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Diagnostic medical device for stabilized image perception of retinal blood vessels using entoptic phenomena

https://doi.org/10.1515/cdbme-2023-1102

Abstract: A diagnostic medical tool is described that allows patients to non-invasively observe, describe and document their own retinal blood vessels using the Purkinje vascular entoptic test. We envision key applications of the Purkinje retinal image stabilization (PRIS) device in monitoring of diabetic retinopathy and cost-effective assessment of retinal visual acuity. To optimize our PRIS principle, we have developed a benchtop device with interchangeable light modules. The modular design is intended to provide maximum flexibility for determining appropriate PRIS stimulation parameters. In self-tests, we found that a pleasant entoptic perception occurs when a green luminous light spot (approx. 525 nm) moves on a circular path. The challenging part is to derive an objective diagnosis from a subjective phenomenon.

Keywords: entoptic, phenomenon, retinal visual acuity, purkinje, diabetes, retinopathy, aneurysm, medical

1 Introduction

1.1 Entoptic phenomena

The Purkinje vascular entoptic test can be used to examine the retinal blood vessels in the patient's own eye. In 1819, Purkinje described his finding that light projected into the eye through the sclera, bypassing the optical system, causes briefly observable shadows of the blood vessels on other retinal receptors [1, 2]. These shadows are not perceived in normal vision due to local adaptation. As already recognized by Purkinje, an image of the retinal vessels is formed in an entoptic manner, which rapidly fades if the light source is not moved. The vessels are perceived as a magnified image representing a complex, branched vascular tree without leaves, the "Purkinje tree" as illustrated in **Figure 1A**. The macula, responsible for high-acuity vision in the center of the retina, can be seen as a granular pattern in the vascular free zone of the Purkinje tree. Entoptic image perception is well described in [1-6]. If a patient perceives abnormalities in the Purkinje tree or if the tree cannot be seen at all, this may indicate retinal disease e.g. diabetic retinopathy. Vessel free areas, with the exception of the macula, may indicate visual field loss (scotoma). The reliability of the entoptic method can be optimized by stabilizing the Purkinje image perception. Using the impressive entoptic phenomenon and our established Purkinje retinal image stabilization (PRIS), we aim to provide a diagnostic medical tool that allows patients to non-invasively observe, describe and document their own Purkinje image. With our PRIS tool (**Figure 1B**) a simple method will be available, also to evaluate the visual performance in patients with media opacities.

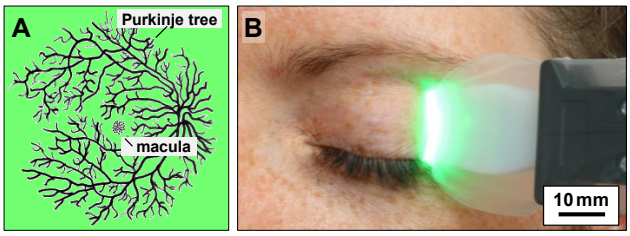

Figure 1: Entoptic image perception with green light stimulation
A: Illustration of a Purkinje tree with macula. No abnormalities are shown.
B: Light module (LM A, light bar) on a closed eye with protective cover.

1.2 Medical use cases

We envision key applications in early detection and monitoring of diabetic retinopathy and cost-effective assessment of the retinal visual acuity. Unless there is media

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opacity (e.g. cataract), the ophthalmologist uses funduscopy as gold standard for ocular fundus examination.

1.2.1 Diabetic retinopathy

In Germany, approx. 4 million people suffer from diabetes mellitus [7]. By 2030, it is estimated that the number of people with diabetes mellitus will exceed 600 million worldwide. 75% of them will live in low and middle income countries [8]. 25 to 35% of diabetics have diabetic retinopathy. If not treated properly, it can lead to blindness which is the most common preventable cause of blindness to adults in many countries [9, 10]. Diabetes patients recognize the progression of their microangiopathy quite late, as the reduction in visual acuity caused by damage to the retinal center occurs late in the course of diabetes. Therefore, diabetic patients should visit the ophthalmologist every 6 to 12 months to determine the status of their disease by observing the retinal blood vessels [7].

1.2.2 Retinal visual acuity

Entoptic perception is used to assess retinal functionality, in cases of severe opacification of the refractive media (cornea, lens, vitreous) [3, 4, 11]. For Africa, it is assumed that approx. 2,000 cataract surgeries per million people (currently 1.3 billion inhabitants) will have to be performed annually in the next 5 to 10 years [12]. Therefore, cost-effective and quick assessments of postoperative visual acuity are important in low-income countries to avoid unnecessary cataract surgery and disappointed patients.

1.3 Limitations of previous methods

To our knowledge, no diagnostic device has been described or is commercially available that allows a simple self-diagnosis of the retinal vessels based on entoptic perception. So far, the entoptic phenomenon of Purkinje's tree is initiated manually with a penlight or by using ophthalmological techniques by the examiner. Applegate and Bradley (1991) previously described an entoptic vascular entoptoscope with a mechanically quite complex setup [13]. Other known setups require fixation of the patient's head [14, 15]. More simply, Dinkulu *et al.* (2021) placed a penlight on the closed eye and moved it slightly up and down with a frequency of 2 to 5 Hz [1], as illustrated in **Figure 2A**. The success of the previously used entoptic techniques is limited by the interaction between patient and examiner. By asking the patient, light stimulation parameters such as frequency of movement, angle of incidence and contact pressure are manually varied by the examiner until the Purkinje tree is perceived by the patient [1, 6]. As a result, the patient has limited control on the quality of the entoptic appearance. Another drawback, already described by Brodie (1987), is that patients have limited understanding of what the examiner is asking for [16]. A stabilized Purkinje image that the patient can focus on to describe his retinal vessels cannot be generated in this way. Furthermore, the vascular image is not accessible for quantification because it fades after only a few seconds due to local adaptation under the conditions mentioned above [15]. The reproducibility of the Purkinje test is thus limited and dependent on the experience and skills of all persons involved, especially the patient. Kluxen and Wilden (1987) successfully trained 136 patients with insulin-dependent diabetes to observe their Purkinje tree and document the microaneurysms (MAs) [17]. MAs are small widenings of the retinal blood vessels with less than 100 µm in diameter. The entoptic appearance was caused by a light pen moved at 2 to 4 Hz by the examiner. Results show an increased error rate in mild retinopathy (less than 20 MAs), which is probably due to the non-stabilized Purkinje image.

2 Materials & Methods

Objectifiability and quantifiability are challenging requirements for the medical use of the entoptic method. To optimize our PRIS principle, we have developed a benchtop device with interchangeable light modules (LMs), see **Figures 3 and 4**. The modular design is intended to provide maximum flexibility for determining appropriate PRIS stimulation parameters (wavelength, light intensity, light source arrangement etc.). The control unit in **Figure 4** contains a programmable microcontroller (Arduino Micro, Arduino LLC, USA), user-control elements and electronics for operating the cable wired LMs. In contrast to manually moved penlights or complex mechanical setups with deflecting mirrors, motors etc. our PRIS technique is based on software-controlled light sources generating a stable, reproducible light stimulation, as demonstrated in **Figure 2B**.

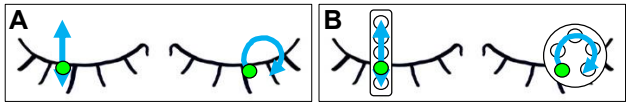

Figure 2: Illustrated principle of light stimulation for entoptic perception
Light spot (green dot) is moved over the closed eye. Blue arrow: up and down (left) and circular (right) movement. **A:** Manually or mechanically generated spot. **B:** PRIS principle with electronically controlled light spot.

Light modules (LMs)

LMs are adapted to the geometry of a closed human eye for optimal placement. The outer radius with eyelid is assumed to be 15 mm. Light emitting diodes (LEDs) in standard 3 mm packages with a small radiation angle (< 20°) are used as light sources. Different geometric LED arrangements were prepared for testing two types of movement: a row configuration (light bar) and four circular arrangements. The row configuration with gapless arranged LEDs (LM A in **Figure 3**) imitates a back and forth light spot movement, as described in [1, 3, 14, 15]. For a rotating light spot, LEDs were arranged symmetrically in circles with different diameters (LMs B to E in **Figure 3**). Light stimulation on circular paths was described in [13, 14]. Control unit interfacing and circuitries were configured to five LEDs, but are expandable. Less than five LEDs can also be tested by user selection. Connected LMs are automatically identified by the control unit so that only suitable stimulation configurations are available for testing. LM housing is composed of a specific 3D printed part and a standard enclosure for D-Sub connectors.

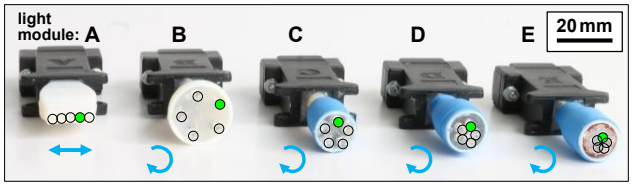

Figure 3: Light modules (LMs) with different geometric LED arrangements Five LEDs in standard 3 mm packages are arranged in row or circular configuration. Row: LM A. Circular: LM B (14.5 mm), LM C (8.3 mm), LM D (5.1 mm) and LM E (3 mm, 30° tilted LEDs). Circle diameter in brackets. Illustrated view of LED positions. Green colored LED represents the moving light spot. Blue arrows: type of light spot movement. Fading is not shown.

Brightness

Brightness is electronically controlled by pulse width modulation (PWM) and can be adjusted to the patient's needs. The control unit provides PWM output signals with a continuous pulse frequency of 490 Hz, not visible as flickering to the human eye. The perceived brightness results from a varied short pulse width (0.2 to 2 ms) and a fixed luminous intensity of the LEDs. PRIS diagnosis is performed on the closed eye, so that the eye is principally protected from intense light intensity. To prevent damage to the eye, the luminous intensity is set to a photobiological safe limit by the LED pulse current.

Wavelength

LMs with different color LEDs in row configuration (LM A) were prepared for selecting a preferred light stimulation color in the visible wavelength range. These experiments led to the standardization of using bright green LEDs (approx. 525 nm) for the PRIS device. We assume that the preferred green LED color is based on the maximum brightness sensitivity of the human eye at 555 nm.

Self-adjustment

In contrast to the known entoptic methods, the patient places the PRIS tool on the closed eye and constantly performs an unnoticed self-adjustment, see **Figure 1B**. For fine tuning, the patient varies intuitively the contact pressure and angle of incidence until the Purkinje vascular structures have a stabilized appearance.

3 Results

The presented PRIS benchtop device, shown in **Figure 4**, was developed for determining light stimulation parameters in first non-clinical tests. Self-tests with LM A with LEDs in row configuration did not provide any clearly preferred settings. In contrast, a majority of self-testers (n = 16) experienced a pleasant entoptic perception with LM type D when a green luminous light spot (approx. 525 nm, PWM 60%) moves with 5 Hz on a circular path 5.1 mm in diameter with fading effect, see **Table 1**. Fading smoothes the fast on-off LED switching and results in a steady movement of the light spot. The direction of light spot rotation did not affect the appearance.

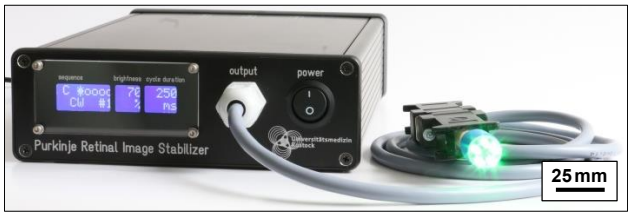

Figure 4: PRIS benchtop device with light spot module

Table 1: Evaluation of different light stimulation parameters in self-tests (n=16) with the developed benchtop device. A colored-coded rating visualizes preferred user settings. Parameter setting with the most votes is marked in bold.

Parameter												Unit
LED arrangement	row									**circular**		
LED color	red		orange		yellow		**green**		blue		white	
Brightness (PWM)	1	5	10	20	30	40	**60**	70	80	90	99	%
Number of LEDs	1		2		3		4		**5**			
Light spot frequency	0.5		1		2.5		**5**		7.5		10	Hz
Light module	A		B		C			**D**		E		
Fading (in % of brightness)	OFF		**30**		50			70				%
Rating:	0 to 4				5 to 11			12 to 16		**n = 16**		

4 Conclusion

The entoptic perception of the retinal vessels and their disease related pathologies is enabled by a simple diagnostic tool and can lead to a standardization of previous methods. The medical benefit for entoptic self-diagnosis in diabetic retinopathy as well as for estimation of retinal visual acuity is given. Nevertheless, the entoptic perception and description of the retinal vessels may vary from patient to patient. The presented benchtop device with interchangeable LMs can be used to evaluate different light stimulation parameters for a pleasant entoptic appearance, see **Table 1**. Self-test findings need to be verified with funduscopic examination.

5 Outlook

The subjective Purkinje appearance becomes both quantifiable and objective by a stabilized entoptic image of the vascular structures combined with assistance methods for the patient. Assistance is primarily provided by the examiner or a physician. Additionally, a medical app will support the patient in device handling and provide necessary knowledge for self-diagnosis and documentation. Measurable results can be achieved by an illustrated decision tree.

Telemedical connectivity to documented health data will also be established for improved medical care. The next development steps will address the miniaturization of the PRIS benchtop device in **Figure 4** into a small handheld diagnostic tool. The PRIS handheld should be durable, easy to use, and also inexpensive to make it available for clinical trials. Clinical studies in patients with and without diabetes are intended to provide information on what assistance needs to be given to a patient to optimize Purkinje self-diagnosis and documentation. The challenging part is to derive an objective diagnosis from a subjective phenomenon.

Author Statement

Research funding: This work was partially funded by the Rostock University Medical Center within the research funding program FORUN. Conflict of interest: Authors state no conflict of interest. Informed consent is not applicable. Ethical approval: Not applicable. Experiments on humans described here are self-tests by the authors and volunteers.

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