UNIVERSITY OF LATVIA

FACULTY OF PHYSICS, MATHEMATICS AND OPTOMETRY

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VISUAL ACUITY AND CONTRAST SENSITIVITY DEPENDING ON THE SHAPE OF ANTERIOR CORNEAL SURFACE

SUMMARY OF DOCTORAL THESIS

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ABSTRACT

Doctoral thesis is written in the Latvian language on 102 pages. The thesis contains 53 illustrations, 5 tables, 143 references and 3 attachments. The study has analysed the quality of vision (visual acuity, contrast sensitivity and high-order aberrations) in keratoconus subjects which is the most common corneal disease with irregular anterior corneal shape depending on changes of corneal shape as keratoconus stage and apex's localization.

The method has been developed to predict visual acuity and contrast sensitivity for irregularly shaped cornea. The contrast sensitivity characterizes quality of vision more than visual acuity in subjects with irregular corneal shape. It is possible to improve contrast sensitivity in subjects with irregular corneal shape by decreasing corneal slope in central part of cornea.

Keywords: keratoconus, quality of vision, visual acuity, contrast sensitivity, higher-order corneal aberrations, corneal apex slope

CONTENTS

1. GENERAL DESCRIPTION OF THESIS

Refractive surgery has been rapidly developing over the last 25 years. It has become increasingly important to understand and to be able to analyse corneal topographic images, to distinguish pathological corneal changes from physiological changes so that laser treatment is not applied to corneas with potentially progressive pathological changes. A better understanding of corneal topographical maps makes it possible to operate a laser more accurate so that the laser would not deteriorate but improve the quality of corneal anterior surface, thereby improving the image quality on the retina. The quality of retinal image is formed by reflected light going through the anterior corneal part. The quality of the retinal image reduces irregular corneal shape, such as corneal astigmatism. The spectacles correct spherical component and astigmatism of refraction, but not the optical aberrations, such as coma or distortion. The irregular astigmatism makes optical aberrations for subjects with keratoconus as the result of changed corneal shape after corneal transplantation or refractive surgery. The irregular corneal shape significantly reduces optical quality of the eye and retinal image in keratoconus subjects. The ocular and higher order corneal aberrations in keratoconus subjects are significantly larger than in the subjects without pathology. The higher order aberrations cause reduction in the quality of the vision. The image of the individual anterior corneal points has been obtained in corneal topography. Although the image of the retina has been generated from light passing through all the corneal points in the area of the pupil, it is not possible to predict the quality of the retinal image only by these points (corneal topography). With the quality of vision, we understand not only high contrast visual acuity but also contrast sensitivity. Contrast sensitivity improvement can be achieved by decreasing higher order aberrations in eye optical system which is critical for peripheral vision and vision under reduced light conditions. The main factor which determines the quality of vision is corneal anterior surface quality – its sphericity in combination with another eye's optical systems surface sphericity – and the corneal clarity.

Historically, keratoconus has been an absolute contraindication to excimer laser exposure because of the possible destabilisation of the cornea and the worsening of the ectasia as it can be formed as excimer laser complication, but actually the excimer laser can be used to reshape anterior corneal surface based on the subject's topography in keratoconus subjects. The treatment is based on corneal anatomical rather than physiological anterior surface improvement. The treatment improving corneal topography improves corrected visual acuity, but at the moment it is not possible to predict the outcome after treatment for all keratoconus subjects. During the treatment cornea in keratoconus subjects has been adjusted to ideal spherical cornea by removing overall tissues to create keratoconus subject's topography more similar to ideal spherical corneal surface – with the laser smoothing corneal apex area on the corneal periphery. As a result, the treatment will not change the quality of vision in all keratoconus subjects equally, because each subject has different corneal apex localization, but the shape of the cornea has been changed by standard protocol. The corneal central part determines the quality of the retinal image; if laser flattens the apex area on corneal periphery than the image quality on the retina will not improve. The treatment will be improved by understanding how corneal irregularities change the quality on the retina. Thus already prior to the treatment, considering individual corneal shape, we will be able to predict how to change the corneal anterior part in order to achieve better quality of the vision on the retina. Currently no studies have been carried out to understand how irregular anterior corneal surface should be changed to improve the quality on retinal image. Therefore, it is necessary to understand how the change of anterior corneal shape will affect the quality of vision on retina in order to decide on the required changes on irregular corneal shape. The quality of vision is determined by high contrast visual acuity, contrast sensitivity and aberrations.

The **aim** of the current study is to achieve irregular corneal surface diagnostics by exploring the impact of anterior corneal surface irregularities on the visual acuity and contrast sensitivity.

The **tasks** of the study to achieve the results are as follows:

1. to explore the impact of corneal irregular shape on visual acuity and contrast sensitivity;
2. to assess the most important corneal irregular shape parameters on which the visual acuity and contrast sensitivity depend;
3. to experimentally evaluate the necessary changes of the corneal irregular shape parameters to improve visual acuity and contrast sensitivity;
4. to develop and clinically approbate the irregular corneal shape diagnostic method based on visual acuity and contrast sensitivity.

1.1. Novelty

The study has:

1. explored how corneal irregular shape affects visual acuity and contrast sensitivity. The degree of irregular corneal shape, such as keratoconus stage, has a stronger effect like apex localization on the quality of vision for irregular shape corneas, however, the impact of apex localization increases on contrast sensitivity increasing spatial frequency;
2. shown that irregular corneal shape defines the quality of vision. The higher order aberrations change the quality of image on the retina. The analysis of higher order aberrations showed that spherical aberration has stronger effect on the quality of vision as the vertical coma aberration, although vertical coma is the dominant irregular corneal shape aberration;

3. created a new method for corneal anterior surface analysis, which allows for the first time to estimate effect of corneal parameters on the quality of vision. The clinical approbation of the method showed that contrast sensitivity improved in all spatial frequencies if the irregular corneal surface decreased in slope for the central corneal area - the sphericity of the cornea improved.

The new method allows eye surgeons to predict the outcome of the topo-guided cross-linking treatment based on individual irregular corneal topography. Currently the topo-guided cross-linking treatment has been performed equally for all irregular corneal shapes, because it is not possible to predict the potential outcome for irregular corneal shape.

1.2. Thesis

1. It has been established that visual acuity and contrast sensitivity affect the irregular corneal shape as keratoconus stage more than corneal apex localization on the corneal surface, although apex effect on the contrast sensitivity increases as spatial frequency increases (Liduma et al, 2020, Proc. SPIE 11312; Liduma et al, 2020, Proc. SPIE 11359; Proceedings of the Latvian Academy of Science, 5(710), 339-246).
1. It has been set experimentally that regularity of central corneal area has a more important effect on visual acuity and contrast sensitivity than the higher and the lower corneal keratometric values.
2. It has been explored that the vertical coma is the dominant aberration for irregular corneal shaped eye, although the spherical aberration has the most important effect on visual acuity (Liduma, S., Krumina, G., 2019, Proc. SPIE 11207).
3. The method developed within the framework of the study has shown that contrast sensitivity improves if the slope in the central corneal area reduced.

1.3. List of publications

1. Liduma, S., Luguzis, A., Krumina, G. (2020). “Keratoconus apex positions impact on visual acuity and contrast sensitivity”, Poc. SPIE 11359, Biomedical Spectroscopy, Microscopy, and Imaging, 113591W (1 April 2020); doi: 10.1117/12.2546319
2. Liduma, S., Luguzis, A., Krumina, G. (2020). “Keratoconus stage impact on visual acuity and contrast sensitivity”, Poc. SPIE 11312, Medical Imaging, 113122J (16 March 2020); doi: 10.1117/12.2543181
3. Liduma, S., Krumina, G. (2019). “The impact of keratoconus apex’s localization on eye aberrations”, Proc. SPIE 11207, Fourth International Conference on Applications of Optics and Photonics, 112070R (3 October 2019); doi: 10.1117/12.2527145

4. Liduma, S., Krumina, G. (2017) “Visual acuity and contrast sensitivity in different keratoconus stages”, *Proceedings of the Latvian Academy of Sciences*, 5(710), pp.339-246. DOI: 10.1515/prolas-2017-0058

1.4. International conferences

1. SPIE Photonics Europe Digital forum 2020 (April 6-10, 2020) “Keratoconus apex positions impact on visual acuity and contrast sensitivity” Liduma, S., Luguzis, A., Krumina, G., oral video presentation
2. SPIE Medical Imaging 2020 (Houston, USA, February 15-20, 2020) “Keratoconus stage impact on visual acuity and contrast sensitivity”. Liduma, S., Luguzis, A., Krumina, G., poster
3. Deutsche Ophthalmologische Gesellschaft DOG 2019 (Berlin, Germany, September 26-29, 2019) „The impact of keratoconus apex' slope on visual acuity and contrast sensitivity”. Liduma, S., Luguzis, A., Krumina, G., poster, p. 130
4. European Society of Cataract & Refractive Surgeons ESCRS 2019 (Paris, France, September 14-18, 2019) “Changes in visual acuity, refraction and pachymetry after cross-linking”, Liduma, S., Vavzika, E., Lukins, F., Karlsone, L., Krumiņa, G., poster
5. IV International Conference on Application in Optics and Photonics AOP 2019 (Lisbon, Portugal, April 31-June 4, 2019) “The impact of keratoconus apex’s localization on eye aberrations”, Liduma, S., Krumina, G., poster, p.44
6. 15th International Young Scientist Conference „Developments in Optics and Communications 2019” (Riga, Latvia, April 11-12, 2019) „The impact of keratoconus apex’ localization on eye aberrations”, Liduma, S., Krumina, G., oral presentation, p.32
7. International Scientific Conference on Medicine 2019 (Riga, Latvia, February 22, 2019) “The evaluation of keratoconus patients’ quality of life”, Liduma, S., Krumina, G., poster
8. 2nd International Symposium on Visual Physiology, Environmentm and Perception VisPEP 2018 (Vilnius, Lithuania, November 30-December 1, 2018) “Visual acuity, refraction, and pachymetry in different keratoconus stages after cross-linking” Liduma, S., Vavzika, E., Krumiņa, G., poster, p. 54.
9. 41st European Conference on Visual Perception conference ECVP 2018 (Trieste, Italy, August 26-30, 2018) “Visual acuity and contrast sensitivity depending on keratoconus apex’s position”, Liduma, S., Krumina, G., poster, p.20.
10. 14th International Young Scientist Conference „Developments in Optics and Communications 2018” (Riga, Latvia, April 12-13, 2018) “Changes in visual acuity, refraction and pachymetry in various stages of keratoconus

after cross-linking operations”, Liduma, S., Vavzika, E., Krumina, G., oral presentation, p.4.

11. Deutsche Ophthalmologische Gesellschaft DOG 2017 (Berlin, Germany, September 28-October 1, 2017) “The impact of keratoconus apex position on visual acuity and contrast sensitivity”. Liduma, S., Krumina, G., poster, p.127.
12. 13th International Young Scientist Conference “Developments in Optics and Communications 2017” (Riga, Latvia, April 6-7, 2017) „The impact of keratoconus apex position on visual acuity and contrast sensitivity”, Liduma, S., Krumina, G., oral presentation, p.2.
13. 1st International Symposium on Visual Physiology, Environment and Perception VisPEP 2016 (Riga, Latvia, October 6-8, 2016) “Visual acuity and contrast sensitivity in different keratoconus stages”, Liduma, S., Krumina, G., poster, pp.48-49.

1.5. Local conferences

1. The 77th scientific conference of the University of Latvia (Riga, Latvia, February 15, 2019), **“**The impact of keratoconus apex localization on corneal higher order aberrations”, Liduma, S., Krumina, G., oral presentation
2. The 76th scientific conference of the University of Latvia (Riga, Latvia, February 16, 2018), **“**The changes of visual quality in different keratoconus stages after cross-linking treatment”, Liduma, S., Vavzika, E., Krumina, G., oral presentation
3. LOOA and the 75th scientific practical conference of the University of Latvia (Riga, Latvia, February 19, 2017), **“**The impact of keratoconus apex localization on visual acuity and contrast sensitivity”, Liduma, S., Krumina, G., oral presentation
4. The 75th scientific conference of the University of Latvia (Riga, Latvia, February 17, 2017), **“**The changes of visual acuity, refraction corneal thickness in different keratoconus stages after cross-linking treatment”, E. Vavzika, S. Liduma, poster

2. THEORETICAL FRAMEWORK

Keratoconus is a non-infectious, progressive bilateral corneal thinning which involves 2/3 parts of the central cornea (*Rabinowitz*, 1998; *Espandar & Meyer*, 2010). Although keratoconus is the most common bilateral, it has an asymmetric course (*Gokhale*, 2013). Corneal thinning and protruding create irregular astigmatism and/or myopia. According to Rabinowitz, in the general population keratoconus occurs in 1 out of 2000 people (*Rabinowitz*, 1998). The only method which stops keratoconus progression and corneal thinning is the cross-linking treatment, which uses riboflavin and ultraviolet-A (UVA) light. In cross-linking treatment additional covalent links are created between collagen molecules, stabilising corneal protrusion and changing corneal tissue properties (*Espandar & Meyer*, 2010; *Boa et al*., 2016), which leads to improved corneal shape increase uncorrected and corrected visual acuity and decreases corneal higher order aberrations, especially coma (*Romero-Jimenez & Santodomingo-Rubido*, 2010). Amsler-Krumeich classification (see Table 1) is the most commonly used and the oldest keratoconus classification, graded keratoconus from first to forth stage based on spectacle correction, central corneal keratometry (corneal curvature), existence of scars and central corneal thickness (Duncan & Belin, 2016).

Table 1

Amsler-Krumeich classification.

I stage	• Eccentric corneal steepening • Induced myopia and/or astigmatism <5 D • Average K value <48 D
II stage	• Induced myopia and/or astigmatism >5 D, <8 D • Average K value <53 D • No central scars • Corneal thickness >400 µm
III stage	• Induced myopia and/or astigmatism >5 D, <10 D • Average K value >53 D • No central scars • Corneal thickness 300 – 400 µm
IV stage	• Refraction not measurable • Average K value >55 D • Central scars, perforation • Corneal thickness 200 µm

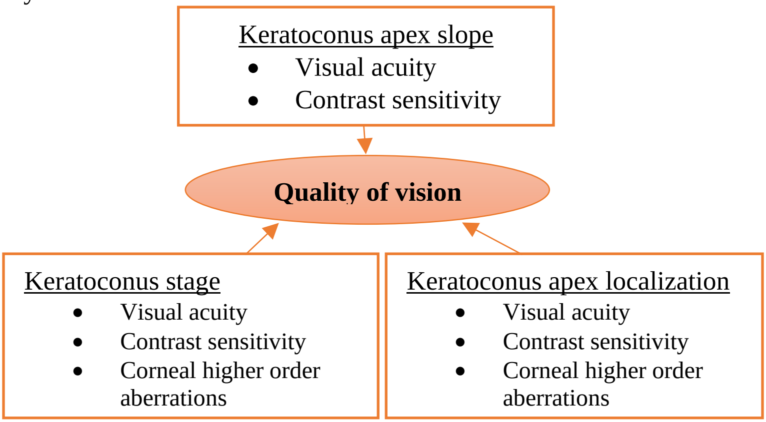
Applegate with colleagues (2006) demonstrated that the correlation between retinal image quality and visual acuity is stronger in low contrast visual acuity, even if subjects with irregular corneal shape has high contrast visual acuity above 1.0 (*Applegate & Marsack*, 2006). Visual acuity differs from contrast sensitivity as visual acuity measurement is based on visual resolution under high contrast conditions (at least 85%) where objects have the same contrast but different size. Contrast sensitivity is the threshold measurement required to see an object, in this case the contrast is different to determine the minimum level of contrast required to recognize the object (*Owsley*, 2003). The complaints about vision do not reflect high contrast visual acuity in keratoconus subjects and low contrast visual acuity is more informative about their vision (*Zadnik et al*., 2000). Maeda and colleagues (2000) study showed that pathological topography significantly reduced letter contrast sensitivity compared to subjects with normal topography without altering best corrected high contrast visual acuity (*Maeda et al*., 2000). Before reduction in high contrast visual acuity, contrast sensitivity reduces at medium and high spatial frequencies for subjects with irregular corneal shape as keratoconus (*Hess & Carney*, 1978; *Zadnik & Mannis*, 1984; *Zadnik et al.*, 1987; *Pesudovs et al*., 2004). Zanik (1987) study showed that reduction of contrast sensitivity starts at 6 cpd for subjects with irregular surface cornea. The maximum contrast sensitivity was observed at 6 cpd in the control group without pathological changes, while 60 % of the subjects with irregular corneal shape had the maximum contrast sensitivity at 3 and 4 cpd, contrast sensitivity proportionally decreased from normal contrast sensitivities at the higher frequencies with the highest difference at 12 and 18 cpd (*Zadnik et al*., 1987).

As the refractive surgery becomes increasingly popular, it is crucial to understand the aberrations of the anterior corneal surface, because the latest technologies make it possible to reshape the anterior surface of the cornea with the aim to reduce corneal aberrations during treatment, thereby improving the quality of the retinal image (*Rosa et al*., 2008). Smolek (2003), on the basis of the assumption that corneas with larger irregularities of the anterior surface will have larger corneal aberrations resulting in the best corrected visual acuity deterioration, showed that not all aberrations have an equal effect on the subject's visual quality, i.e. a major improvement in the best corrected visual acuity can be achieved by correcting 4th order aberrations, but correcting 10th order aberrations visual acuity improves less (*Smolek & Klyce*, 2003). Paranhos (2011) study of the quality of life showed that the quality of life is influenced the most by following parameters, such as gender (men are more satisfied with life), changes in cylinder size above 1 D and contrast sensitivities changes at 3 and 6 cpd spatial frequencies. This shows that daily functional vision improves by improving the contrast sensitivity at 3 and 6 cpd spatial frequencies and reducing the cylinder size by at least 1 D (*Paranhos et al*., 2011).

Keratoconus has been an absolute contraindication to the excimer laser because of possible destabilisation of the cornea and the worsening of ectasia condition, since ectasia can be formed as a complication of an excimer laser treatment. However, it is possible for keratoconus subjects to use a laser to correct the anterior corneal surface based on subject's topographical data. It is possible to combine cross-linking and topography based corneal anterior surface improvement by laser to improve the corneal anterior surface, reducing irregular astigmatism and error of refraction at the same time improving visual acuity and stopping keratoconus progression (*Shetty*, 2013).

3. RESEARCH

The study analyses the quality of vision for irregular shape corneas depending on the location of the corneal surface apex and degree of corneal surface changes. The quality of vision has been defined by visual acuity, contrast sensitivity and higher order aberrations. The study analysed the impact of corneal surface changes as keratoconus stage and localization of corneal apex on quality of vision, as well as impact of corneal apex slope on quality of vision. The aim was to develop a method that would allow to predict necessary changes of irregular corneal shape to improve the quality of vision.



3.1. Slope of the irregular corneal surface apex

3.1.1. Method

The study analysed 45 keratoconus subjects (77 eyes) with keratoconus. Keratoconus has four stages of development based on Amsler-Krumeich classification. Only the subjects with the first three keratoconus stages were examined (see Table 2).

Table 2

Keratoconus subjects depending on the stage and apex localization.

	I stage	II stage	III stage	TOGETHER:
Central apex	7 (26%)	10 (32%)	16 (76%)	**33**
Peripheral apex	20 (74%)	21 (68%)	5 (24%)	**46**
TOGETHER:	**27**	**31**	**21**	

It was assumed on the basis of corneal topography that the keratoconus apex is in the area where the cornea has the highest value of the curvature. The cornea apex is usually located below the visual axis. If the keratoconus apex was in a 1.5

mm large radius around the centre of the cornea then it was assumed that the keratoconus apex was at the centre (see Fig. 1). If the apex was outside the circle with a 3 mm diameter then it was assumed that the apex was located on the periphery of the cornea.

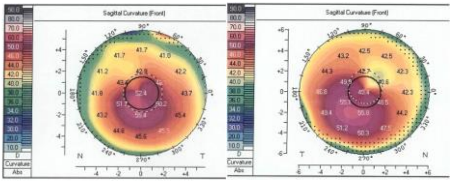


Fig. 1. The left image is for a patient's topography with the keratoconus apex at the centre and the right one is with the keratoconus apex on the periphery. The dark circle line around the central part of the cornea represents 1.5 mm radius, while the dotted line represents pupils' border.

In keratoconus subjects were determined subjective correction of refraction, visual acuity with and without spectacle correction, corneal topography, measurement of pupil size in twilight conditions, biomicroscopy in order to exclude subjects with corneal scarring and contrast sensitivity to 8 spatial frequencies with and without spectacle correction.

The study introduced and analysed various parameters characterizing geometric shape of the cornea designed to measure the slope between different parts of cornea. The shape of cornea is described using measurements from the elevation map of the corneal anterior surface (with respect to the ideal shape of cornea) in subjects obtained from ALLEGRO Oculyzer. A real corneal surface elevation from the ideal corneal sphere has been expressed in micrometres (μm) (see Fig. 2).

Corneal measurements were read at the following locations (see Fig. 3):

(1) the corneal centre – (C);

(2) the points evenly distributed on the circles of 1, 2, 3 mm radius around the corneal centre (grey-colored points);

(3) the points located at distances of 1, 2, 3 mm from the corneal centre on an axis which goes through the corneal centre and corneal surface apex (ax), and on an axis perpendicular to it (P ax).

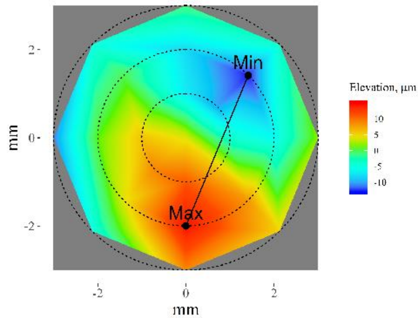


Fig 2. A schematic illustration of the corneal anterior surface demonstrates a real corneal surface elevation from an ideally spherical corneal surface, i.e. each point in the graph represents an elevation (measured in micrometres) from the imaginary ideally spherical corneal surface. The particular image also shows the maximum (Max) and the minimum (Min) elevation points. Dotted circular lines represent the analysed circles of 1, 2 and 3 mm radius. Red colour represents higher points while blue color – lower points.

The study introduces parameters characterising the corneal surface in order to determine their correlation with the parameters characterising visual quality, such as visual acuity and contrast sensitivity. On the basis of the measurements at points (2) described above, the highest and the lowest corneal points were identified, i.e. the points with the greatest and the smallest elevation, respectively, taking an imaginary ideal corneal sphere as a reference, as well as a difference between these points. On the basis of the measurements at points (3), changes in the elevation from the corneal centre in four directions (defined by the location of corneal protrusion) were obtained for all eyes. More precisely, change in elevation was measured:

a) in the direction of corneal protrusion and in the opposite direction of it along a line passing though the centre and corneal surface apex (ax);
b) on both sides from the corneal centre along a line which is perpendicular to the line of the centre-corneal surface apex (P ax).

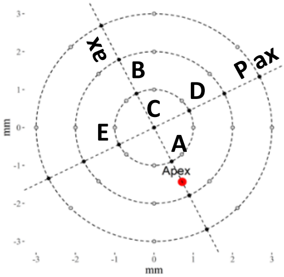


Fig. 3. A schematic example of the locations of measurement points.

3.1.2. Results

Parameters characterising the corneal surface

All subjects with irregular corneal shape together demonstrated a medium correlation in absolute values between the visual acuity and the highest corneal point of the corneal anterior surface (r=0.30, p<0.01), while a correlation between the visual acuity and the lowest corneal point was weaker (r=0.21, p=0.06). In subjects with central corneal surface apex, the visual acuity had no statistically significant correlations with either the highest corneal point (r=0.10, p=0.61), the lowest corneal point (r=0.15, p=0.44). Subjects with peripheral corneal surface apex had statistically significant correlations with either the highest corneal point (r=0.44, p<0.01), the lowest corneal point (r=0.34, p=0.02).

Parameters characterising the corneal surface had higher correlations with the contrast sensitivity than visual acuity. In all subjects together, the correlation between contrast sensitivity and change in elevation (slope) of the corneal surface varied across spatial frequencies of the contrast sensitivity. The correlation (in absolute values) between the highest corneal elevation and contrast sensitivity in different spatial frequencies ranged from r=0.25 (p=0.03) at 3 cpd to r=0.47 (p<0.01) at 9 cpd. In subjects with central corneal surface apex, correlations between contrast sensitivity and elevation of the highest corneal point ranged from r=0.10 (p=0.61) at 3 cpd to r=0.38 (p=0.05) at 9 cpd. As to the subjects with peripheral corneal surface apex, the correlation between the contrast sensitivity and elevation of the highest corneal point ranged from r=0.33 (p=0.02) at 3 cpd to r=0.53 (p<0.01) at 9 cpd. In all subjects together, the absolute value of correlation between the lowest corneal point and contrast sensitivity ranged from r=0.33 (p=0.09) at 5 cpd to r=0.40 (p<0.01) at 11 cpd. In subjects with central corneal surface apex the absolute value of correlation between the lowest corneal point and contrast sensitivity ranged from r=0.32 (p=0.09) at 7 cpd to r=0.49 (p<0.01) at 15 cpd. As to the subjects with peripheral corneal surface apex, correlation ranged from r=0.32 (p=0.03) at 3 cpd to r=0.47 (p<0.01) at 11 cpd.

The study focused on two directions characterising changes in the surface (slope) – the direction through the corneal centre and corneal surface apex (ax), and the direction perpendicular to it (P ax). Visual acuity had higher correlations with the changes in elevation along the (ax) direction.

Analysing the change in elevation along the axis that goes through the corneal centre and the corneal surface apex (ax), separately in the direction from the corneal centre to the opposite direction of the corneal surface apex (CB) and to the corneal surface apex (CA), visual acuity had higher correlations with the (CB) direction and smaller correlations with the (CA) direction from corneal centre.

The highest correlation of visual acuity in all subjects together was that with the changes in elevation along the axis which goes through the corneal centre and corneal surface apex in a 1 mm radius (ax direction CB). A situation was similar in the subjects with peripheral apex, namely the highest correlation of visual acuity was that with an elevation change in a 1 mm radius along the axis passing through the corneal surface apex (ax) direction, while the subjects' eyes with central corneal surface apex do not demonstrate statistically significant correlations between shape of cornea parameters and visual acuity at any distance from the corneal centre.

Higher correlation between the change in elevation (slope) and contrast sensitivity for all subjects together was associated with the direction which goes through the corneal surface apex and the corneal centre (ax) rather than the direction perpendicular to it (P ax). The highest correlation between -contrast sensitivity and changes in the elevation can be observed in the central area of the cornea in a 1 mm radius around the corneal centre for the direction (CB), both for all subjects together and individually with the central and peripheral apex.

Regression model

Previous results showed that central corneal slope has stronger correlations with contrast sensitivity than visual acuity, so in regression model the analysis was focused on the difference made in contrast sensitivity by changing central slope by 1 µm. The highest correlations between contrast sensitivity and difference in slope were in the direction (ax) with a radius 1 mm around the central cornea. The visual axis forms the visual acuity at the central point of the eyeball (fovea). Correlations between contrast sensitivity and change in corneal slope suggest that subjects will experience changes in daily life, if there is a difference in the corneal central part with 1 mm radius in the opposite direction of the corneal surface apex. Changes in corneal elevation will result in a change in subjects contrast sensitivity.

A regression model was created within the context of the study allowing to predict the expected contrast sensitivity if corneal slope changes in central part are known (in the line through corneal surface apex). With the regression model it is possible to predict contrast sensitivity at each spatial frequency:

Log-contrast sensitivity = Intercept (a) + regression coefficient (b) * change in slope (µm)

Regression model (see Fig. 4) describes the predictability of the regression model, i.e. how well the contrast sensitivity can be described by the slope value. In higher contrast sensitivity spatial frequencies (9, 11, 13 and 15 cpd) it is possible to describe contrast sensitivity more accurately following the slope change.

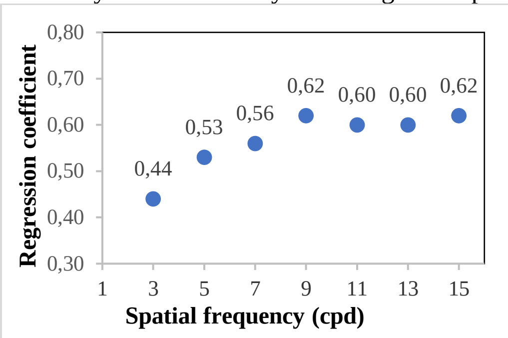


Fig. 4. Regression coefficient in different spatial frequencies for all subjects together.

The regression coefficient b describes the change in contrast sensitivity in each of the spatial frequencies if the slope increases by 1 µm. According to the figure, when a slope changes by one unit (1 µm), the log-contrast sensitivity is more affected in high spatial frequencies, i.e. log-contrast sensitivity decreases (see Fig. 5 b). The intercept (a) coefficient can be interpreted as a reference point (corneal surface without slope) from which the expected log-contrast sensitivity is calculated according to the observed slope (see Fig. 5 a). If the spatial frequency increases, then the intercept decreases while the b factor increases. Since the slope values were negative and a lower coefficient (higher than absolute) means a higher slope, the regression results indicate that higher frequencies already have lower contrast sensitivity at low corneal slope, while corneal slope increases, the contrast sensitivity decreases even more rapidly than lower frequencies.

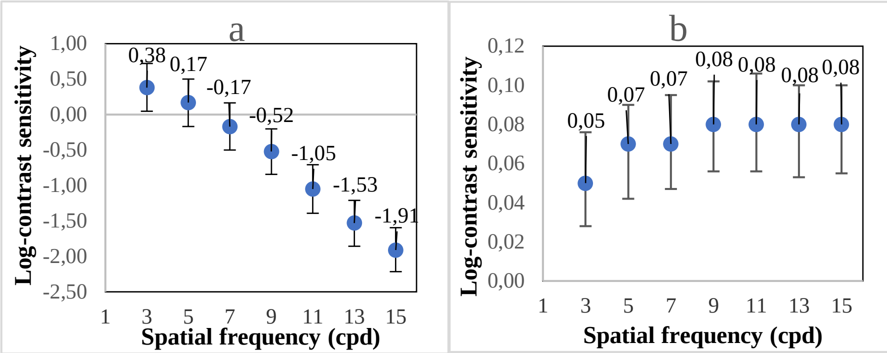


Fig. 5. Figure shows average intercept coefficient of contrast sensitivity value in all special frequencies for all subjects together, while figure b shows average change of contrast sensitivity if the slope changes by 1 µm for subjects. Assessment ± confidence interval.

3.2. Contrast sensitivity of the irregular corneal shapes

3.2.1. Method

Visual acuity and contrast sensitivity were measured at 3 m with and without the best possible spectacle correction using the FrACT software 3.9.3 (Bach, 2007) measurement was taken only once. The grading contrast sensitivity test was used, and measurements were taken at the following frequencies: 1, 3, 5, 7, 9, 11, 13, and 15 cpd. Contrast sensitivity was measured taking 10 measurements in four directions using the psychometric method, and visual acuity was measured using the C optotype. Visual acuity measurements started with C optotype recognition and depending on the subject's response, the sizes were increased or reduced. To compare contrast sensitivity for subjects with keratoconus to subjects without corneal pathology, contrast sensitivity was measured also for a subject without pathology (9 eyes). These measurements were taken only once per subject. Measurements were done in 10 lux illuminances to control pupil size and to ensure that the subject looks through the central part of the pupil. Illuminance was measured with a Konica Minolta T-10M luxmeter. Contrast sensitivity was measured on the computer display at 3 m distance by 10 consecutive measurements. The average luminance from the computer display was 99 cd/m2 and luminance from surrounding walls was 0.83 cd/m2. Luminance was measured with a Konica Minolta Chroma meter CS-100A.

3.2.2. Results

We assumed that different degrees of corneal irregularities as keratoconus stages and apex localizations will create different amount of reduction in each contrast sensitivity spatial frequency comparing to subjects without ocular pathology. For example, for subjects with larger corneal irregularities lower spatial frequencies will be affected and higher amount of contrast sensitivity will be reduced at lower spatial frequencies comparing to subjects with smaller corneal irregularities. Figure 6 shows contrast sensitivity for subjects with irregular corneal shape in different keratoconus stages. The results showed that if keratoconus stage increases, then the amount of contrast sensitivity decreases equally in all spatial frequencies. Mixed effect model showed that effect of spectacles correction on contrast sensitivity is statistically significant ($p<0.01$), but there are differences of spectacles created effect on contrast sensitivity between keratoconus stages. The first and the second stage subjects do not have statistically significant difference in corrected and uncorrected difference of contrast sensitivity ($p=0.91$), while the second and the third stage have it ($p=0.0$). Spectacle correction changes contrast sensitivity statistically significantly for the first stage keratoconus subjects, while third stage keratoconus subjects do not have statistically significant improvement in contrast sensitivity ($p=0.27$).

The average corrected visual acuity and standard deviation for the first stage keratoconus subjects were 0.72±0.27 decimal units, the average uncorrected visual acuity was 0.38±0.36 decimal units, t-test ($p<0.01$). The average corrected visual acuity and standard deviation for the second stage keratoconus subjects were 0.55±029 decimal units, uncorrected visual acuity was 0.37±0.30 decimal units, t-test ($p<0.01$). The third stage corrected visual acuity and standard deviation for keratoconus subjects were 0.39±0.23 decimal units and uncorrected visual acuity was 0.16±0.11, t-test ($p<0.01$).

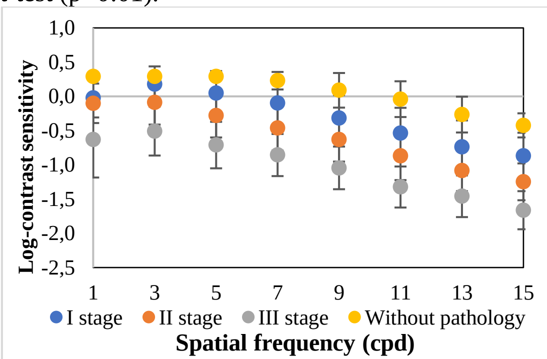


Fig. 6. Corrected contrast sensitivity depending on the keratoconus stage in subjects with irregular corneal anterior surface compared to contrast sensitivity with the subjects without pathology ± standard deviation.

Analysing keratoconus subjects by apex position (see Fig. 7) the conclusions were very similar to the previous results. Keratoconus subjects with central apex position had the lower contrast sensitivity, compared to subjects with peripheral apex position. The difference in contrast sensitivity between all spatial frequencies slightly increased with the spatial frequency between subjects with peripheral and central apex position. Mixed effect model showed that spectacle correction significantly improves contrast sensitivity (p=0.0) for subjects with different apex positions. Different keratoconus apex localization has statistically significant impact on contrast sensitivity (p=0.01) for subjects with irregular corneal shape, although corneal surface apex localization does not have statistically significant impact on spectacle correction (p=0.38).

The average corrected visual acuity and standard deviation for keratoconus subjects with central keratoconus apex were 0.47±027 decimal units, without correction –0.26±0.22 decimal units, t-test (p<0.01). The average corrected visual acuity and standard deviation for keratoconus subjects with peripheral keratoconus apex were 0.62±0.26 decimal units, without correction –0.38±0.34 decimal units, t-test (p<0.01).

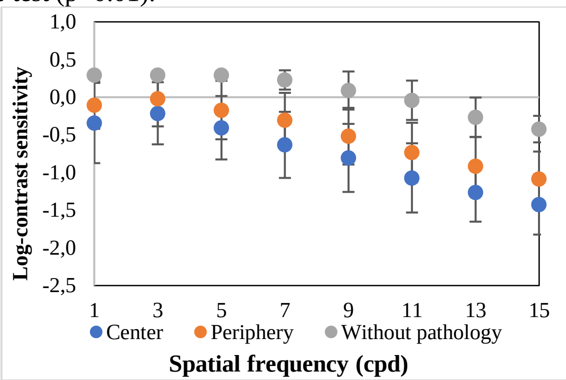


Fig. 7. Contrast sensitivity depending on apex localization with spectacle correction for subjects with irregular corneal shape ± standard deviation.

Analysing contrast sensitivities deviation from the subjects without pathology in each spatial frequency for subjects with irregular corneal shape (see Fig. 8), in different keratoconus stages and in different apex localizations the lowest difference from subjects without pathology is at 3 cpd. The difference in log-contrast sensitivity between subjects with and without pathology increased up to 11 cpd but remained rather constant at the highest spatial frequencies – 11, 13 and 15 cpd for subjects with irregular corneal shape in different keratoconus stage and apex localization.

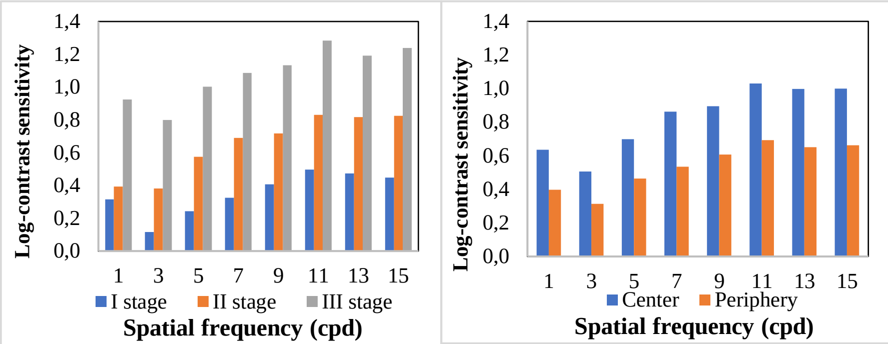


Fig. 8. The difference in contrast sensitivity from subjects without pathology in each spatial frequency for subjects with irregular corneal shape depending on keratoconus stage and apex position ± standard deviation.

Mixed effect model shows that contrast sensitivity has statistically significantly effect in each spatial frequency (p=0.0) and between keratoconus stages (between first and second stage p=0.08; between first and third stage p=0.0), while corneal apex localization has statistically significant effect only together with spatial frequency (p=0.04). Statistically significant interaction between spatial frequency and corneal surface apex localization means that the effect of spatial frequency on contrast sensitivity depends on corneal surface apex localization – in irregular shaped corneas subjects with peripheral apex localization, the contrast sensitivity decreases slower when spatial frequency increases, the effect of apex position is different in different spatial frequencies – in low frequencies contrast sensitivity, on average, is less different from subjects without pathology comparing to high frequencies.

3.3. Aberrations of the irregular corneal shapes

3.3.1. Method

The study has analysed corneal anterior surface 3rd and 4th order higher order aberrations with different keratoconus stage and apex localization for keratoconus subjects. The study used a control group which consisted of subjects without corneal or other pathology and without physiological corneal astigmatism in order to compare higher order aberrations between subjects with irregular corneal shape and subjects without pathology. The control group consisted of 7 subjects (9 eyes). Higher order aberrations were measured by videokeratoscopy method to 8 mm large pupil.

The higher order aberration measurements will be more precisely with wavefront aberometroskopy method because of irregular corneal anterior surface for keratoconus subjects. The corneal topography measured corneal anterior surface and described with parameters as elevation, tilt and curvature. The elevation data described the corneal height relative to reference surface. The tilt describes the orientation of the tangential line to the surface point. The curvature describes the “curve” of the cornea and is inverted proportionally to the radius of the curvature. The most important measurement of the cornea is considered a corneal elevation map, which shows the difference between the subject’s cornea and the perfect surface. On the elevation topography map, it is possible to see subjects’ corneal irregularities because the topographer compares the “real” corneal surface to the hypothetical sphere, where areas are located either “above” (µm) or below (µm) the ideal sphere.

3.3.2. Results

The average corneal RMS aberrations and standard deviation for all subjects with irregular corneal shape together were 2.0±0.56 µm and for subjects without pathology 1,14±0,52 µm. For the first stage keratoconus subjects the average RMS aberrations and standard deviation were 1.51±0.26 µm, for the second stage keratoconus subjects the average RMS aberrations and standard deviation were 2.09±0.38 µm, while for the third stage keratoconus subjects the average RMS aberrations and standard deviation were 2.64±0.45. For irregular corneal surface subjects with central apex localization the average RMS and standard deviation were 2.27±0.61 µm, and for subjects with peripheral apex localization were 1.86±0.46 µm.

The results of the study showed that corneal anterior surface dominant aberrations in Zernike polynomials were Z(3,-1) and Z(4,0) aberrations, namely, vertical coma and spherical aberration. For all subjects with irregular corneal surface together, the average vertical coma and standard deviation were -2.6±1.3 µm. The average spherical aberration and standard deviation were 0.6±0.8 µm.

As the keratoconus stage increases, the vertical coma increases as well. The average vertical coma was -0,2 µm for subjects without pathology. The average vertical coma for the first stage keratoconus subjects was -1.3±0.7 µm, for the second stage keratoconus subjects it was -2.7±0.8 µm and for the third stage keratoconus subjects it was -4.0±0.9 µm, namely, the vertical coma increased for the first stage keratoconus subjects by 1.1 µm, for the second stage keratoconus subjects by 2.5 µm and for the third stage keratoconus subjects by 3.8 µm comparing to the subjects without pathology (see Fig. 9). Despite the fact that the vertical coma Z(3,-1) was different between the first and the third stage keratoconus subjects, the difference was not statistically significant (p=0.34) by Mann-Whitney U two-tailed test, a statistically significant difference was not also found for the second and the third stage keratoconus subjects but it was established for the first and the third keratoconus subjects by Mann-Whitney U two-tailed test, p=0.31 and p=0.04 respectively.

The average spherical aberration and standard deviation for subjects with irregular corneal surface without pathology were 1.3 µm which reduces as keratoconus stage increases. The average spherical aberration and standard deviation for the first stage keratoconus subjects were 1.1±0.3 µm, and it decreased comparing to the subjects without pathology by 0.2 µm. For the second stage keratoconus subjects the average spherical aberration and standard deviation were 0.7±0.6 µm, it decreased comparing to the subjects without pathology by 0.6 µm. For the third stage keratoconus subject's spherical aberration decreased by 1.6 µm and become negative comparing to the subjects without pathology -0.3±0.9 µm. Mann-Whitney U two-paired test did not show any statistically significant difference for spherical aberration between all keratoconus stages, between the first and the second keratoconus stage p=0.60, between the second and the third keratoconus stage p=0.35 with significance level 0.05. Also, results did not show any statistically significant difference for keratoconus stages comparing to the subjects without pathology.

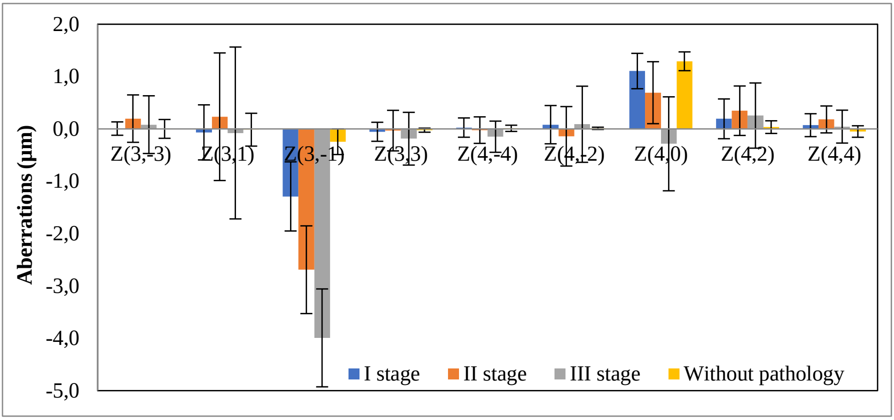


Fig. 9. The average corneal anterior surface higher order aberration depending on the keratoconus stage ± standard error.

The study revealed that the dominant aberrations for all subjects with different apex localization were vertical coma and spherical aberration (see Fig. 10). The average vertical coma and standard deviation for corneal anterior surface were -0.2±02 µm, the average vertical coma and standard deviation for keratoconus subjects with central apex localization were -2.9±1.4 µm, while for subjects with peripheral keratoconus apex they were -2.3±1.2 µm. Comparing to the subjects without pathology it increased by -2.1 µm but comparing to the subjects with central apex localization it decreased only by 0,6 µm. Vertical coma was not significantly different statistically for subjects with different apex localization – central and peripheral – comparing to the subjects without pathology by Mann-Whitney two paired U test ($p=0.51$) with significance level 0.05.

The average spherical aberration and standard deviation for subjects without pathology were 1.3±0.2 µm, while for subjects with central corneal surface apex the spherical aberration was negative -0.1±0.1 µm and for subjects with peripheral corneal surface apex the spherical aberration was positive 1.0±1.0 µm. Spherical aberration has a statistically significant difference by Mann-Whitney two paired U test ($p<0.01$) with significance level 0.05.

The strongest correlation between the corrected visual acuity and the spherical aberration was for the first stage keratoconus subjects ($r=0.59$; $p<0.01$). The results did not show statistically significant correlation between the visual acuity and aberrations for subjects with second and third keratoconus stage. The strongest correlation between the spherical aberration and the visual acuity was for central apex localization ($r=0.45$; $p<0.01$).

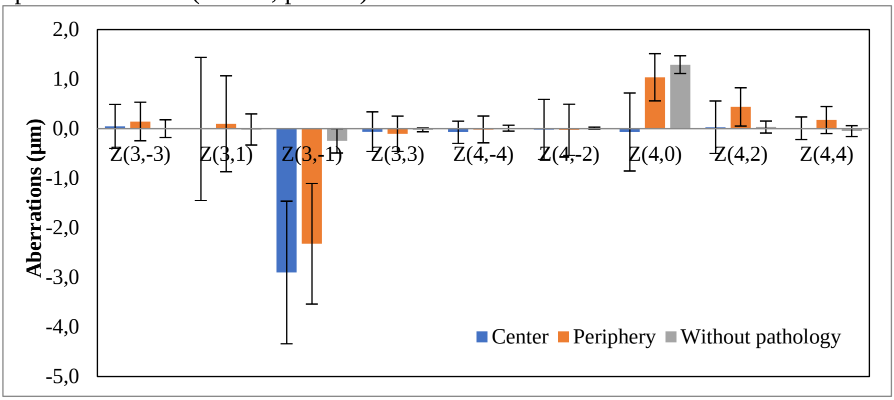


Fig. 10. The average corneal anterior surface higher order aberration depending on the corneal surface apex localization ± standard error.

DISCUSSION

Previous studies have showed that the most informative assessment of daily functional vision for keratoconus subjects is not visual acuity in high-contrast conditions, but an assessment of contrast sensitivity (*Zadnik et al.*, 2000; *Abdu & Mohidin*, 2014; *Hess & Carney*, 1978; *Zadnik et al*, 1984; *Zadnik et al*., 1987; *Pesudovs et al*., 2004). Low contrast visual acuity is more informative about the subjects with irregular corneal surface functional vision than high contrast visual acuity. Keratoconus subjects with fine high contrast visual acuity still may have complaints about the quality of vision. Fine quality of vision does not require high contrast sensitivity at all spatial frequencies equally. The functional visual acuity in subjects with irregular corneal surface will reduce more if reduction will be in low and medium spatial frequencies rather than in high spatial frequencies.

Contrast sensitivity haven't been studied a lot for keratoconus subjects, although these studies have shown reduction in contrast sensitivity at medium and high spatial frequencies for subjects with irregular corneal surface. The only study whose results can be compared with the results of the present study is the Zadnik (1987) research, which showed that the maximum contrast sensitivity for subjects with irregular corneal surface is at 3 and 4 cpd, following by a reduction in the contrast sensitivity from subjects without pathology, reaching the maximum difference at the high spatial frequencies. The results of the Zadnik (1987) study coincide with the results of our study. Our results demonstrated the maximum contrast sensitivity at 3 cpd for subjects with irregular corneal surface followed by reduction in higher contrast sensitivity for subjects with different keratoconus stages and different apex localizations. If the keratoconus stage increases, the contrast sensitivity decreases. Subjects with central corneal surface apex localization have lower contrast sensitivity than subjects with peripheral corneal surface apex. The changes in contrast sensitivity caused by the spectacle correction in the various spatial frequencies for subjects with different apex localizations suggest that there is an impact of central corneas slope apex on contrast sensitivity. Spectacle correction change contrast sensitivity equally in all spatial frequencies for subjects with peripheral corneal apex localization, while subjects with central corneal apex localization have various improvement in all spatial frequencies. The peripheral apex localization for subjects with irregular corneal surface has smaller effect on the central part of the cornea comparing to subjects with central apex localization when corneal surface apex creates slope in the central corneal part.

The larger the total corneal aberrations, the worse the best corrected visual acuity (Alio et al., 2011). The interaction between visual acuity and RMS aberration shows that the larger corneal total aberrations, the worse the best corrected visual acuity will be. Therefore, aberrations play the major role in the quality of vision. It has been proven (Fathy et al., 2016) that for keratoconus subjects the dominant higher order aberrations are a vertical coma and a spherical aberration which also appeared in our study. The analysis of keratoconus subjects vertical coma Zernike polynomials Z(3,-1) shows that if keratoconus stage is increasing then vertical coma has a tendency to increase, although the increase is not significant in statistical terms. The spherical aberration decreases and becomes negative when the stage of keratoconus subjects increases comparing to subjects without pathology. The difference is not statistically significant, it is a trend.

The different apex localization has the statistically significant difference in the vertical coma aberration for subjects with irregular corneal shape. The vertical coma is higher by 0.6 μm for subjects with a central corneal apex comparing to subjects with a peripheral corneal apex. The spherical aberration has a difference in subjects with different apex localizations, subjects with central apex localization have a negative spherical aberration, while subjects with peripheral apex localization have a positive spherical aberration. The difference is statistically significant. The dominant aberration for subjects with irregular corneal shape is the vertical coma, although the stronger correlation with the best corrected visual acuity has the spherical aberration.

The results show correlations between the quality of vision (visual acuity and contrast sensitivity) and parameters characterising the corneal surface and corneal apex slope showing stronger correlation with contrast sensitivity than visual acuity. The study shows that the contrast sensitivity describes better the quality of vision for subjects with irregular corneal shape, therefore subjects will feel changes in contrast sensitivity more in everyday life than the changes in visual acuity.

The study showed that the parameters characterising the corneal surface as the maximum, minimum corneal height describing the geometrical shape of the cornea are not the main determinants of visual quality. The changes in corneal slope in the central corneal have higher correlations with contrast sensitivity, i.e. the slope of corneal surface apex on the central cornea determines contrast sensitivity for subjects with irregular corneal shape.

The highest corneal point (apex) is closer to the central cornea for subjects with central apex position, so it makes steeper slope in the central part of the cornea comparing to subjects with peripheral apex localization. The highest corneal point (apex) is located further from the central cornea for subjects with peripheral corneal surface apex, so the slope in the central part of the cornea is less apparent. It is a reason why correlations between the contrast sensitivity and the slope were stronger for the subjects with peripheral apex localization.

The study showed that the most important corneal area which determines the quality of vision for subjects with irregular corneal shape is the area above the corneal centre with a radius of 1 mm in the opposite direction of the corneal surface apex localization. The next step is to understand how changes in the slope in the central part of the cornea will change the quality of vision to predict to which keratoconus subject and what amount the topo-guided cross-linking treatment will improve the quality of vision.

The regression model has been established to predict contrast sensitivity for keratoconus subjects by changing the slope of the corneal central part caused by the corneal apex. The regression model allows to calculate how contrast sensitivity for keratoconus subjects will change at each spatial frequency if the corneal slope will decrease by 1 µm. The regression model is more accurate at higher spatial frequencies and for keratoconus subjects with central corneal surface apex. Contrast sensitivity tends to decrease for central corneal surface apex localization in the higher spatial frequencies more than for keratoconus subjects with peripheral apex localization, particularly for higher spatial frequencies in the regression model.

CONCLUSIONS

The aim of our current study has been to achieve irregular corneal surface diagnostics by exploring the impact of anterior corneal surface irregularities on the visual acuity and contrast sensitivity. It will help to predict how changing irregular corneal shape of the eye would improve the visual acuity and contrast sensitivity. In order to achieve the aim of the study, the quality of vision parameters, such as the visual acuity and the contrast sensitivity, has been analysed depending on corneal irregular shape.

The analysis of the corneal surface parameters showed that the changes in the central corneal area has a stronger impact on the quality of vision than corneas higher and lower keratometric values which are usually located on the corneal periphery. As a result, the study has established a regression model to describe how contrast sensitivity will change when corneal slope reduces in the central area. The analysis of the regression model showed that the contrast sensitivity characterizes the quality of vision better than visual acuity.

The results of vision acuity and contrast sensitivity analysis showed that the degree of corneal irregular shape like keratoconus stage has stronger impact on visual acuity and contrast sensitivity, such as apex localization for irregular corneal shaped eyes. The impact of corneal surface apex on contrast sensitivity is not equal in all spatial frequencies – the impact of corneal surface apex increases when spatial frequency increases.

The higher order aberration analysis has determined that vertical coma and spherical aberration are the dominant aberrations for irregular corneal shaped eyes. The vertical aberration is the largest aberration while spherical aberration has the most important impact on the quality of vision.

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