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BIOPHYSICS

THE BIOPHYSICAL PROPERTIES OF CORNEA IN ANALYZING GLAUCOMA RISK

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Abstract. The corneal properties in connection with glaucoma risk were studied on 4343 eyes. These include the stress generated by the increase of the intraocular pressure, corneal hysteresis and optic nerve properties as determined by optical coherence tomography. A new biophysical ocular parameter, denoted as corneal damping, φ, has been defined. Correlations between optic nerve thickness, intraocular pressure and corneal viscoelastic properties and φ parameter were obtained. The data evidenced that after 40 years at an intraocular pressure over 30 mmHg corneal viscoelasticity decrease and explain 36% of variance in the optic nerve thickness.

Keywords: corneal viscoelasticity, corneal hysteresis, specific damping capacity, optical coherence tomography.

1. INTRODUCTION

Glaucoma screening is an important goal in ophthalmology, to avoid the risk of blindness. The common denominator for glaucoma is a characteristic optic neuropathy, which derives from various risk factors including Intraocular Pressure (IOP), the most frequent involved; attempts to define glaucoma only on the basis of ocular tension are no longer advised [1]. Biomechanical features of cornea and sclera may enhance or reduce this risk [2]. Corneal properties reflect biophysical properties of the eye walls, including papillary area [3]. Measured IOP is over- or under-estimated through a more viscous or more elastic cornea. The viscous-elastic ocular model [4] considers that just a part of this IOP is transmitted toward posterior pole; partial is absorbed in the ocular walls and other ocular structures (Fig. 1). Decrease in peripapillary Retinal Nerve Fiber Layer (RNFL) thickness, frequent occurring in relation with IOP, lead to diagnosis of glaucoma [5].

The analysis of a number of 4 343 eyes, showed that age and corneal viscoelastic properties are more important than IOP, to be considered in glaucoma risk. Based on the above data, a biophysical ocular parameter has been defined and correlated with this risk.

2. EXPERIMENTAL METHOD

In order to obtain information on cornea and optic nerve damage, the IOP and corneal viscoelasticity have been measured by Ocular Response Analyzer (ORA), and RNFL thickness by optical coherence tomography (OCT).

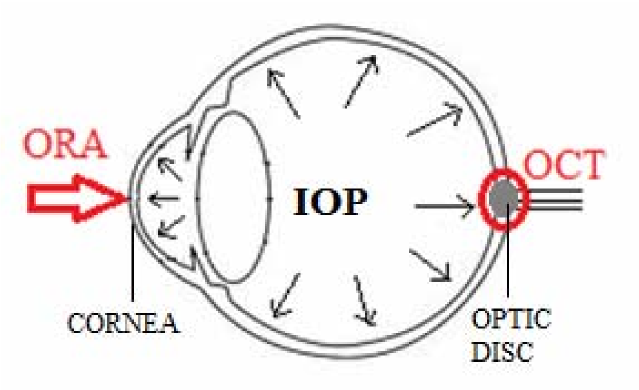

Fig. 1 – Cross section of the eye; site where ORA and OCT measurements were made are noted (red arrow and circle).

In ORA method a metered collimated air-pulse, presses on the cornea and changes its concavity into an applanatic form (Fig. 1). After stopping the air pulse, cornea return to its normal configuration. Intraocular pressure (IOPg) is determined from the time evolution of the corneal shape [6]. Corneal hysteresis (CH) is defined as the difference between inward and outward pressure values obtained during applanation process, as a result of corneal viscous damping. IOPcc is the IOPg adjusted in correlation with the corneal viscoelastic properties.

On the same eyes the retinal area around the optic disc, by a time domain optical coherence tomography, was scanned. In this method [7], a superluminiscent diode focalized a broadband near-infrared light beam on the retina. By analyzing the reflected part of the projected light we obtain information about scanned retinal nerve fiber layers (RNFL), around the optic disc. In this way we determined the average thickness in the entire circumference of the optic disk, labeled as t_{AV} and quadrant average thickness of RNFL, labeled as t_S, t_I, t_T, t_N – for superior, inferior, temporal and nasal quadrants respectively (Fig. 2).

All these data were collected in a database by a computerized method, using a set of virtual instruments (vi) in Labview (National Instruments). This software extracted the necessary information from the devices' reports and automated stocked in the database [8].

After the completion of the database, information was analyzed using the statistical package for social sciences method (SPSS version 13).

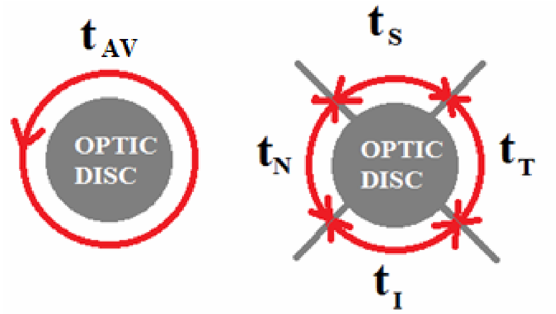

Fig. 2 – OCT scan line around the optic disc (red circle).

3. RESULTS

The 4 343 studied eyes are coming from a group of patients with ages between 8 and 95 years, 36% being male and 64% female patients. Data obtained for the whole group of patients are listed in Table 1.

Table 1

Descriptive statistics for the studied patients

Instrument	Parameters	Minimum	Maximum	Media
OCT	t_{AV} (μm)	23.9	150.2	99.8 +/– 15
	t_S (μm)	9	191	124.1 +/– 23
	t_N (μm)	10	174	79.9 +/– 19
	t_T (μm)	15	175	70.8 +/– 15
	t_I (μm)	1	199	124.3 +/– 23
ORA	IOPg (mmHg)	4.1	65.9	18.3 +/– 5
	IOPcc (mmHg)	6.2	70.7	18.9 +/– 5
	CH (mmHg)	0	26.6	9.9 +/– 2
	φ	0	1.19	0.3 +/– 0.1

In the studied group of patients, statistically significant correlations (all with $p < 0.001$) were found between all ORA and OCT parameters (Table 2). The test values evidences only a weak correlation between IOPg and t_T , t_N ($0.05 < r < 0.07$) and a better one between IOPcc, CH with t_{AV} ($r = 0.16$). These data suggest that the above parameters can be incorporate in a relation which give more accurate information about the glaucoma risk of the patients. Consequently, a corneal damping parameter, φ, was introduced in order to describe corneal viscoelastic properties:

$$\varphi = \frac{\text{CH}}{2\ \text{IOPg}}.$$

The damping parameter has a significant statistical correlation with RNFL thickness, especially with $\boldsymbol{t_{AV}}$ and $\boldsymbol{t_I}$, where $r = 0.15$ (Table 2).

Table 2

Correlation coefficient *r* between ORA and OCT measured parameters, on quadrants

		OCT parameters				
		$\boldsymbol{t_{AV}}$	$\boldsymbol{t_S}$	$\boldsymbol{t_T}$	$\boldsymbol{t_I}$	$\boldsymbol{t_N}$
ORA parameters	IOPcc	–0.16	–0.14	–0.07	–0.16	–0.10
	IOPg	–0.11	–0.09	–0.05	–0.11	–0.07
	CH	0.17	0.15	0.07	0.16	0.10
	φ	0.15	0.13	0.05	0.15	0.10

In Fig. 3 are represented RNFL ($\boldsymbol{t_{AV}}$) correlations with CH ($R^2 = 0.028$). This correlation is better than between RNFL ($\boldsymbol{t_{AV}}$) and IOPg ($R^2 = 0.011$).

Multiple regression stepwise [9, 10] was used to search if *age,* in addition to *ORA* parameters, are able to predict *RNFL damage* as a marker for glaucoma disease. Thus, a *multilayered stratified* statistical analyze has been performed. The database was divided in three subgroups: (1) patients with the age under 40 years (< 40y), (2) patients over 40 years with IOPg under 30 mmHg (> 40 y, IOPg < 30 mmHg) and (3) patients over 40 years with IOPg over 30 mmHg (> 40 y, IOPg > 30 mmHg). Variation of RNFL depending on IOP, was studied in the above 3 subgroups of patients, and correlation coefficients were computed. The R^2 parameter which refers to the fraction of variance and tell us how good one parameter is at predicting another, has been determined; the results are listed in Table 3. Fraction of variance (R^2) referring to RNFL ($\boldsymbol{t}$) increases with increasing the IOP (max 0.06) and decreasing CH and φ (max 0.07). The most significant values were obtained for damping parameter at patients over 40 years and with IOP > 30 mmHg, where fraction of variance reached a value of 0.36. This mean that 36% of variance in RNFL ($\boldsymbol{t}$) thickness is accounted for by the variance in φ, at this subgroup, so age is an important factor to be considered.

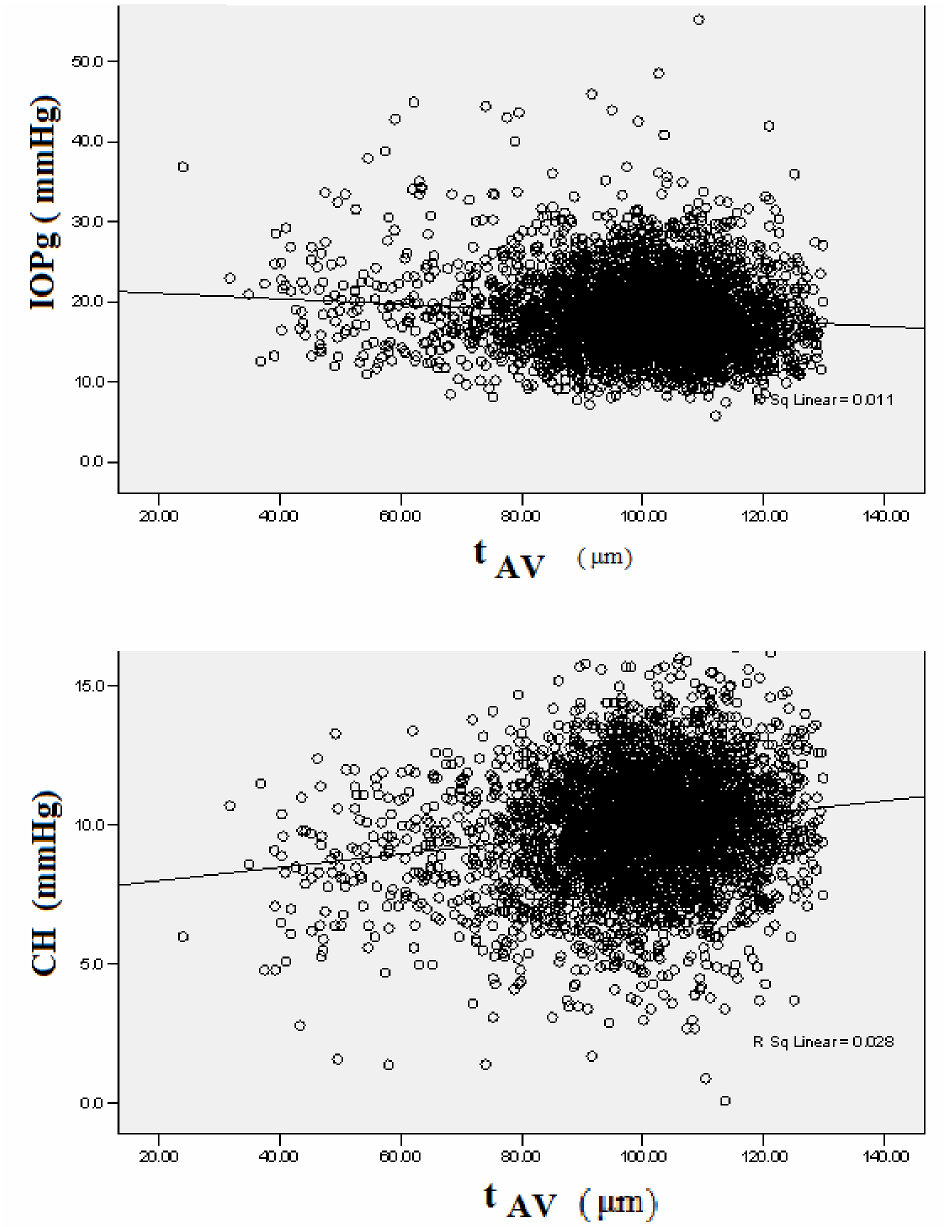

Fig. 3 – RNFL (t_{AV}) correlation with IOPg and CH.

Table 3

Multiple regression stepwise: R^2 and p computed for ORA and OCT parameters in the studied subgroups of patients

			ORA parameters (mmHg)							
			IOPg		CH		φ		age + φ	
			R^2	*p*	R^2	*p*	R^2	*p*	R^2	*p*
OCT parameters (μm)	t_{AV}	all patients	0.01	0.000	0.02	0.000	0.03	0.000	0.11	0.000
	t_{AV}	<40 y	0.002	0.141	0.008	0.004	0.010	0.001	0.012	0.309
		>40 y , IOPg<30 mmHg	0.011	0.000	0.024	0.000	0.021	0.000	0.148	0.000
		>40 y, IOPg>30 mmHg	0.018	0.190	0.023	0.140	0.053	0.024	0.343	0.035
	t_S	<40 y	0.000	0.735	0.005	0.020	0.003	0.095	0.009	0..279
		>40 y , IOPg<30 mmHg	0.009	0.000	0.018	0.000	0.015	0.000	0.129	0.000
		>40 y, IOPg>30 mmHg	0.065	0.011	0.028	0.098	0.072	0.008	0.360	0.010
	t_N	<40 y	0.001	0.397	0.006	0.008	0.006	0.009	0.006	0.059
		>40 y , IOPg<30 mmHg	0.006	0.000	0.008	0.000	0.011	0.000	0.066	0.000
		>40 y, IOPg>30 mmHg	0.011	0.297	0.002	0.642	0.003	0.616	0.227	0.000
	t_T	<40 y	0.000	0.614	0.001	0.050	0.000	0.640	0.002	0.389
		>40 y , IOPg<30 mmHg	0.001	0.078	0.004	0.001	0.002	0.016	0.031	0.000
		>40 y, IOPg>30 mmHg	0.038	0.057	0.017	0.209	0.046	0.035	0.114	0.001
	t_I	<40 y	0.006	0.009	0.004	0.349	0.013	0.000	0.013	0.605
		>40 y , IOPg<30 mmHg	0.009	0.000	0.023	0.000	0.020	0.000	0.100	0.000
		>40 y, IOPg>30 mmHg	0.007	0.405	0.020	0.169	0.045	0.039	0.223	0.000

All mentioned computed correlations (Tables 2, 3) are statistically significant, having a probability $p < 0.001$ to obtain the test result by chance alone in comparison with the studied distribution of data.

4. DISCUSSION

The previous published data evidenced that IOP induces a certain amount of stress and strain at the optic nerve head and lead to apoptosis of the ganglion cells [11]. The process depends on biomechanical properties of eye walls, of which cornea is part. The subjects with low CH ("stiff" cornea), a process that occurs with age, are suggested to be candidates for a variety of ocular diseases [12]. The risk of glaucoma with ageing as previously reported [13, 14] was also found in the present study. With increasing age, the corneal hysteresis (CH) decreases, the cornea is stiffer, and these correlate well ($r = 0.16$) with a lower RNFL average thickness, that is a sign of glaucoma (Fig. 3 and Table 2). The correlation is better than between RNFL ($\boldsymbol{t_{AV}}$) and IOPg ($r = 0.11$).

Damping is the result of mechanical energy conversion of a structure into thermal energy [15, 2]. This phenomenon is useful to reduce the amplitude of dynamic instabilities in a structure [16, 17]. The present data revealed that corneal specific damping capacity, φ, can describe the RNFL damage (positive correlation with $\boldsymbol{t_{AV}}$) under high IOP as aggressor factor (Table 2). Studies on ocular hypertension show a rate of 11% conversion to glaucoma in time [18]. For the whole group of data, fraction of RNFL variance in relationship with damping parameter, has been found to be 11% (R^2 = 0.11), in agreement with the previously published results.

The correlations between ORA and OCT parameters were found to be better for the subgroup (3) over 40 years with IOP > 30 mmHg than for the lower age range (subgroup under 40 years). For the third subgroup, fraction of RNFL variance reached 0.36 (Table 3) in relation with the damping parameter, which means that φ justify a rate of 36% of RNFL variability (loss).

Corneal viscoelastic properties (corneal hysteresis and damping parameter) are therefore more important to be considered (in association with age) than intraocular pressure alone, in assessment of glaucoma risk.

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