Tohoku J. Exp. Med., 2025, **265**, 39-45

Development of a Low-Cost Scanning Laser Ophthalmoscope Using Semiconductor Laser Technology

Hiroki Takizawa,[1] Hiroshi Kunikata,[1,2] Takeshi Yabana,[1] Masataka Sato,[1] Takahiro Ninomiya,[1] Neelam Kaushik,[1] Parmanand Sharma,[1] Noriko Himori,[1,3] Mitsuru Sugawara,[4] Seiji Morino,[4] Makoto Suzuki,[4] Makoto Ishikawa[1] and Toru Nakazawa[1,2,5,6]

[1]Department of Ophthalmology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan
[2]Department of Retinal Disease Control, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan
[3]Department of Aging Vision Healthcare, Tohoku University Graduate School of Biomedical Engineering, Sendai, Miyagi, Japan
[4]QD Laser Corporation, Kawasaki, Kanagawa, Japan
[5]Department of Ophthalmic Imaging and Information Analytics, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan
[6]Department of Advanced Ophthalmic Medicine, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

In recent years, the use of scanning laser ophthalmoscopy (SLO) has emerged as a valuable tool in ophthalmic diagnostics. However, its widespread adoption has been prevented by substantial costs associated with existing devices. This study reports on the development of a low-cost SLO that is safe, requires no pupil dilation and no focus adjustment, and uses semiconductor laser technology for scanning. A prototype SLO equipped with red (638 nm) and infrared (IR; 795 nm) lasers was developed, and eyes with ocular diseases including glaucoma, branch retinal vein occlusion (BRVO), and diabetic retinopathy (DR) were examined using the SLO. We examined 53 patients (average age 62.0 ± 13.0 years; 93 eyes) with glaucoma (65 eyes), BRVO (11 eyes), and DR (17 eyes) using the low-cost SLO. Successful images were obtained from 83 eyes of 47 patients. The process was non-invasive, allowing for clear observation of the optic nerve head (ONH) and retinal vessels using both red and IR lasers. Furthermore, ophthalmological findings such as ONH cupping, macular edema, and retinal hemorrhage were detectable. Using a semiconductor laser, the prototype SLO successfully obtained high-quality images of ocular morphology and pathology without requiring pupil dilation and without focus adjustment. This low-cost SLO has the potential to enhance the accessibility of ophthalmic diagnostics, particularly in resource-limited settings, and contribute to the early detection and management of various ocular diseases.

Keywords: branch retinal vein occlusion; diabetic retinopathy; glaucoma; semiconductor laser; scanning laser ophthalmoscopy
Tohoku J. Exp. Med., 2025 January, **265** (1), 39-45.
doi: 10.1620/tjem.2024.J072

Introduction

Recently, color scanning laser ophthalmoscopy (SLO) has become widely used in fundus examination (Lompado et al. 2000) because of its clearer images compared to conventional color fundus photography (Terasaki et al. 2021). Generally, color SLO generates high-resolution color images of the retina by combining blue, green, and red lasers. The blue (short-wavelength) light captures images of the retinal surface, green (medium-wavelength) light captures images of the intermediate layer, and red (long-wavelength) light captures images of the deeper retinal layers (Terasaki et al. 2021). This way, the SLO can contribute to diagnosis even in cases where it is difficult to directly

Received February 13, 2024; revised and accepted July 16, 2024; J-STAGE Advance online publication August 1, 2024
Correspondence: Hiroshi Kunikata M.D., Ph.D., Department of Ophthalmology, Tohoku University Graduate School of Medicine, 1-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8574, Japan.
e-mail: drkunikata@gmail.com

observe and photograph the fundus with a conventional fundus camera or slit lamp, such as in patients with cataract or vitreous opacity (Terasaki et al. 2021). Furthermore, SLO is useful for in vivo imaging of different retinal cells and for monitoring changes over time (Miyahara et al. 2008; Tsuda et al. 2016; Ito et al. 2019; Asano et al. 2020), making it a valuable tool that offers hope for understanding the pathogenesis of ocular diseases.

Though SLO enables ophthalmologists to detect and monitor various ocular diseases with high precision, the widespread adoption of SLO has been prevented by the considerable costs associated with existing devices, limiting the accessibility of this valuable tool. Namely, the high costs traditionally associated with SLO have prevented its integration into routine ophthalmic practice, particularly in resource-limited clinical settings. Thus, to overcome the barriers to its widespread adoption, we developed a prototype of a small, low-cost SLO that requires no pupil dilation and no focus adjustment and uses a semiconductor laser for scanning.

The purpose of this study is to report on the development of a small, low-cost SLO and describe its clinical utility for ocular diseases including glaucoma, branch retinal vein occlusion (BRVO), and diabetic retinopathy (DR).

Methods

This was a single-center, cross-sectional study. The research followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Tohoku University Graduate School of Medicine (protocol No. 2021-1-434). Written informed consent was obtained from all subjects.

Subjects

Fifty-three patients (24 males and 29 females; mean age 62.0 ± 13.0 years old [YO], range 44-95 YO) with ocular diseases attending the outpatient clinic of Tohoku University Hospital were included in this study. These included 65 eyes with glaucoma, 11 eyes with BRVO, and 17 eyes with DR.

Ophthalmological examinations

Our prototype SLO, along with optical coherence tomography (OCT) and fundus photography, was used without pupil dilation. The OCT devices used were spectral-domain OCT (Cirrus HD-OCT, Carl Zeiss Meditec, Inc., Dublin, USA) or swept-source OCT (DRI OCT Triton, Topcon, Inc., Tokyo, Japan). Among the 53 patients, 14 had their pupil diameters previously measured clinically with anterior segment OCT (CASIA or CASIA2, Tomey Corporation, Nagoya, Japan), and all 14 were glaucoma patients.

The prototype SLO system

Fig. 1 shows the external appearance (Fig. 1A) and internal structure (Fig. 1B) of the optical imaging device. Its external dimensions are 226 mm (width) × 115 mm (height) × 297 mm (depth), with a 65-mm-diameter eyepiece lens positioned 37.5 mm from the top surface. The internal structure measures 218 mm (width) × 104 mm (height) × 292.6 mm (depth), with the 65-mm-diameter eyepiece lens mentioned above. The SLO optical system is located behind the eyepiece lens, and the circuit board is placed at the rear of the device.

Fig. 2 illustrates the layout of the optical system. The unpolarized laser light is emitted radially from the lasers and passes through a collimating lens to become parallel. The beams are either reflected or transmitted by a plate-type beam splitter with color selectivity, then pass through a prism-type beam splitter dependent on polarization. The collimated beams, after being adjusted in distance between the focusing lens and the relay lens to match the subject's eye diopter value, are swept to a predetermined field of view by the micro electro-mechanical systems (MEMS) mirror, becoming a return beam. The beam's diameter emanating from the MEMS mirror is 1.6 mm. After raster scan-

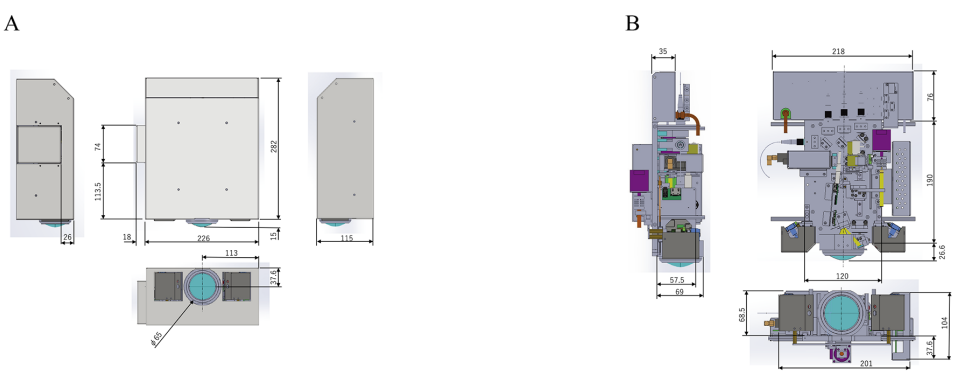

Fig. 1. External and internal dimensions of the semiconductor laser–based SLO system.
A) The external appearance with dimensions of 226 mm (width) × 115 mm (height) × 297 mm (depth), with a 65-mm-diameter eyepiece lens positioned 37.5 mm from the top surface. B) The internal structure, measuring 218 mm (width) × 104 mm (height) × 292.6 mm (depth), with a similar eyepiece lens arrangement. The SLO optical system is located behind the eyepiece, with the circuit board situated at the device's rear.

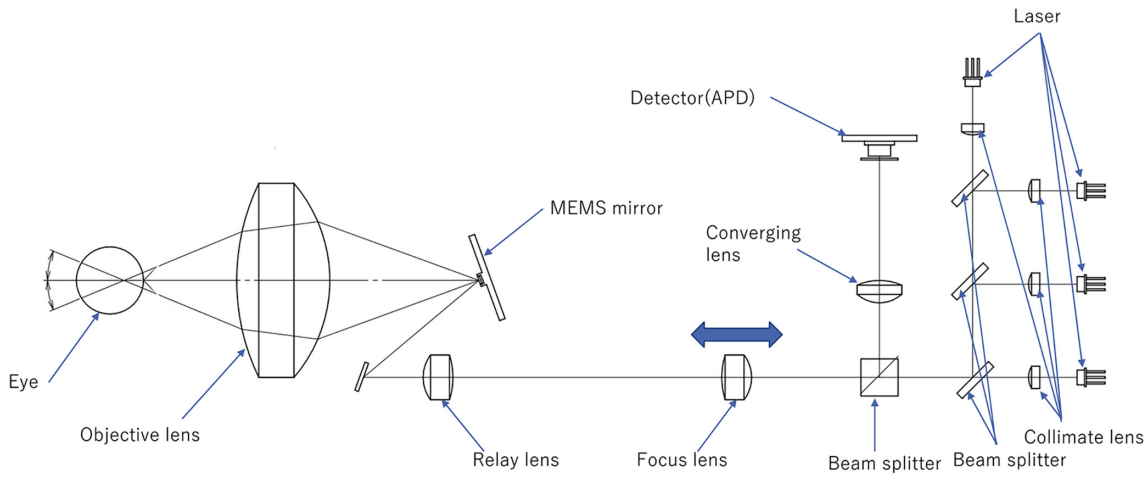

Fig. 2. Schematic and optical design of the SLO system.
This diagram illustrates the path of polarized laser light through the optical system, including its emission from the laser, collimation, selective reflection/transmission by a color-selective plate-type beam splitter and polarization-dependent prism-type beam splitter, adjustment for eye diopter, and sweeping across a predetermined field of view by the MEMS mirror. It also shows the light's focus on the retina, polarization plane changes upon reflection, and the path back to the polarization beam splitter, where corneal and retinal reflections are differentiated and detected by the avalanche photodiode.

ning by the MEMS mirror, the light passes through the objective lens and focuses. Upon passing through the eye's pupil, each spot of light reaches the retina in a concentrated state. The direction of the reflected light's polarization plane changes on the retina. The reflected light retraces the path of the incident light to reach the polarization beam splitter. The corneal reflection light, which does not change its polarization plane, passes through, while the retinal reflection light, which does change, is reflected. This light then passes through a converging lens and is received by a detector (an avalanche photodiode) where it undergoes photoelectric conversion; the retinal brightness signal is then transmitted to the analog-digital converter (ADC) circuit.

The laser diodes serve as light sources: infrared (IR), 795 nm; red, 638 nm; green, 520 nm; and blue, 520 nm. This study used the IR and red lasers.

Results

This study included 93 eyes of 53 patients with ocular diseases attending the outpatient clinic of Tohoku University Hospital. There were 65 eyes of 33 cases of glaucoma, 11 eyes of 11 cases of BRVO, and 17 eyes of 9 cases of DR. Successful data were obtained from 83 eyes of 47 patients. The process of the SLO measurement was smooth and successful, without the need for pupil dilation or focus adjustment, allowing for clear observation of the optic nerve head (ONH) and retinal vessels using both red and IR lasers. Furthermore, it was possible to make ophthalmological findings such as ONH cupping, macular edema, and retinal hemorrhage.

Successful imaging data could not be obtained for 10 eyes of 6 patients, all of whom had glaucoma. There were no significant differences in age between the 27 glaucoma patients with successful images and the 6 glaucoma patients with failed images (mean age of 55.1 ± 9.3 and 56.8 ± 0.3 years, respectively, P = 0.66). Previous data on pupil diameter were available for 14 patients with glaucoma (mean 5.4 ± 1.2 mm, range 3.4-7.0 mm). The device was able to acquire good SLO images from the eye with the smallest pupil of 3.4 mm without dilation. A review of the medical records of the 10 eyes of the 6 patients who could not be imaged successfully suggested that the reasons for failed imaging may be due to poor fixation caused by cataract (four eyes), postoperative capsular opacification (two eyes), and visual field abnormalities due to glaucoma (four eyes).

Three representative cases are presented below. For comparison, color fundus camera photos and OCT images are shown.

Case 1 was a 56-year-old male with bilateral glaucoma (Fig. 3). The images are of the right eye, showing enlargement of the ONH cupping. No retinal diseases were observed. No obvious retinal lesions were seen in the fundus photos or OCT map. SLO also showed no notable findings in the macula. However, ONH cupping was clearly visible in the red-laser image.

Case 2 was a 76-year-old male with bilateral proliferative DR and diabetic macular edema in the left eye, showing laser scars and dot hemorrhage (Fig. 4). The SLO images are of the left eye. There was swelling in the macula due to edema in the OCT map. Corresponding to the OCT map, shadows are visible in the red-laser image. Additionally, laser scars are visible in the both red-and IR-laser images.

Case 3 involves BRVO and associated macular edema in the left eye, showing inner retinal hemorrhage (Fig. 5). There was swelling in the macula due to edema in the OCT map. Extensive shadows are visible in both red-and IR-laser images, reflecting retinal hemorrhages and macular

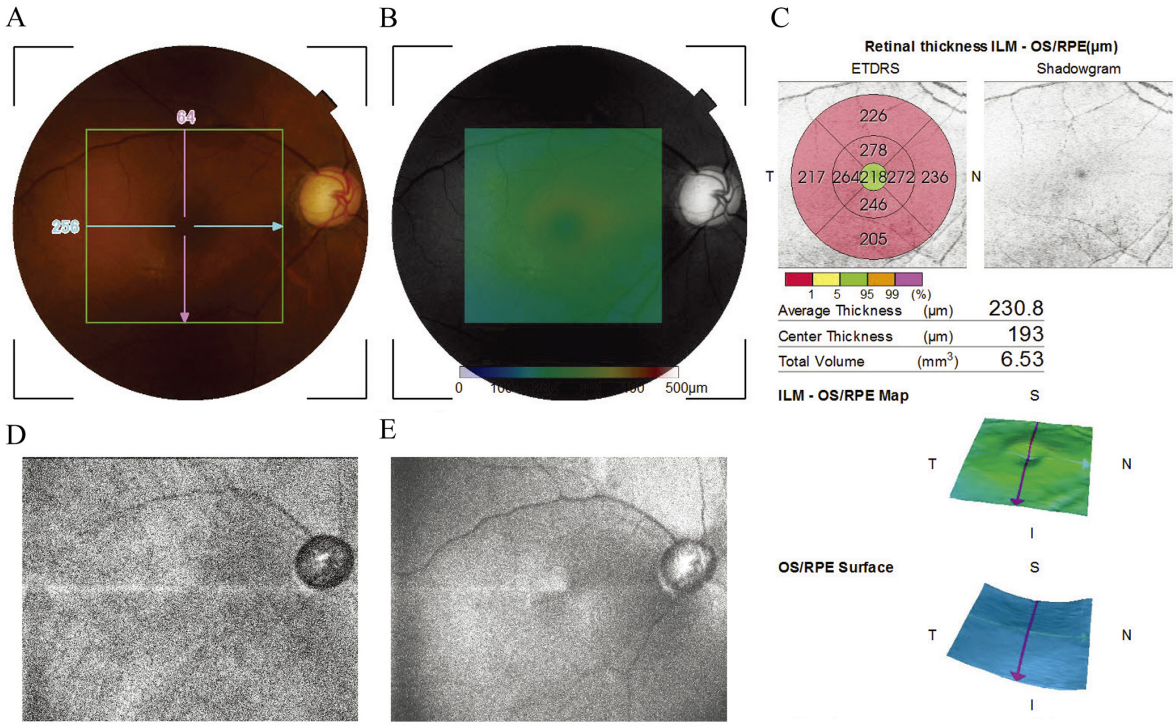

Fig. 3. Representative case of glaucoma.
Imaging results from a patient with glaucoma (Case 1). A) Color fundus photograph. B,C) OCT maps, imaged using Triton OCT. D,E) Images captured with SLO, where D) is IR and E) is red.

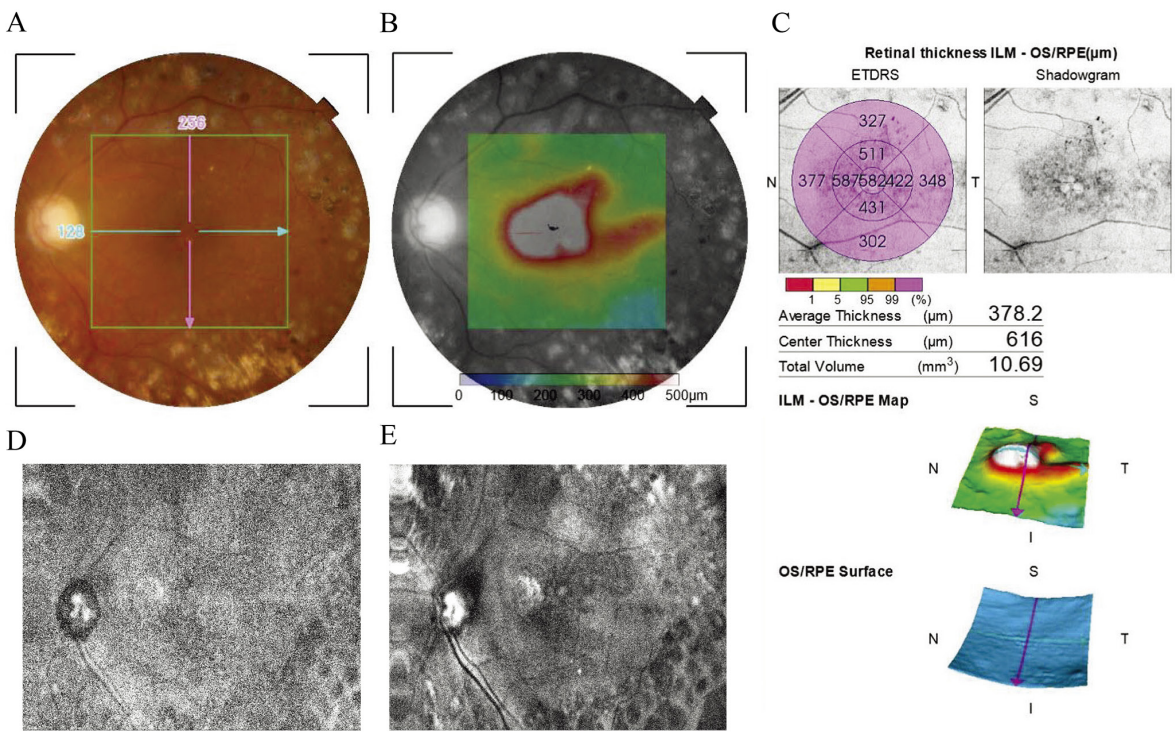

Fig. 4. Representative case with DR.
Imaging results from a patient with diabetic retinopathy (Case 2). A) Color fundus photograph. B,C) OCT maps, imaged using Triton OCT. D,E) Images captured with SLO, where D) is IR and E) is red.

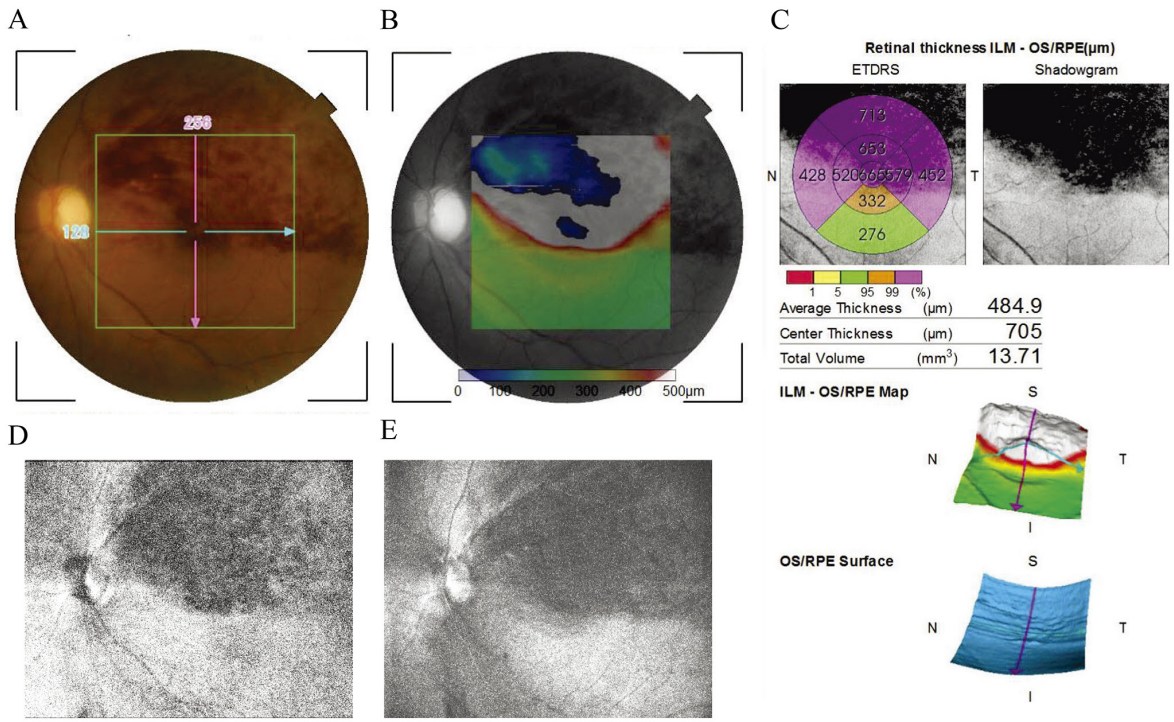

Fig. 5. A representative case with BRVO.
Imaging results from a patient with branch retinal vein occlusion (Case 3). A) Color fundus photograph. B,C) OCT maps, imaged using Triton OCT. D,E) Images captured with SLO, where D) is IR and E) is red.

edema in the upper quadrants.

Discussion

We set out to report on the development of a small, low-cost SLO equipped with red and IR lasers that is safe, requires no pupil dilation and no focus adjustment, and uses semiconductor laser technology for scanning. Eyes with ocular diseases including glaucoma, BRVO, and DR were successfully examined using the SLO. The SLO was non-invasive, allowing for clear observation of the ONH and retinal vessels using both red and IR lasers. Furthermore, we were able to make ophthalmological findings such as ONH cupping, macular edema, and retinal hemorrhage.

Advances in SLO technology

The integration of semiconductor laser technology represents a revolutionary shift in SLO, with innovations that have increased the safety and efficiency of the device. In particular, color SLO with short, medium, and long wavelength lasers was able to capture the retinal layers in unprecedented detail (Terasaki et al. 2021). The small SLO prototype we developed was equipped with red and IR lasers, both of which are long wavelengths of light, which allowed imaging through the different layers of the eye and enabled a strong ability to capture detailed images of the intraocular structures. Indeed, we could detect ONH cupping in glaucoma and retinal hemorrhages associated with BRVO, thus demonstrating the potential of the device in clinical use due to the high prevalence of these diseases (Quigley and Broman 2006; Rogers et al. 2010; Tham et al. 2014; Song et al. 2019). In general, subretinal lesions can be seen more clearly in long-wavelength IR spectra than in color fundus photographs. Although this study did not include eyes with age-related macular degeneration (AMD) with choroidal neovascularization, this SLO may be useful for detecting this type of AMD due to the disease's characteristics, and we would like to recruit sufficient cases to investigate the SLO's usefulness in the future. The ability to successfully capture images sufficient to make medical findings in the affected eyes using this SLO highlights the potential for applying this technology to a variety of real-world clinical situations.

Clinical significance and non-invasiveness

We used the SLO to non-invasively test 93 eyes with a variety of ocular diseases and were able to obtain important ocular findings such as ONH cupping, macular edema, and retinal hemorrhage, demonstrating the clinical utility of the SLO. The non-invasive nature of the process is particularly noteworthy, eliminating the need for pupil dilation and focus adjustment. This means that side effects such as allergic reactions can be avoided, as no eye drops are used to dilate the pupil (Tayman et al. 2010; Sefi-Yurdakul and Sancakli 2021), and the examination is completed very smoothly, with the major advantage that no focus adjustment is required. Thus, the SLO can non-invasively provide detailed images of the ONH and retina, which may help clinicians to assess various ophthalmic diseases in a

safe, location-independent manner.

High accessibility leads to the early detection of ocular diseases

One of the most promising aspects of semiconductor laser–based SLO is its potential to improve the accessibility of ophthalmic diagnostics, especially in resource-limited settings. Conventional SLOs are equipped with two types of mirrors: a polygon mirror and a galvanometer mirror; they scan the retina in two axes by orthogonalizing the scanning directions of these two mirrors. The SLO prototype uses a single MEMS mirror for scanning, which oscillates at high speed around two XY axes and has the advantages of being smaller and less expensive than a galvanometer mirror. Low-cost SLOs are distinctive in nature and may provide a valuable option for healthcare facilities with limited financial capacity and difficulty in making expensive investments. This will have important implications for global health, as early detection and intervention in glaucoma and retinal disease can prevent irreversible visual impairment and improve patient outcomes. We have successfully developed a cost-effective SLO proof-of-concept device to address the need to reduce costs while maintaining the high utility of SLOs. This low-cost SLO is small, portable, and cost-effective, making it ideal for use in mobile clinics and community health settings. As a result, it has the potential to extend the reach of ophthalmic diagnostics to disadvantaged populations who often have limited access to specialized health services. Since early detection of ocular disease is important to prevent irreversible visual impairment, the ability of this SLO prototype to detect changes in the ONH and retina indicates its potential as a valuable tool for proactive healthcare.

Limitations

There are several limitations to this study. Firstly, research on blue and green lasers could not be conducted. This was because both lasers were too bright, making photography difficult. Therefore, we did not study color SLO in this research project. Secondly, the number of cases examined was small. Other retinal degenerative diseases, such as AMD, were not examined. Thirdly, since the device could not measure or monitor pupil size during the capture of SLO images, pupil diameter data were only available in the current study from previous anterior OCT data for 14 of the 53 patients. Therefore, since our device could obtain good SLO images from eyes with a pupil as small as 3.4 mm without dilation, although the SLO images may be minimally influenced by pupil diameter, the smallest precise pupil diameter required to obtain SLO imaging should be investigated. Further research and clinical validation will be essential to establish the widespread applicability and effectiveness of this technology across diverse healthcare settings. This prototype SLO will be improved in the future with a wider angle of view and higher resolution.

Conclusion

Using IR and red semiconductor lasers, we successfully used the prototype SLO to obtain high-quality images of ophthalmological structures; these images were sufficient to make ophthalmological findings and did not require pupil dilation or focus adjustment. This small, low-cost SLO has the potential to enhance access to ophthalmic diagnostics, particularly in resource-limited settings, and contribute to the early detection and management of various ocular diseases.

Acknowledgment

The principal investigator, Hiroki Takizawa, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Author Contributions

H.T., T.Y. and T.N. designed and conducted the study; H.T. collected the data; H.T., H.K., T.Y. and T.N. interpreted the data; H.T. and H.K. wrote the main manuscript text; H.T. prepared all figures. All authors reviewed and approved the final paper.

Conflict of Interest

The authors declare no conflict of interest.

Funding

This paper was supported by JST grants from JSPS KAKENHI Grants-in-Aid for Scientific Research (C) (H.K. 17K11445) and COI-NEXT (JPMJPF2201). The funders had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

References

Asano, T., Nagayo, Y., Tsuda, S., Ito, A., Kobayashi, W., Fujita, K., Sato, K., Nishiguchi, K.M., Kunikata, H., Fujioka, H., Kamiya, M., Urano, Y. & Nakazawa, T. (2020) Companion Diagnosis for Retinal Neuroprotective Treatment by Real-Time Imaging of Calpain Activation Using a Novel Fluorescent Probe. *Bioconjug. Chem.*, **31**, 2241-2251.

Ito, A., Tsuda, S., Kunikata, H., Toshifumi, A., Sato, K. & Nakazawa, T. (2019) Assessing retinal ganglion cell death and neuroprotective agents using real time imaging. *Brain Res.*, **1714**, 65-72.

Lompado, A., Smith, M.H., Hillman, L.W. & Denninghoff, K.R. (2000) Multispectral confocal scanning laser ophthalmoscope for retinal vessel oximetry. In Spectral Imaging: Instrumentation, Applications, and Analysis., edited by Bearman, G.H. Cabib, D. & Levenson R.M., SPIE, 3920, pp. 67-73.

Miyahara, S., Almulki, L., Noda, K., Nakazawa, T., Hisatomi, T., Nakao, S., Thomas, K.L., Schering, A., Zandi, S., Frimmel, S., Tayyari, F., Garland, R.C., Miller, J.W., Gragoudas, E.S., Masli, S., et al. (2008) In vivo imaging of endothelial injury in choriocapillaris during endotoxin-induced uveitis. *FASEB J.*, **22**, 1973-1980.

Quigley, H.A. & Broman, A.T. (2006) The number of people with glaucoma worldwide in 2010 and 2020. *Br. J. Ophthalmol.*,

90, 262-267.
Rogers, S., McIntosh, R.L., Cheung, N., Lim, L., Wang, J.J., Mitchell, P., Kowalski, J.W., Nguyen, H., Wong, T.Y. & International Eye Disease, C. (2010) The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia. *Ophthalmology*, **117**, 313-319. e311.
Sefi-Yurdakul, N. & Sancakli, O. (2021) Tropicamide and anaphylaxis: A case report. *Saudi J. Ophthalmol.*, **35**, 71-72.
Song, P., Xu, Y., Zha, M., Zhang, Y. & Rudan, I. (2019) Global epidemiology of retinal vein occlusion: a systematic review and meta-analysis of prevalence, incidence, and risk factors. *J. Glob. Health*, **9**, 010427.
Tayman, C., Mete, E., Catal, F. & Akca, H. (2010) Anaphylactic reaction due to cyclopentolate in a 4-year-old child. *J. Investig. Allergol. Clin. Immunol.*, **20**, 347-348.
Terasaki, H., Sonoda, S., Tomita, M. & Sakamoto, T. (2021) Recent Advances and Clinical Application of Color Scanning Laser Ophthalmoscope. *J. Clin. Med.*, **10**, 718.
Tham, Y.C., Li, X., Wong, T.Y., Quigley, H.A., Aung, T. & Cheng, C.Y. (2014) Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*, **121**, 2081-2090.
Tsuda, S., Tanaka, Y., Kunikata, H., Yokoyama, Y., Yasuda, M., Ito, A. & Nakazawa, T. (2016) Real-time imaging of RGC death with a cell-impermeable nucleic acid dyeing compound after optic nerve crush in a murine model. *Exp. Eye Res.*, **146**, 179-188.