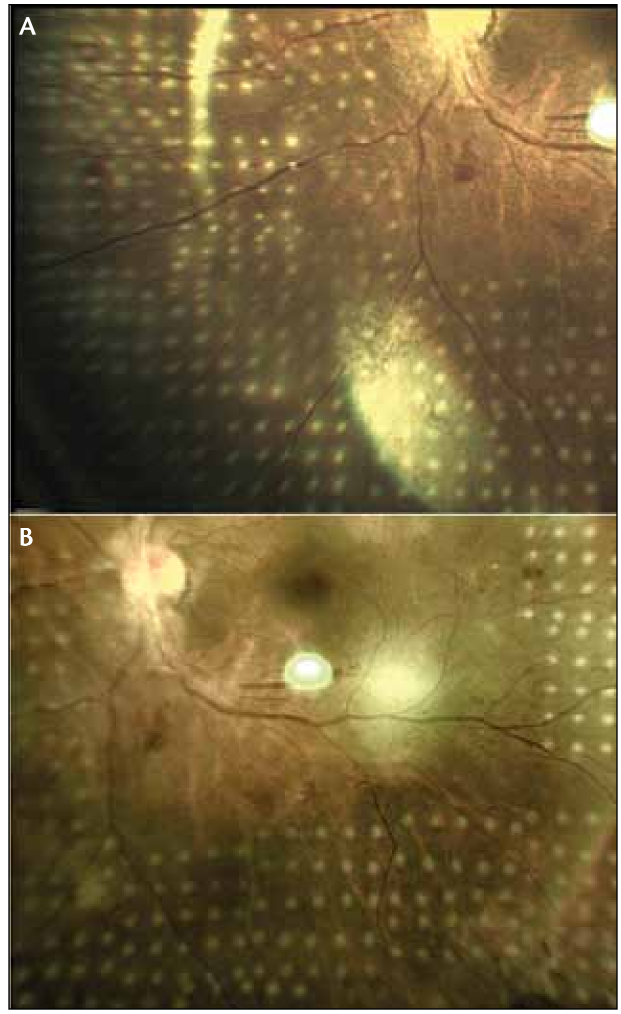

Figure 2. Images A and B show that the static wide field of view of 63° x 50° (80° diagonal) displayed on the touch screen corresponds to different regions of the retina in different eyes. By moving the joystick laterally or up and down, the operator can move to the next region to treat.

grid patterns with the following parameters were used: pulse duration 30 ms, spot size 300 µm, and power to achieve a mild white burn. Burns were placed 1 spot diameter apart.

Patients were asked to rate their pain from 1 to 10 (10 being most severe) and whether PRP with the Navilas was more or less painful compared with their previous treatment using indirect ophthalmoscopy. Pretreatment and posttreatment visual acuity were measured using ETDRS charts. Central macular thickness was measured by spectral-domain optical coherence tomography (Cirrus, Carl Zeiss Meditec). A paired Student *t*-test was used for statistical comparisons, with $P < .05$ denoting statistical significance.

RESULTS

As seen in Figure 1, the Navilas rapid PRP contact lens offers a field of view up to the equator without the need for eye movements or contact lens tilt. In this figure, black circles denote the field of view with spacing of 10° between circles. Particular circles are labeled for 30° (usual fundus camera), 80° (static field of view for Navilas rapid PRP), and 136° (equator). The green rectangle marks the central static field of view that is covered by Navilas and fully displayed on the screen. By moving Navilas laterally and vertically, the aerial image produced by the contact lens may be sampled. This aerial image diameter corresponds to more than the equator at 136°. As shown in Figure 2, Navilas instantly displays a static wide field of view of 63° x 50° (80° diagonal) on its touch screen. By moving the joystick laterally or up and down, the operator was able to move to the next region to treat. Imaging and treatment of the periphery reaching the equator was achieved with relative ease.

Focusing the Navilas onto the aerial image is guided and supported by an optical focus finder. Two bars of infrared light are projected onto the retina. With optimum focus, the 2 bars will line up vertically, whereas the bars will move apart horizontally when Navilas moves out of focus.

The size (diameter) for the laser spots may be adjusted within a range of 75 µm to 750 µm. Because the Navilas Rapid PRP contact lens is specifically designed for use with the Navilas, the given spot size states the diameter of the resulting spot on the retina without requiring the physician to recalculate size for lens magnification.

Single spots or different types of patterns may be selected and applied. Most useful for a speedy PRP treatment was the square pattern, which could be placed via touch screen, mouse, or a trackball mounted onto the joystick of the device. The trackball, furthermore, allows for precise adjustment of position by moving it slowly or for jumping by a full pattern to the next position by moving the trackball faster toward the desired direction.

Laser delivery can be done under light color or infrared mode. When performing treatments under light color, laser uptake is confirmed live while laser spots are delivered. After noticing a gray white burn, power intensity is kept the same during the treatment session, and uptake tends to be consistent across 4 quadrants. If laser is delivered under infrared mode, laser uptake can be confirmed any time by taking a color image. The color image is taken by pressing the trackball of the joystick, and a color snap is seen on the screen. By pressing the trackball again, the color snap is closed and the live image under infrared is on screen again to continue the treatment session.

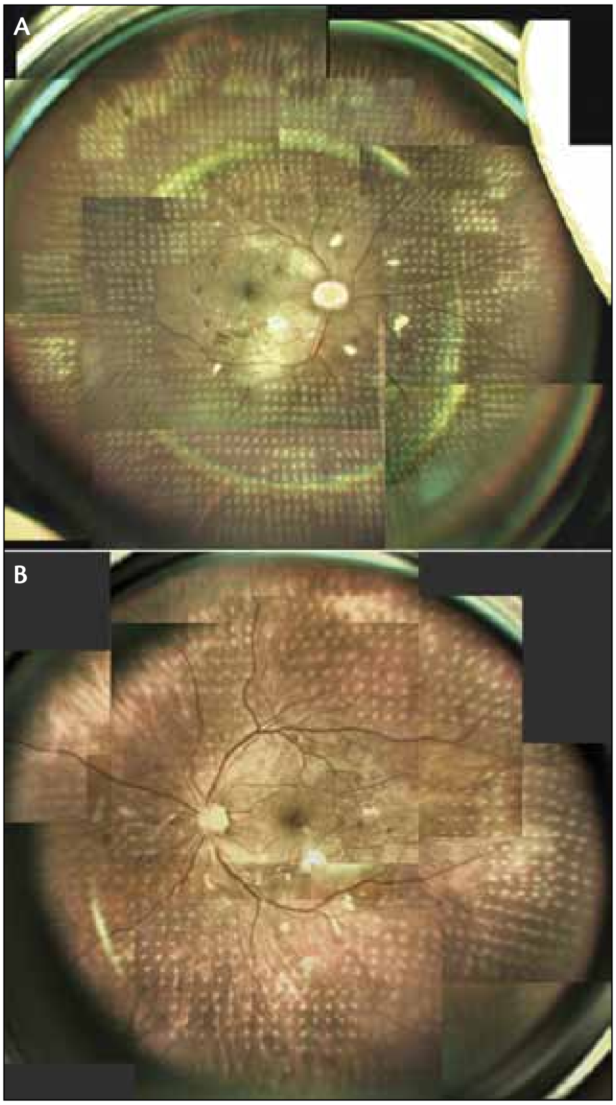

Figure 3. Images A an B correspond to 2 cases in which a full PRP was performed in 1 session. Multiple images were taken after treatment and stitched together to get a full field of view of the retina.

This case series included 31 consecutive eyes of 24 patients with high-risk PDR. Six eyes had concurrent macular edema on presentation, and 4 of them received intravitreal bevacizumab (Avastin, Genentech) injection during the study period. Twenty-five eyes had received previous PRP treatment using indirect ophthalmoscopy (Iridex OcuLight GL Green 532 nm laser). All patients tolerated the Navilas PRP treatment without complications. Five eyes presented with mild vitreous hemorrhage, and infrared mode imaging maintained a good quality view of the fundus during treatment. In all other cases, clear color fundus images were obtained with ease. The average treatment time was 8.2 ±1.7 minutes (range 3.9–10 minutes). The total number of laser spots applied to each eye was calculated per quadrant. A total of 1532 ±599 spots were delivered per eye with an average of 640 ±240 spots per quadrant.

Three eyes received complete PRP in a single session with an average of 2006 ±340 spots and an average treatment time of 7.1 minutes. Figure 3 illustrates 2 cases of a full PRP completed in 1 session. In 12 eyes, laser treatment corresponded to fill-ins, and in most of the cases (10/12) it was possible to complete the PRP during the session. In 2 eyes, a complete treatment was not achieved due to a corneal scar and a patient who was not able to position the chin on the chin rest correctly.

Visual acuity and macular thickness remained stable after 3 months. Average corrected distance visual acuity was 20/70 at baseline and 20/63 at 3 months. Central macular thickness was 279 ±87 µm at baseline and 274 ±114 µm at 3 months ($P > 0.05$). With exclusion of eyes with concurrent diabetic macular edema, central macular thickness before and after the treatment did not change significantly (276 ±47 µm at baseline vs 272 ±79 µm at 3 months, $P > 0.5$). There were no complications during or after the laser treatment.

Patients who received previous PRP were able to complete laser treatment with the Navilas system, and this cohort of patients unanimously reported significantly less pain with the Navilas system; the pain score was 2.7 ±1.9.

DISCUSSION

In this study, we reported for the first time the technical features, clinical use, safety, comfort, and ease of use of this novel laser system, the Navilas laser, for the treatment of PDR. We have shown that Navilas can be a safe and efficient platform for laser delivery in patients with retinal disorders such as diabetic retinopathy.

PRP has been the gold standard for the treatment of diabetic retinopathy for several years.[5-7] Using either a slit lamp or an indirect ophthalmoscope, laser burns can be placed as single laser spots, and sequential spots are laid down by moving the aiming beam or in a semiautomated pattern scan mode in which a variety of patterns can be delivered by a single footpedal depression. In our study, we have introduced a new modality of laser delivery in which the laser is attached to a digital fundus imaging system. As result, treatments are performed on a computerized image with target-assistance systems that allow higher precision and reproducibility.

We have demonstrated that the Navilas imaging and delivery platform reduces variations in fluence delivered to the retina, enabling a more even application of laser burns.

Three systematic factors have been identified for lasers attached to slit lamp delivery systems that lead to variations of the fluence delivered to the retina. These factors are the operator's variable accommodation, the astigmatism introduced by the contact lens, and the depth of focus of the observation system.[18,19] Variations in these factors tend to increase the beam size, leading to a decreased effective fluence. To achieve blanching at the necessary fluence level, the most commonly used parameter is to increase the power, thereby increasing the thermal load to the anterior segment. Depth of focus of the slit-lamp microscope is defined by the distance by which the microscope can be moved in relation to the patient's retina before the observer notices any deterioration of the image. In this case, fluence may vary by a factor of 2.25.[19] The Navilas system has an optical focusing aid, which ensures accurate focussing. The defocus detectable by the operator corresponds to a spot size change of less than 9%. Therefore, the fluence may vary by less than 20%.

CONCLUSIONS

We have demonstrated that the Navilas imaging and delivery platform reduces variations in fluence delivered to the retina, enabling a more even application of laser burns.

In conventional slit-lamp based lasers, variable accommodation of the operator gazing through the slit-lamp microscope's oculars during the procedure is inevitable, and this results in a variation of fluence by a factor of 9.[19] The Navilas system focuses onto a the real image of the retina that is aided by an optical focus finder and remains fixed; hence, this factor is eliminated.

In regard to the astigmatism induced by the contact lens, conventional slit-lamp laser treatments present a variable amount of astigmatism that is introduced into the laser beam by oblique incidence of the beam on the (flat) surface of the contact lens. As a result, the final energy density on the retina is completely unpredictable and one can observe a variation in the size and shape of the laser spot. This variation increases when treating the periphery of the retina, particularly when tilting the contact lens is necessary to obtain a better view of the area to treat. The Navilas system requires the use of a PRP lens designed for this system. No other contact lens can be used to obtain an image in this system. It requires minimal tilt of the contact lens while still achieving the field for PRP. Therefore, the effects of astigmatism should be reduced. Ultimately, the reduced astigmatism is the reason for more homogeneous spots. Moreover, tilting the lens does not help to obtain a better view of the target area. Because the optical head and the lens need to be lined up to obtain the image on screen, tilting the lens can lead to misalignment of the optical axes and loss of the image on screen.

Retinal photocoagulation can be painful, presumably due to local ocular inflammatory responses that enhance outer retinal neurogenic inflammation in ocular pain terminals and higher-order neurons,[20] leading to significant suboptimal laser application in patients.[21] Our results showed a low level of pain with consistent laser burns and tissue uptake, suggesting better comfort for the patient.

The patient experience and compliance during Navilas PRP is greatly improved by the ability to perform the treatment under infrared illumination invisible to the patient's eye. The patient will be dazzled by bright white light illumination only for short time spans for acquiring color images for treatment evaluation.

The fact that we did not experience any complications during the procedures indicates that Navilas laser offers safe treatments. Taken together, navigated laser offers a safe and efficient platform for the treatment of diabetic retinopathy.

As with any new device, there is a learning curve involved to become acquainted with the Navilas and the behavior of this new technology. The most time-consuming step here is to learn how to align the Navilas Rapid PRP contact lens and center it to the Navilas optical head so that the optical axes are in line. If any part is not centered, the image is not visualized. It is expected that the learning curve may quickly be overcome, as shown with focal treatments.[22]

This study demonstrated safety and ease of use. Larger prospective studies, however, are required to observe the long-term clinical efficacy and measure the correlation with the total coagulated area.

In summary, this study reports the first clinical experience with the Navilas panretinal photocoagulator. It delivers safe and fast treatments that are comfortable for the physician and the patient. ■


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