Tracking scanning laser ophthalmoscope (TSLO)

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ABSTRACT

The effectiveness of image stabilization with a retinal tracker in a multi-function, compact scanning laser ophthalmoscope (TSLO) was demonstrated in initial human subject tests. The retinal tracking system uses a confocal reflectometer with a closed loop optical servo system to lock onto features in the fundus. The system is modular to allow configuration for many research and clinical applications, including hyperspectral imaging, multifocal electroretinography (MFERG), perimetry, quantification of macular and photo-pigmentation, imaging of neovascularization and other subretinal structures (drusen, hyper-, and hypo-pigmentation), and endogenous fluorescence imaging. Optical hardware features include dual wavelength imaging and detection, integrated monochromator, higher-order motion control, and a stimulus source. The system software consists of a real-time feedback control algorithm and a user interface. Software enhancements include automatic bias correction, asymmetric feature tracking, image averaging, automatic track re-lock, and acquisition and logging of uncompressed images and video files. Normal adult subjects were tested without mydriasis to optimize the tracking instrumentation and to characterize imaging performance. The retinal tracking system achieves a bandwidth of greater than 1 kHz, which permits tracking at rates that greatly exceed the maximum rate of motion of the human eye. The TSLO stabilized images in all test subjects during ordinary saccades up to 500 deg/sec with an inter-frame accuracy better than 0.05 deg. Feature lock was maintained for minutes despite subject eye blinking. Successful frame averaging allowed image acquisition with decreased noise in low-light applications. The retinal tracking system significantly enhances the imaging capabilities of the scanning laser ophthalmoscope.

Keywords: ophthalmoscopy, confocal imaging, retinal tracking, image stabilization

1. INTRODUCTION

The scanning laser ophthalmoscope (SLO) is a popular research tool with increasingly widespread clinical use since its invention.\textsuperscript{1-3} The SLO applies the principles of confocal microscopy to ophthalmology. A confocal imaging system rejects scattered light from all planes but the focal plane by use of an aperture placed at the detector plane conjugate to the focal plane. Most SLOs use a flying spot illumination beam and some achieve high light collection efficiency by use of disparate entrance and exit pupil sizes. The SLO is therefore able to achieve relatively high resolution depth sectioning, higher contrast, and multi-wavelength operation without the illumination power required for other clinical instruments. The tracking scanning laser ophthalmoscope (TSLO) is a variant of the SLO with a retinal tracker as the primary feature.\textsuperscript{4}

The TSLO uses a different optical arrangement than commercially-sold scanning laser ophthalmoscopes from Heidelberg Engineering, Laser Diagnostics Technologies, and Rodenstock. The primary difference is the use of a scanning line rather than a flying spot.\textsuperscript{5} In the TSLO, a cylindrical lens is used to create a line, a single galvanometer scans and de-scans that focused line on the retina, and a line array is used for detection. This setup offers several advantages over other commercial and research SLOs. First, the TSLO has simplified hardware. Since scanning is reduced to a single axis, there is at least one less moving part and no requirement...
of synchronization between scanners. Spinning polygons and resonant scanners that are required by flying spot imaging instruments to achieve kHz line rates and video frame rates are made superfluous. Second, the TSLO has an extremely compact optical setup and the long (folded) pathlengths in commercial SLOs are unnecessary. Third, the TSLO is inherently safer and thus requires a less complicated fail-safe mechanism. If a scanner fails in a traditional SLO, the laser energy will be focused to a small spot. If the image scanner fails in the TSLO, laser energy remains spread out over a line. The TSLO is significantly less expensive than other instruments with similar capabilities in terms of total hardware costs. Line array detectors are now available at a similar price as PIN or avalanche photodiodes used in other SLOs. One drawback to the current instrument is that higher power is required to achieve the same imaging performance as other research SLOs (but not commercially-sold systems). The typical TSLO illumination laser power is 0.5 mW. However, this is a limitation of the CCD detector sensitivity used in the current version. One of the changes we will implement in the near-future is a CMOS detector that should lower the power to less than 100 μW, near the level used by other research SLOs.

As expected, an analysis of the imaging performance in terms of transverse point spread function (PSF) and longitudinal depth sectioning (i.e., confocality) of the line-scanning optical setup shows its performance to be significantly better than instruments that use area detectors and flood illumination (e.g., fundus camera) and slightly worse than a true flying spot SLO. In terms of transverse performance, neglecting scattering and ocular aberrations, the PSF of the flying spot system is ideal because there is no contribution to background signal from adjacent illuminated regions. In the TSLO only two adjacent regions (pixels) contribute weakly to background levels. In terms of longitudinal performance and sectioning capability in a volume sample with scattering, the total reflected light intensity is a depth integral of the range gate function, which depends upon source illumination and sample reflectivity. For a flying spot SLO the range gate function is inversely proportional to the square of depth, \((z - z_0)^2\) (i.e., confocal), and for a flood illumination-area detection instrument is independent of depth (i.e., no sectioning capacity). The range gate function for the TSLO has inverse proportionality with depth, \(|z - z_0|\), and thus is termed “quasi-confocal”.

The primary feature of the ophthalmoscope reported herein is retinal tracking. Frequent eye motion causes serious difficulties for many therapeutic and diagnostic ophthalmic technologies. Scleral magnetic search coils, electro-oculography, and double Purkinje trackers are among the techniques that have been previously used for eye tracking. Most of the development effort on video image based trackers has focused on pupil tracking. The extraction of retinal coordinates from pupil coordinates is not straightforward. The video based systems employ a passive image processing approach and the system bandwidth is thus limited by the camera frame rate. The genesis of the current research program was the development of a system for robotic laser photoagulation. That system, still under development, uses a similar approach for transverse retinal tracking and coagulation reflectance for control of the depth of laser damage. The use of retinal tracking in diagnostic instruments such as the scanning laser ophthalmoscope resulted from that initial effort.

2. METHODS

2.1. Optical Setup

The generic optical setup for the TSLO is shown in Fig. 1. A complete description can be found elsewhere. The imaging component of the TSLO is comprised of a laser diode source, image scanning galvanometer, line-scan array detector, and lenses. The source is collimated and then focused in one axis with a cylindrical lens. The source line is scanned on the retina with the imaging galvanometer through the scan and ophthalmic lenses. The field of view of the TSLO was adjustable from 28.6 to 9.3 deg (lateral) by use of Volk ophthalmic lenses with powers ranging from 66D to 20D. Backscattered light collected through the pupil is de-scanned with the same imaging galvanometer and focused onto the line-scan array detector. The image entrance and exit pupils are ~4 and 13 mm, respectively.

The TSLO has been built to support several different diagnostic modes. The imaging source module has two FC-fiber-coupled ports for multi-wavelength illumination. The ports are combined with dichroic beamsplitter with a cutoff at 720 nm (reflects \(\lambda = 450 - 720\) nm and transmits \(\lambda > 720\) nm). A stimulus source port is also included for a variety of functional and electrophysiological applications such as micro-perimetry or MFERG. An integrated monochromator is included for fluorescent and hyperspectral imaging applications, for
example to target and quantify macular pigment and photopigment or subretinal structures. Also, the TSLO was designed with ports for two pairs of tracking galvanometers (four mirrors) for eventual implementation of simultaneous retinal and pupil tracking. This paper will focus on characterization of the tracking performance of the TSLO.

2.2. Retinal Tracking

The tracking portion of the TSLO is comprised of tracking galvanometers, dither scanners, and confocal tracking reflectometer. The entire scanned image field passes through the tracking galvanometers, the position of which are locked to the \( x \)- and \( y \)-axis translational movements of the eye. The confocal reflectometer consists of a tracking beam source and detector. The tracking beam is generated with a low-power (\( \sim \) 25 \( \mu \)W) light-emitting diode (LED). Resonant dither scanners driven at 8 kHz and locked with a 90\(^\circ\) phase separation trace a circular tracker beam profile on the retina. The reflectometer detector senses small changes in fundus reflectance. Since a confocal reflectometer is used, only changes in reflectance at the retinal layer are detected. Once locked onto a target, a phase-sensitive detection scheme is employed to generate error signals when eye motion occurs. The error signals are fed into a feedback control loop, the output of which is control signals for the tracking galvanometers. The control loop is implemented with a real-time digital signal processor (DSP) to achieve a closed-loop bandwidth of \( \sim 1 \) kHz. The principles of tracking and the signal processing of the TSLO are illustrated in Fig. 2.

Hardware-based active retinal tracking implemented in the TSLO can achieve a higher overall system bandwidth than software-based passive trackers, which are limited to the acquisition frame rate (typically 30 frames/sec for the SLO). Figure 3 illustrates image distortion that occurs from rapid eye motion when acquired at 30 frames/sec. This distortion would prevent or seriously degrade the ability of a software tracking algorithm to remain locked to local image landmarks. Although advances have been made in high-speed video imaging systems, they require a higher illumination power and thus are still confined by the physical limit imposed by the laser safety standard for posterior segment tracking. Other approaches include anterior segment tracking using multiple Purkinje reflections. However, these systems require calibration data on every individual to extract retinal coordinates from corneal coordinates.

2.3. Human Subject Tests

To date, only a limited number of human volunteers have been tested in experiments designed to quantify instrument parameters \((n = 7)\). The volunteers all had a normal retina absent of disease with the exception of one with central serous retinopathy and hypopigmentation. All subjects were tested without mydriasis. The experiments included: a) imaging with various fields using different ophthalmic lenses; b) very long duration tracking (minutes) for image stabilization and co-addition of up to 1000 frames; c) a test of tracking performance compared to fixation; d) characterization of tracking for large and rapid saccades; e) evaluation of the automatic
re-lock algorithm; and f) tracking on various retinal features. The procedure for the experiments reported in this paper (c–f) are explained below.

To gain qualitative and quantitative data on tracking performance in comparison to fixation, images were co-added for a 6-sec duration for four situations: 1) no tracking and no fixation, 2) no tracking and fixation, 3) tracking and no fixation, and 4) tracking and fixation. Fixation was accomplished by placing a small white target on a large black board several feet in front of the subject in the field of view of one eye while the other eye was imaged. For no fixation, the white target was removed and the subject was instructed to relax their eyes and to look generally toward the black board. The tracking feature was the bright lamina cribrosa in the optic nerve disc. Videos were acquired for each scenario with or without tracking initiated. The width of a retinal blood vessel for each of the four cases was measured and compared to a single frame for quantification of tracking accuracy.

In order to test retinal tracking robustness during large and rapid saccades, tracking was initiated in one eye while the subject viewed a target with the contralateral eye with an arrangement similar to that used for comparison to fixation. Subjects were instructed to shift their gaze rapidly between four white targets on the black board separated by between approximately 10 and 20 deg. Videos were also recorded without tracking during similar rapid eye excursions. For this and similar experiments, the tracking accuracy was also quantified by measurement of the variability of a vessel edge over a number of frames when the TSLO was locked onto a target.
Figure 3. Rapid eye motion can create problems for software-based retinal trackers. (a) Single frame of fundus when eye is stationary, (b) single frame when eye slews in the opposite direction as the image scanner, (c) single frame when eye slews in the same direction as the image scanner, and (d) single frame when eye slews in a direction perpendicular to the image scan. Video rate is 30 frames/sec.

One important feature for clinical use of the TSLO is the ability to rapidly re-lock after the subject blinks. For some very fast blinks, the TSLO will remain locked through the blink since any system bias is removed in the software. Thus the tracker beam will tend not to drift from its current position when presented with a uniform field absent of a tracking target. However, for most longer duration blinks, the tracker will lose lock when the eyelid passes across the tracked point. For this circumstance, we have designed and implemented a re-lock algorithm to rapidly and automatically re-position the track beam to the previously tracked position. The algorithm automatically determines the occurrence of loss of lock when the reflectance signal passes out of a region determined by upper and lower thresholds. When loss of lock occurs, the algorithm re-positions the tracker beam to the last locked position. As long as the subject does not shift their gaze by a large amount during the blink, the system will re-acquire the target as soon as the subject opens their eyes after the blink. Video, galvanometer position, and reflectance signals were acquired to test the re-lock algorithm. During these experiments, the subject repetitively and purposely closed their eyes for a fraction of a second and the time to re-lock for each ‘blink’ was recorded.

The easiest and most repeatable retinal target for tracking was the optic nerve head. More specifically, the target was the region of bright lamina cribrosa. However, since the position of the tracking beam could be adjusted independently from the imaging field, many different targets could be used while imaging important areas of the retina. Several different features of the fundus were used as tracking targets, including blood vessel junctions, scleral crescent, foveal pit, and regions of hypopigmentation in the subject with the diseased eye.

3. RESULTS

Figure 4 illustrates the results from the comparison of tracking and fixation for one subject. The results from another subject were similar. The width of the vessel edge in the images in Fig. 4 was compared to that for
Figure 4. Comparison of 90 frames (6 sec) co-added for a single subject (a) without tracking and fixation (moderate saccades), (b) without tracking but with fixation, (c) with tracking but without fixation, and (d) with tracking and fixation. Foveal pit is visible in (a)–(c) and indicated by an arrow. Cross-section of vessel used for analysis is also indicated (horizontal white bar).

Figure 5 shows an image of co-added frames and the corresponding position and reflectance signals for an experiment tracking on rapid and large saccades for a single subject. The largest angular excursion for this subject’s eye was 18.4 deg. An image with a similar number of co-added frames taken without tracking for equivalently-sized saccades is shown for comparison. The results of other subjects were similar. Tracking was robust even for saccades up to 500 deg/sec (e.g., 21.3 deg in 46 ms for one subject, 291 μm/deg on the retina). The position of the edge and the width of the vessel measured with cross-sectional analysis over 235 frames was 14.57±1.38 and 11.55±1.35 pixels, respectively. The inter-frame accuracy was therefore 1.38 pixels or 0.0473 deg. Although loss-of-lock often occurred from blinks, vignetting, or the subject re-positioning their head, it rarely occurred simply from the movement of the subject’s eyes within the field of view.

The reflectance and galvanometer position signals during a portion of the re-lock experiment is shown in Fig. 6. The unshaded regions indicate a locked period (constant high reflectance from lamina cribrosa and little variation in positions), the lightly shaded regions indicate a blink (constant low reflectance) and the darker shaded regions indicate the re-lock period. The average time to re-lock for 17 blinks in this experiment was 0.65 ± 0.15 second. Although lock was always re-established after a blink, in 29% of the blinks (5 of 17), there was a brief period where the system lost lock a second time before lock was finally established. In these cases, the re-lock time was 0.85±0.02 seconds, compared to 0.56±0.07 seconds when lock was established immediately. The fourth blink in Fig. 6 is an example. This situation was caused by longer blinks and timing in software. After loss-of-lock is detected, there is a variable user-defined software delay before the hardware is commanded
Figure 5. Tracking on rapid, large saccades. (a) Image of 235 co-added frames (~15.7 sec.) with retinal tracking. Cross-section of vessel used for analysis is indicated (horizontal white bar). (b) Image of 256 co-added frames (~17.1 sec.) without retinal tracking. (c) Position signals acquired from galvanometers during tracking. (d) Reflectometer signal during tracking. N: nasal, T: temporal, I: inferior, S: superior.

to re-lock (i.e., galvanometers re-positioned). If the delay is shorter than the blink time, when the system tries to re-establish lock, it will not detect the target. Therefore, the appropriate software delay is a function of individual blink duration. Since that information cannot be known a priori, a slightly longer re-lock period may occur. However, as mentioned previously, in all cases re-lock was established.

Figure 7 shows the wide variety of fundus features on which the TSLO was able to lock. In this figure, images are shown of co-added frames when locked onto the target for durations between 4 and 6 seconds. In general, tracking was most robust for optic nerve head (lamina cribrosa) and blood vessel junctions. Tracking on hypopigmentation was also robust and was determined by the size and contrast of the pigmented region. For scleral crescent and foveal pit, tracking robustness depended upon the characteristics of the subject’s anatomy and thus was quite variable.

4. DISCUSSION

The preliminary results shown above indicate the TSLO was able to achieve robust retinal tracking in a small number of normal subjects. Stabilization of virtually all eye movements with speeds of 500 deg/sec was achieved
Figure 6. Demonstration of automatic tracking re-lock algorithm. (a) Position signals during 4 blink and re-lock cycles. (b) Reflectometer signals for same period. Shading indicates region of blink (light) and re-lock (darker).

with an accuracy of <0.05 deg. The ultimate imaging improvement in a clinical setting will require testing on a population with various retinal disease states. Also, all TSLO diagnostic modes will have to be rigorously tested to determine the usefulness of those features. The initial results indicate that tracking will greatly improve the utility of the SLO for such research and clinical applications as hyperspectral imaging, psychophysical measurements, MFERG, perimetry, quantification of macular pigment and photopigment, imaging of neovascularization and subretinal structures (drusen, hyper-, and hypo-pigmentation), and endogenous fluorescence imaging. Retinal tracking will also remove the limitation imposed by eye movements upon advanced ophthalmic imaging technologies such as optical coherence tomography and adaptive optics scanning laser ophthalmoscopy.

The qualitative improvement in imaging can be seen immediately in Figs. 4 and 5. Fig. 4 compares the motion stabilization of tracking and fixation in normal healthy eyes. Relatively good image stabilization was achieved with fixation (compare Fig. 4a to 4b). However, the images with tracking (Figs. 4c and d) illustrate sharp, high-contrast large and small retinal vessels that are smeared or entirely washed out in Fig. 4b. For patients with a loss of central vision and/or the ability to fixate due to disease or age, and for pediatric exams, the improvement would be even more dramatic. Although the rapid and fast saccades of Fig. 4 would not occur during a normal clinical examination, they depict the ability of the TSLO to track any and all translational eye movements and verify the very high system bandwidth of ~1 kHz. Even for these large voluntary saccades of ~20 deg, the system tracked with an accuracy <0.05 deg. In normal subjects with typical eye movements
Figure 7. Co-added images during retinal tracking of four fundus features on which the TSLO locked: (a) foveal pit (65 fr, 3.8 deg), (b) hypopigmentation (71 fr, 5.5 deg), (c) blood vessel junction (90 fr, 5.1 deg), and (d) scleral crescent (60 fr, 1.6 deg). Tracking point (tracking beam size and dither amplitude) indicated by concentric circles. The number of frames co-added and the maximum angular excursion for each image is listed above. All videos from which the co-added images are derived were acquired at 15 frames/sec.

The re-lock algorithm was sufficiently robust to re-initiate tracking within one second of all blinks. Although the algorithm requires calibration in that a software delay must be set differently for each subject, this procedure is quite simple and takes only one or two minutes. The re-lock algorithm makes possible longer duration tracking of many minutes in a realistic clinical scenario. In the next software version, automatic blink extraction routines will be implemented where software frame co-addition and video acquisition functions will proceed by suspension during and re-initiation after a subject’s blinks.

Figure 7 illustrates the wide variety of features on which the TSLO can track. Tracking was most robust on the optic nerve head. Blood vessel junctions also made good targets. The scleral crescent was able to track, although not extremely robustly because of its large size and highly asymmetric shape. For targets with an elliptical shape asymmetry, we have created a software algorithm that automatically adjust control parameters to accommodate the asymmetry. Foveal pit tracking was highly dependent on subject anatomy: in some patients there was a clear reflectance feature while in others no such tracking feature existed. Although every subject is different, there are always abundant retinal targets from which to choose.

For lock to be robust, the tracking beam size and dither amplitude must approximately match the feature size. If the ophthalmic lens is changed, the tracker beam size will also change. This can be considered a drawback if a single feature is tracked because tracking performance will be dependent on which lens is used. However,
it enables the user to rapidly switch tracking targets simply by switching lenses. The system is designed so that by swapping reflectometer input fibers, the tracker beam size can be adjusted. This crude design will be replaced in future systems with a pinhole wheel to rapidly dial a particular beam diameter.

The TSLO thus achieves stabilized, high-contrast, quasi-confocal imaging in a relatively compact, low-cost design. Future studies on the TSLO will emphasize testing of the advanced functionality modules, such as dual wavelength illumination/detection, hyperspectral imaging with the monochromator, and perimetry with the stimulus module.

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