ΠΑΝΕΠΙΣΤΗΜΙΟ ΔΥΤΙΚΗΣ ΑΤΤΙΚΗΣ
UNIVERSITY OF WEST ATTICA

RAP 2023
INTERNATIONAL CONFERENCE ON RADIATION APPLICATIONS | In Physics, Chemistry, Biology, Medical Sciences, Engineering and Environmental Sciences
May 29 - June 2, 2023 | Hellenic Centre of Marine Research | Anavyssos | Attica | Greece

# Evaluating changes in retinal nerve fiber layer and photopic negative response for patients under glaucoma treatment

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## Abstract

We assessed the structural and functional changes of the optic nerve in patients under glaucoma treatment. Our study was carried out by evaluating: (a) the retinal nerve fiber layer (RNFL) thickness taken from the spectral-domain optical coherence tomography (OCT) system and (b) the photopic negative response (PhNR) of the electroretinogram (ERG) test recorded by the RETeval portable device. The RETeval system and the corresponding sensor strip electrodes were provided from the LKC Technologies Inc. We performed examinations at the Ophthalmology Clinic of the “Elpis” General Hospital of Athens on a sample of 114 eyes in total. Several parameters were examined under statistical correlations via the SPSS software package. Amongst the most important were the: age, RNFL, Pmin, W-Ratio, a-wave and b-wave. Statistical analysis was performed by bivariate linear correlation tests with RNFL as the independent parameter. Results showed that there were no statistical differences between age interval subgroups (30-50 and 51-80 years old) for the control group, especially on the time responses of amplitudes on PhNR parameters. In addition, statistical difference was found between the control group and the group under glaucoma treatment for both OCT and RETeval parameters, including RNFL thickness and PhNR. More specifically, RNFL turned out to be correlated to bwave (ms) and W-ratio parameters. Our findings indicate that the PhNR obtained by the RETeval system may be a useful tool to accompany the routine diagnostic systems on Opthalmology, in order to follow up the patients under glaucoma treatment.

## Introduction

One of the most important eye diseases is glaucoma, which is considered a worldwide leading cause of irreversible visual damage and blindness [1, 2]. More specifically, gradual loss and degeneration of retinal ganglion cells (RGCs) have been observed, which cause changes in the optic nerve and reduction of the RNFL thickness [3]. The major risk factor that conducts to glaucoma is considered to be the elevated intraocular pressure (IOP) [2, 4]. The individuals with IOP greater than 21 mmHgn must be carefully managed with the appropriate treatment, usually with ocular hypotensive drops [2, 5], in order to reduce the IOP . Glaucoma has a slow and asymptomatic progression until advanced stages thereby it is essential to detect early functional and structural changes before vision loss. Electroretinography (ERG) is considered an important functional and objective diagnostic tool to monitor RGCs activity [6-10]. In particular, there is a specific extended protocol that describes an extension to the ERG Standard, namely photopic negative response (PhNR) that provides information about the function of retinal ganglion cells and their axons [8, 9]. It has been shown that glaucoma patients with visual field defects demonstrate pathologic PhNR values [11, 12]. The RETeval ERG system (LKC Technologies Inc.) is a new portable device, easy-to-use and non-invasive, that provides the PhNR and requires minimal patient’s cooperation. The main objective of the present work is to: (a) study the structural and functional changes that have occurred in early glaucoma Caucasian patients under treatment by using OCT and RETeval ERG system, (b) compare possible correlations with control subjects (b) compare the numeral outcomes of electrophysiology with RNFL thickness, the traditionally used diagnostic parameter in glaucoma.

## Materials and Methods

The overall workflow of the study is analytically described in reference 13.Below is briefly provided the workflow of the study as well as the main system and parameter assessment.

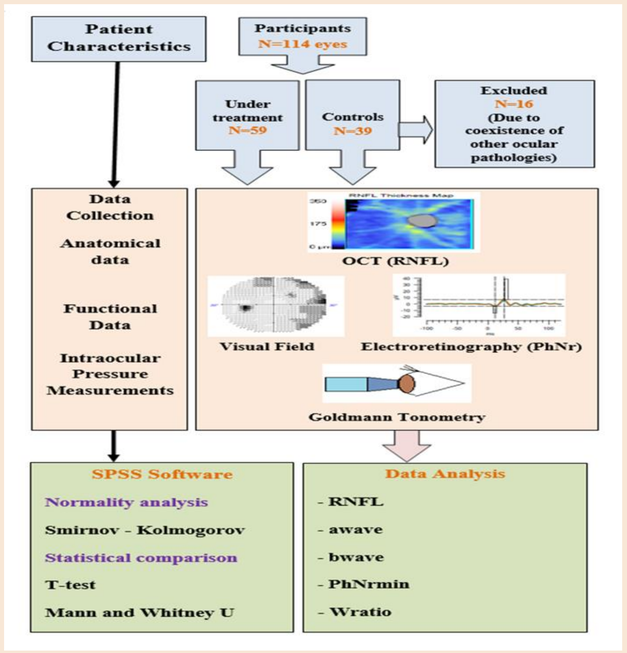


Figure 1. The patient recruitment process the exclusion criteria, and the workflow of our study

Figure 2. The spectral-domain OCT optical coherence tomography used in the present study (Cirrus HD-OCT 4000).

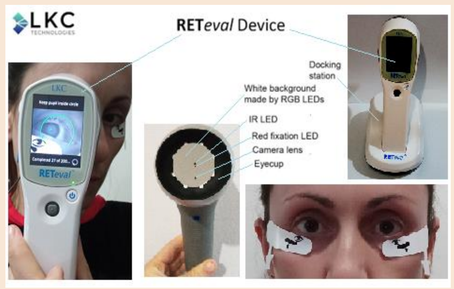


Figure 3 The RETeval recording system used in the present study.

## Parameter assessment and statistical analysis

The following parameters are invastogated: (i) the a-wave amplitude (μV) and time response (ms), (ii) the b-wave amplitude (μV) and time response (ms), (iii) the implicit time of minimum PhNR (ms), (iii iv) the minimum (Pmin) PhNR amplitude and implicit time (ms), (iv) the W-ratio. The parameters as Pmin, Wratio, a-wave, b-wave were obtained with RETeval, using PhNR protocol. The reported values of the reports were from -100 ms to +120 ms, with the center of the flash at 0 ms. The W-ratio is defined as follows: W-ratio = (b – pmin) / (b – a), where a, b and pmin are the voltages relative to baseline defined as a: a-wave peak, b: b-wave peak, pmin: minimum voltage between 30 ms and 100 ms. The W-ratio is the inverse of PTR (Ratio b-wave / PhNR measured from peak-to trough) [2]. The output parameters were statistically analyzed and tested using the SPSS software package. All data were checked for normality with the Smirnov - Kolmogorov test. Thereafter, on the data following the normal distribution, statistical comparisons were carried out with a t-test while on the rest of the data independent samples of Mann and Whitney U tests were performed

## Results and Discussion

Table 1: The characteristics of the subjects involved in this study

| | Mean value ± Standard Deviation | |
|---|---|---|
| **Variables** | Under glaucoma treatment (n=59) | Control (n=39) |
| **Age (y)** | 67.7 ±10.3 | 51.8±14.1 |
| **RNFL (μm)** | 76.9 ± 12.9 | 93 ± 8.6 |
| **a-wave (μV)** | -7.4 ± 2.4 | -8.6 ± 2.9 |
| **a-wave (ms)** | 12.8 ± 1.1 | 12.1 ± 0.8 |
| **b-wave (μV)** | 20.8 ± 6.0 | 25.7 ± 7.4 |
| **b-wave (ms)** | 30.5 ± 2.1 | 28.8 ± 1.4 |
| **PhNrmin (μV)** | -4.4 ± 1.3 | -5.7 ± 1.7 |
| **PhNrmin (ms)** | 60.9 ± 9.2 | 58.8 ± 8.7 |
| **Wratio** | 0.86 ± 0.05 | 0.89 ± 0.07 |
| **IOP (mm Hg)** | 15.3 ± 2.7 | 14.4 ± 1.8 |

Table 2: p-values of the statistical comparisons between the control group and the case group

| Parameters | p-value |
|---|---|
| **RNFL (μm)** | **<0.001** |
| **awave (ms)** | **<0.001** |
| **awave (μV)** | **0.079** |
| **bwave (ms)** | **<0.001** |
| **bwave (μV)** | **<0.001** |
| **PhNrmin (ms)** | **0.034** |
| **PhNrmin (μV)** | **<0.001** |
| **Wratio** | **0.003** |

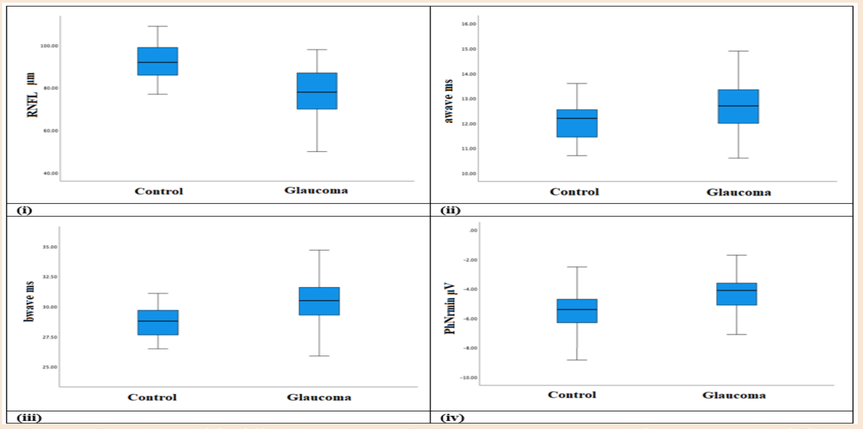


Figure 4: Comparisons of the following parameters: RNFL (μm) (i), awave (ms) (ii), bwave (ms) (iii) and PhNrm (μV) (iv) between the control group and the group under glaucoma treatment.

## Conclusions

Statistical difference was found between the control group and the group under glaucoma treatment for both OCT and RETeval parameters, including RNFL thickness and PhNR. More specifically, RNFL turned out to be correlated to bwave (ms) and W-ratio parameters. Our findings indicate that the PhNR obtained by the RETeval system may be a useful tool to accompany the routine diagnostic systems on Opthalmology, in order to follow up the patients under glaucoma treatment.

**Acknowledgements** The team from LKC Technologies for their technical support and assistance.

**Ethical approval:** Approval by the Research Ethics Committee of the University of West Attica, Greece, Approval number 82608/19-09-2022.

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