·Clinical Research·

Corneal biomechanical changes and intraocular pressure in patients with thyroid orbitopathy

Zofia Pniakowska, Anna Klysik, Roman Gos, Piotr Jurowski

Department of Ophthalmology and Visual Rehabilitation, the Veterans Central Hospital, Lodz 90-710, Poland

Correspondence to: Zofia Pniakowska. Department of Ophthalmology and Visual Rehabilitation, the Veterans Central Hospital, Zeromskiego 113 Street, Lodz 90-710, Poland. zofia.pniakowska@gmail.com

Received: 2014-07-31 Accepted: 2015-01-31

Abstract

• AIM: To determine the relevance of the objective parameters addressing the altered biomechanical properties of cornea for glaucoma monitoring in patients with mild or moderate thyroid associated orbitopathy (TAO), and in healthy individuals.

• METHODS: Twenty-five patients with TAO (group 1) and 25 healthy adults (group 2) were included to the study. Both groups were of a similar age and the ratio women:man. For each patient, the following parameters of both eyes were measured with ocular response analyzer (ORA): corneal hysteresis (CH), corneal resistance factor (CRF), Goldmann correlated intraocular pressure (IOPg) and corneal compensated intraocular pressure (IOPcc). In both groups participating in our study, all measurements were performed within minutes to reduce the diurnal effects.

• RESULTS: The mean age in group 1 was 56±11y and 76% were women, 24% were men. The mean age in group 2 was 64±11y and 68% were women, 32% were men. CH correlated negatively with IOPg in group 1 (r^2= 0.10, P<0.05). IOPg strongly correlated with IOPcc in both groups (group 1: r^2=0.79, P<0.0001; group 2: r^2= 0.85, P<0.0001). There was positive correlation between CRF and IOPg in group 1 (r^2=0.12, P<0.05) and in group 2 (r^2=0.31, P<0.0001). Statistical analysis revealed no significant correlation between CRF and IOPcc in group 1 (r^2=0.009, P>0.05) and also no significant correlation in group 2 (r^2=0.04, P>0.05). CRF mean value in group 2 (11.51±1.72 mm Hg) was higher than in group 1 (10.85±1.45 mm Hg) (P<0.05). IOPg strongly correlated with IOPcc in both groups (group 1: r^2=0.79, P<0.0001; group 2: r^2=0.85, P<0.0001). There was also strong correlation between CRF and CH in both populations: group 1: (r^2=0.58, P<0.0001), group 2: (r^2= 0.41, P<0.0001).

• CONCLUSION: Biomechanical parameters of cornea, as quantified by CH and CRF, and measured together with IOPcc, precisely reveal glaucoma staging in TAO and thus are reliable for diagnosing and follow-up in clinical practice.

• **KEYWORDS:** corneal hysteresis; corneal resistance factor; glaucoma; intraocular pressure; thyroid associated orbitopathy

DOI:10.18240/ijo.2016.03.20

Pniakowska Z, Klysik A, Gos R, Jurowski P. Corneal biomechanical changes and intraocular pressure in patients with thyroid orbitopathy. *Int J Ophthalmol* 2016;9(3):439-443

INTRODUCTION

Thyroid associated orbitopathy (TAO) is the most common ocular manifestation of Graves' disease. Increased intraocular pressure (IOP) in eyes with TAO leads frequently to glaucoma or glaucomatous neuropathy, which are one of the main causes of visual field loss and blindness in these patients [1-5]. IOP measurement for glaucoma monitoring in patients with TAO can be inaccurate due to the altered biomechanical properties of the cornea, such as higher corneal hydration, connective tissue decomposition, altered rigidity and bio-elasticity, which are not addressed by the standard tonometers[6-8].

Therefore, innovative parameters addressing the altered biomechanical characteristics of the cornea could potentially constitute the diagnostic algorithm of the glaucoma monitoring in patients with TAO. Biomechanical parameters of the cornea [corneal hysteresis (CH), corneal resistance factor (CRF)] and parameters of intraocular pressure [Goldmann correlated intraocular pressure (IOPg), corneal compensated intraocular pressure (IOPcc)] are all measured with ocular response analyzer (ORA) (2010 Reichert, Inc.)[7-13]. IOPcc eliminates the bias related to the individual corneal properties, such as elasticity and thickness.

The aim of the study was to determine the relevance of the objective parameters addressing the altered biomechanical properties of cornea for glaucoma monitoring in patients with mild or moderate TAO, and in healthy individuals.

SUBJECTS AND METHODS

Prospective, noninvasive study was conducted in the Department of Ophthalmology and Visual Rehabilitation of the Medical University of Lodz in Poland. Approval of the Ethics Committee of Medical University of Lodz was

Table 1 Severity classification of GO, as recommended by EUGOGO

Severity score	Definition
1 (sight-threatening GO)	Patients with dysthyroid optic neuropathy and/or corneal breakdown.
2 (moderate to severe GO)	Patients with any one or more of the following: lid retraction ≥2 mm, moderate or severe soft tissue involvement, exophthalmos ≥3 mm above normal for race and gender, inconstant or constant diplopia.
3 (mild GO)	Patients usually with one or more of the following: minor lid retraction (<2 mm), mild soft tissue involvement, exophthalmos <3 mm above normal for race and gender, transient or no diplopia, corneal exposure responsive to lubricants.

GO: Graves' orbitopathy; EUGOGO: European group on Graves' orbitopathy.

obtained for the study. Informed consent was obtained from all participants of the study. Twenty five patients with TAO (group 1) and twenty five healthy volunteers with no history of ocular disease (group 2) were enrolled to the study. Both eyes of each patient with diagnosis of orbitopathy were subjected to clinical examination according to the recommendations of European group on Graves' orbitopathy (EUGOGO)[14].

Patients with TAO, who were originally recruited to participate in our study, presented a variety of eye conditions, resulting from different stages/activity of Graves' orbitopathy (GO) and stages of glaucoma/ocular hypertension. Numerous additional variables would need to be controlled in such a large and heterogeneous group of patients; otherwise the results would be at high risk of large bias with decreased statistical power. Thus, we decided on the moderate but homogenous sample size, which is suitable to achieve statistically significant and reliable results. To standardize the study group and eliminate the above-mentioned risk factors, which could affect measurement of IOP, CH or CRF, we determined the specific inclusion criteria. Based on the clinical examination, patients were classified to three groups of GO stage: 1: sight-threatening GO, 2: moderate to severe GO and 3: mild GO (Table 1). For the study we enrolled patients in second stage of GO (2: moderate to severe GO). The second inclusion criterion was based on evaluation of the activity of orbitopathy. Following the currently EUGOGO recommendations, the 7-point scale clinical activity score (CAS) (CAS convergent with the first seven points of the original scale CAS) was used (Table 2)[14]. CAS ratio ≥3 shows the activity of the inflammatory process, which was accepted by us as a second inclusion criterion. Finally, the third inclusion criterion was the stage of glaucoma/ocular hypertension, estimated in accordance with the universally accepted glaucoma staging system (GSS) based on the visual field evaluation [15]. The GSS comprises of 6 stages according to the recommendation by Mills *et al* [15], based on the Humphrey visual field.

To the study we included patients with the ocular hypertension (stage 0), early glaucoma (stage 1) and moderate glaucoma (stage 2).

Patients classified to the stage 3 (advanced glaucoma), 4 (severe glaucoma), and 5 (end-stage of glaucoma/blind) of the ocular hypertension were excluded. Patients with history of corneal surgery procedures, past or existing corneal trauma independent of its etiology, other corneal dystrophies, keratoconus, cataract, and diabetes mellitus were excluded from the study.

Table 2 Clinical activity of GO, according to Bartalena *et al*[14], modified by EUGOGO; CAS ≥3/7 indicates active GO

CAS	Clinical manifestation
1	Painful, oppressive feeling on or behind the globe, during the last 4wk
2	Pain on attempted up-, side-, or down-gaze, during the last 4wk
3	Redness of the eyelid (s)
4	Diffuse redness of the conjunctiva, covering at least one quadrant
5	Swelling of the eyelid (s)
6	Chemosis (conjunctival oedema)
7	Swelling of caruncle and/or plica

GO: Graves' orbitopathy; EUGOGO: European group on Graves' orbitopathy; CAS: Clinical activity score.

The qualification procedure was performed also on healthy volunteers with the following exclusion criteria: corneal pathological conditions which could affect measurement of IOP, CH or CRF, past or existing corneal trauma, history of corneal surgery procedures, history of elevated IOP, ocular hypertension or glaucoma, as well as with cataract and diabetes mellitus. Both groups were of a similar age and the sex ratio.

Finally, according to the qualification procedure, 25 patients were included to the study group and 25 healthy individuals comprised control group.

For each patient the following parameters of both eyes were measured with ORA: CH, CRF, IOPg and IOPcc. Elasticity of the corneal tissue is quantified by CH. CRF describes visco-elastic response of cornea, *i.e.* corneal "resistance". For measurement, ORA generates an air-pulse against cornea, which in turn moves inwards, past applanation, and into a slight concavity. A few milliseconds later, the cornea recurs to its normal shape and passes through the applanated phase once more, resulting in two different pressure values. Their average value is IOPg and their difference is CH. The quality of each measurement was determined by waveform score value, presented on a scale of zero (0) to ten (10). The three consecutive ORA readings of each eye with the best quality

Table 3 Characteristics of the selected parameters of the patients assessed in the study and differences between the study group and the control group

Parameters	$\bar{x} \pm s$		Median		Min		Max		T	P
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Age (a)	56±11	64±11	58	63	28	72	42	87		
IOPg (mm Hg)	16.39±3.31	17.56±4.52	15.76	16.91	10.30	27.90	7.70	29.93	-1.45	0.1475
IOPcc (mm Hg)	16.53±3.85	17.16±4.72	16.50	16.25	8.56	25.40	9.30	29.66	-0.71	0.4754
CRF (mm Hg)	10.85±1.45	11.51±1.72	10.70	11.61	7.96	15.10	8.10	15.93	-2.08	0.0400
CH (mm Hg)	10.60±1.68	10.99±1.74	10.70	11.35	6.53	15.00	6.30	13.30	-1.12	0.2617
Waveform	7.60±1.41	7.16±1.31	7.91	7.28	2.62	9.36	3.49	9.15		

Group 1: Study group; Group 2: Control group; IOPg: Goldmann-correlated intraocular pressure; IOPcc: Corneal compensated intraocular pressure; CRF: Corneal resistance factor; CH: Corneal hysteresis; Waveform: The quality of ORA measurement.

and waveform score above 3.0 were taken for further evaluation. In both groups participating in our study, all measurements were done in primary gaze, to exclude the influence of globe position on IOP. Additionally, all measurements were performed within minutes to reduce the diurnal effects.

For all measurable variables we tested the compatibility of their distribution with a normal distribution using λ-Kolmogorov test. For comparison between two measurements of the same parameter in both groups, we used Student's t-test for independent samples. The relationship between the two variables was calculated with the rectilinear correlation coefficient r. Coefficient of determination, which is the square of the correlation coefficient, assessed the impact between two variables. We found the differences between the mean values and the dependencies between attributes as statistically significant where the error of probability P was less than 0.05.

RESULTS

The mean age in group 1 was 56±11y and 76% were women, 24% were men. The mean age in group 2 was 64±11y and 68% were women, 32% were men.

CRF mean value in group 2 (11.51±1.72 mm Hg) was higher than in group 1 (10.85±1.45 mm Hg) (P<0.05) (Table 3). The study revealed no statistically significant difference in the mean value of IOPg between groups (P>0.05) (Table 3). The mean value of IOPcc in group 1 did not differ from the mean IOPcc value in group 2 (P>0.05) (Table 3). There were also no significant differences of CH values between both groups (P>0.05) (Table 3).

CH correlated negatively with IOPg in group 1 (r^2=0.10, P<0.05), but in group 2 there was no statistically significant correlation between CH and IOPg (r^2=0.07, P=0.058). CH also correlated negatively with IOPcc in the group 1 (r^2=0.51, P<0.0001) and in the control group 2 (r^2=0.37, P<0.0001). There was positive correlation between CRF and IOPg in group 1 (r^2=0.12, P<0.05) and in group 2 (r^2=0.31, P<0.0001). Statistical analysis revealed no significant correlation between CRF and IOPcc in group 1 (r^2=0.009, P>0.05) and also no significant correlation in group 2(r^2=0.04, P>0.05).

Table 4 Correlation among CH, CRF, IOPg and IOPcc in study group and control group

Parameters	Groups	Correlation		
		r	r^2	P
CH				
IOPg	1	-0.31	0.10	0.023
	2	-0.26	0.07	0.058
IOPcc	1	-0.71	0.51	<0.0001
	2	-0.61	0.37	<0.0001
CRF	1	0.76	0.58	<0.0001
	2	0.64	0.41	<0.0001
CRF				
IOPg	1	0.35	0.12	0.011
	2	0.55	0.31	0.0001
IOPcc	1	-0.094	0.009	0.496
	2	0.2	0.04	0.151
IOPg				
IOPcc	1	0.89	0.79	<0.0001
	2	0.92	0.85	<0.0001

1: Study group; 2: Control group; CH: Corneal hysteresis; CRF: Corneal resistance factor; IOPg: Goldmann-correlated intraocular pressure; IOPcc: Corneal compensated intraocular pressure.

IOPg strongly correlated with IOPcc in both groups (group 1: r^2=0.79, P<0.0001; group 2: r^2=0.85, P<0.0001). Moreover, we found correlation between CRF and CH in both populations group 1:(r^2=0.58, P<0.0001), group 2:(r^2=0.41, P<0.0001) (Table 4).

DISCUSSION

TAO is clinically manifested by soft tissue involvement, eyelid retraction, proptosis, exposure keratopathy, optic neuropathy and muscle fibrosis [16-17]. Advanced proptosis alters adequate lid closure and may lead to severe exposure keratopathy and corneal ulceration. Aetiologically, TAO is an endocrine orbitopathy, caused by the excessive production of the thyrotropin receptor antibodies, which leads to swelling and hypertrophy of extraocular muscles, cellular infiltration of interstitial tissues, proliferation of the intraorbital adipose and connective tissues and excessive production of glycosaminoglycans [18-22]. Ocular mobility is restricted by

oedema in the infiltrative and fibrotic stages of disease [17]. The morphological changes in cornea can lead to glaucoma, and the early diagnosis is essential to avoid irreversible consequences.

In patients with TAO, diagnosis of the primary open angle glaucoma (POAG) can be challenging. Even if an elevated IOP is detected in these patients, the question arises whether the elevated IOP is just a sign of orbitopathy or if glaucoma or ocular hypertension should be considered[23]. Prevalence of normal-tension glaucoma, POAG or ocular hypertension among patients with Graves' disease was reported in range from 0.8% to 13.5% [4,24]. Goldmann applanation tonometry (GAT) was designed to assess IOP, unaffected by the ocular rigidity [25]. GAT is currently the preferred method of IOP measurement, also in patients with glaucoma [24]. However, numerous studies demonstrated that applanated intraocular pressure (IOPg) is not equal to the real intraocular pressure[4,26-27]. Recent studies proved that GAT-IOP is strongly dependent on central corneal thickness (CCT), which suggests that CCT should be the basis for IOP correction algorithm [7-8]. Nevertheless, weak correlation of CCT and IOPg limits the efficacy of GAT [11]. Therefore, Pascal dynamic contour tonometry and ORA tonometry have emerged as techniques of IOP estimation in early glaucoma detection [12,25]. As given above, IOPcc describes intraocular pressure more accurately as it is less influenced by corneal properties. In our study IOPg correlated with IOPcc in group 1 and 2, however, the difference in results between groups in our series pointed out necessity of the more detailed analysis regarding influence of CRF and CH on IOPg and IOPcc in patients with orbitopathy. Independent association was previously found between CH and glaucoma damage, and thus CH could act as an objective parameter for diagnosing the glaucoma progression risk [28]. CH was significantly lower in patients diagnosed with glaucoma when compared to glaucoma suspects, ocular hypertensives and in control group [12,25]. As previously reported, the lowered CH was a predictive factor of visual field loss progression in the glaucoma patients, while altered IOPg showed no relationship with visual field changes [29]. In our study, CH showed only small negative correlation with IOPg, both in patients with TAO and in healthy individuals. In turn, we observed significant correlation between decreasing CH and increasing IOPcc in both groups of patients. According to above, IOPcc acts as a marker of the early subclinical stages of glaucoma in patients with TAO.

Correlation between CH and CRF was previously seen in patients with orbitopathy and in healthy people[30]. Shah *et al*[30] mentioned that CH, CCT and CRF correlated with one another but the correlation was only moderate. This suggests that CH and CRF are parameters measuring separate traits of the corneal rigidity and these variables may be more useful when trying to adjust IOP measurements in patients with altered ocular rigidity [31]. Similarly, our results revealed the marked positive correlation between CRF and CH in both groups.

CRF represents an overall resistance to deformation and is useful for differentiating between individuals with false-positive results of IOPg and glaucoma [12]. Corneas with elevated CRF values (*i.e.* greater rigidity) require higher pressure to achieve applanation, when compared to corneas with lowered CRF. In our series, CRF was significantly lower in the study group in comparison with the control group. We found weak correlation between CRF and IOPg in both groups. According to the above, the lowered CRF of corneas in patients with TAO can lead to the relatively underestimated values of IOPg and the missdiagnosed glaucoma [12]. Interestingly, we did not see any correlation between CRF and IOPcc in both groups (Table 4), which suggests that CRF affected IOPg value but not IOPcc. Our finding proves that IOPcc is not prone to bias related to the affected biochemical corneal characteristics in patients with TAO [11,32]. As a consequence, CRF and IOPcc are more reliable in early glaucoma detection than IOPg.

In conclusion, biomechanical parameters of cornea, as quantified by CH and CRF, and measured together with IOPcc, precisely reveal glaucoma staging in TAO and thus are reliable for diagnosing and follow-up in clinical practice.

ACKNOWLEDGEMENTS

Conflicts of Interest: Pniakowska Z, None; **Klysik A,** None; **Gos R,** None; **Jurowski P,** None.

REFERENCES

1 Yamazaki S, Inoue R, Tsuboi T, Kozaki A, Inoue T, Inoue T, Inoue Y. A characteristic optic disc appearance associated with myopia in subjects with Graves' ophthalmopathy and in subjects with primary open-angle glaucoma. *Clin Ophthalmol* 2013;7:47-53.

2 Konuk O, Onaran Z, Ozhan Oktar S, Yucel C, Unal M. Intraocular pressure and superior ophthalmic vein blood flow velocity in Graves' orbitopathy: relation with the clinical features. *Graefes Arch Clin Exp Ophthalmol* 2009;247(11):1555-1559.

3 Nassr MA, Morris CL, Netland PA, Karcioglu ZA. Intraocular pressure change in orbital disease. *Surv Ophthalmol* 2009;54(5):519-544.

4 Herzog D, Hoffmann R, Schmidtmann I, Pfeiffer N, Preussner PR, Pitz S. Is gaze-dependent tonometry a useful tool in the differential diagnosis of Graves' ophthalmopathy? *Graefes Arch Clin Exp Ophthalmol* 2008;246 (12):1737-1741.

5 Behrouzi Z, Rabei HM, Azizi F, Daftarian N, Mehrabi Y, Ardeshiri M, Mohammadpour M. Prevalence of open-angle glaucoma, glaucoma suspect, and ocular hypertension in thyroid-related immune orbitopathy. *J Glaucoma* 2007;16(4):358-362.

6 Dayanir V, Sakarya R, Ozcura F, Kir E, Aktunc T, Ozkan BS, Okyay P. Effect of corneal drying on central corneal thickness. *J Glaucoma* 2004;13 (1):6-8.

7 Brandt JD, Gordon MO, Gao F, Beiser JA, Miller JP, Kass MA, Ocular Hypertension Treatment Study Group. Adjusting intraocular pressure for central corneal thickness does not improve prediction models for primary

open-angle glaucoma. *Ophthalmology* 2012;119(3):437-442.

8 Bayhan HA, Aslan Bayhan S, Can I. Comparison of central corneal thickness measurements with three new optical devices and a standard ultrasonic pachymeter. *Int J Ophthalmol* 2014;7(2):302-308.

9 Pepose JS, Feigenbaum SK, Qazi MA, Sanderson JP, Roberts CJ. Changes in corneal biomechanics and intraocular pressure following LASIK using static, dynamic, and noncontact tonometry. *Am J Ophthalmol* 2007; 143(1):39-47.

10 Broman AT, Congdon NG, Bandeen-Roche K, Quigley HA. Influence of corneal structure, corneal responsiveness, and other ocular parameters on tonometric measurement of intraocular pressure. *J Glaucoma* 2007;16(7): 581-588.

11 Luce DA. Determining *in vivo* biomechanical properties of the cornea with an ocular response analyzer. *J Cataract Refract Surg* 2005;31 (1): 156-162.

12 Sullivan-Mee M, Billingsley SC, Patel AD, Halverson KD, Alldredge BR, Qualls C. Ocular Response Analyzer in subjects with and without glaucoma. *Optom Vis Sci* 2008;85(6):463-470.

13 Deol M, Taylor DA, Radcliffe NM. Corneal hysteresis and its relevance to glaucoma. *Curr Opin Ophthalmol* 2015;26(2):96-102.

14 Bartalena L, Baldeschi L, Dickinson A, *et al* Consensus statement of the European group on Grave's orbitopathy (EUGOGO) on management of GO. *Eur J Endocrinol* 2008;158(3):273-285.

15 Mills RP, Budenz DL, Lee PP, Noecker RJ, Walt JG, Siegartel LR, Evans SJ, Doyle JJ. Categorizing the stage of glaucoma from pre-diagnosis to end-stage disease. *Am J Ophthalmol* 2006;141(1):24-30.

16 Lantz M, Abraham-Nordling M, Svensson J, Wallin G, Hallengren B. Immigration and the incidence of Graves' thyrotoxicosis, thyrotoxic multinodular goiter and solitary toxic adenoma. *Eur J Endocrinol* 2009;160 (2):201-206.

17 Dagi LR, Elliott AT, Roper-Hall G, Cruz OA. Thyroid eye disease: honing your skills to improve outcomes. *J AAPOS* 2010;14(5):425-431.

18 Dharmasena A. Selenium supplementation in thyroid associated ophthalmopathy: an update. *Int J Ophthalmol* 2014;7(2):365-375.

19 Perros P, Neoh C, Dickinson J. Thyroid eye disease. *BMJ* 2009; 338: b560.

20 Shah Y. Thyroid ophthalmopathy. *J Assoc Physicians India* 2011;59 Suppl:60-65.

21 Fang ZJ, Zhang JY, He WM. CT features of exophthalmos in Chinese subjects with thyroid-associated ophthalmopathy. *Int J Ophthalmol* 2013;6 (2):146-149.

22 Chng CL, Lai OF, Chew CS, Peh YP, Fook-Chong SM, Seah LL, Khoo DH. Hypoxia increases adipogenesis and affects adipocytokine production in orbital fibroblasts-a possible explanation of the link between smoking and Graves' ophthalmopathy. *Int J Ophthalmol* 2014;7(3):403-407.

23 Wiersinga WM, Kahaly GJ, eds. Graves' orbitopathy: a multidisciplinary approach-questions and answers. 2nd revised ed. Basel, Switzerland: Karger;2010;33-39.

24 Kashkouli MB, Pakdel F, Kiavash V, Heidari I, Heirati A, Jam S. Hyperthyroid vs hypothyroid eye disease: the same severity and activity. *Eye (Lond)* 2011;25(11):1442-1446.

25 Sullivan-Mee M. The role of ocular biomechanics in glaucoma management. *Review of Optometry* 2008;145(10):49-54.

26 Touboul D, Roberts C, Kérautret J, Garra C, Maurice-Tison S, Saubusse E, Colin J. Correlations between corneal hysteresis, intraocular pressure, and corneal central pachymetry. *J Cataract Refract Surg* 2008;34 (4): 616-622.

27 Iyamu E, Ituah I. The relationship between central corneal thickness and intraocular pressure: a comparative study of normals and glaucoma subjects. *Afr J Med Sci* 2008;37(4):345-353.

28 Congdon NG, Broman AT, Bandeen-Roche K, Grover D, Quigley HA. Central corneal thickness and corneal hysteresis associated with glaucoma damage. *Am J Ophthalmol* 2006;141(5):868-875.

29 Kirwan C, O'Keefe M, Lanigan B. Corneal hysteresis and intraocular pressure measurement in children using the reichert ocular response analyzer. *Am J Ophthalmol* 2006;142(6):990-992.

30 Shah S, Laiquzzaman M, Cunliffe I, Mantry S. The use of the Reichert ocular response analyzer to establish the relationship between ocular hysteresis, corneal resistance factor and central corneal thickness in normal eyes. *Cont Lens Anterior Eye* 2006;29(5):257-262.

31 Kotecha A. What biomechanical properties of the cornea are relevant for the clinician? *Surv Ophthalmol* 2007;52(2):S109-114.

32 Kotecha A, Elsheikh A, Roberts CR, Zhu H, Garway-Heath DF. Corneal thickness- and age-related biomechanical properties of the cornea measured with the ocular response analyzer. *Invest Ophthalmol Vis Sci* 2006;47(12):5337-5347.