EXTENDED SUMMARY OF DOCTORAL DISSERTATION

Computer image analysis algorithms in the analysis of corneal deformation

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1. Introduction

This summary of doctoral dissertation includes a series of 7 publications and is the culmination of the author's literature studies and research on the use of computer image analysis algorithms for the analysis of corneal deformation and the assessment of biomechanical parameters to support the process of ophthalmic diagnostics.

Currently, image analysis and processing is a dynamically developing interdisciplinary field. Owing to the quantitative assessment of processed images, it is possible to distinguish the characteristic properties and features of the objects contained in the images. This discipline is particularly important in medicine, where innovative devices used, among others, for eye examinations, enable the imaging of structures invisible to the naked eye, and thanks to dedicated software, which uses image analysis tools, medical information, understandable for doctors, is obtained. There are a number of tools that allow for the imaging of the organ of vision, such as the slit lamp, ultra-biomicroscopy (UBM), rotating Scheimpflug camera or optical coherence tomography (OCT). Currently, there are many algorithms dedicated for the analysis of the images of morphological structures of the eye. Among others, for OCT, successive layers of the fundus are determined and measured [8–10], the depth of the anterior chamber (ACD) and other parameters used in ophthalmic diagnostics are calculated [11–14]. However, due to the development of modern technologies in the field of imaging diagnostics of the organ of vision, there is a growing need for constant improvement of the existing methods and search for new solutions for the analysis of sight organ images.

Corvis ST non-contact tonometer meets the above need. Although the tonometer is a device whose main task is to measure intraocular pressure (IOP), in this case a much more extensive analysis is possible. The afore-mentioned device is equipped with an ultra-fast Scheimpflug camera, which records a sequence of images of corneal deformation (Figure 1) caused by an air puff.

The possibility of analysing corneal deformation images allows for the determination of parameters [15–17] previously unavailable to traditional devices in in vivo measurements, including those relating to the corneal biomechanics and other phenomena occurring during this process [18, 19]. It should be noted that as of the day of starting the doctorate, the Corvis ST tonometer was commonly used by ophthalmologists only for IOP measurements, whereas the parameters based on the analysis of corneal deformation, available in the commercial tonometer software, were used sporadically.

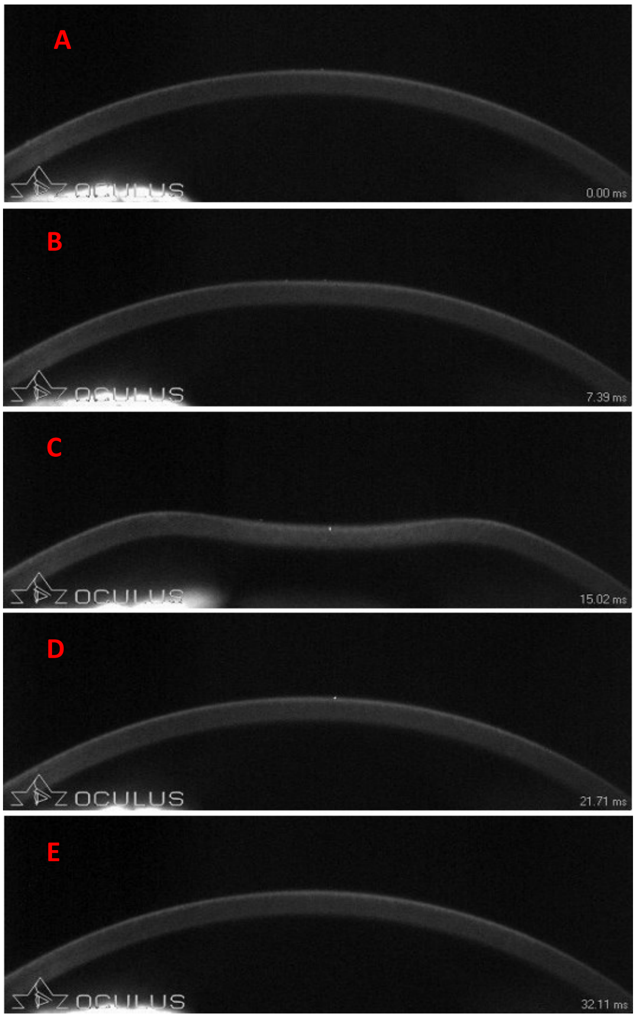

Figure 1 Images showing the complete process of corneal deformation: a) recording begins when the cornea is in its natural convex shape; b) the air puff flexes the cornea which reaches the point of first applanation; c) the cornea continues to deform until its greatest concavity; d) the air puff is turned off, and the cornea returns to its natural shape by passing through the second applanation phase; e) the measurement process ends when the cornea reaches its natural convex shape.

In recent years, papers have been published [20–22] describing the repeatability and the possibility of practical application of the above-mentioned parameters. It was confirmed that the analysis of dynamic deformation of diseased corneas, e.g. in patients with keratoconus, provides new, diagnostically important information. The keratoconus is related to, among others, a greater amplitude of corneal deformation (DA) compared to normal corneas. The information obtained from the analysis of the course of dynamic corneal deformation during the IOP examination also allows for a more complete assessment of the condition of the cornea in patients during their qualification for refractive surgery, which, on the other hand, helps to prevent possible complications such as corneal ectasia. It is also worth pointing out that the obtained information is also used when monitoring patients with keratoconus before and after the collagen cross-linking (CXL) procedure. Confirmation of the usefulness of the parameters available in the first version of the Corvis ST tonometer software contributed to their popularization in the practice of ophthalmologists, where they are increasingly used in the diagnosis of eye diseases and in the correction of intraocular pressure values, although not all relationships between them are known. The above became an impulse to search for new parameters, because on the basis of images of dynamic corneal deformation under the influence of an air puff, it is possible to obtain much more information. In recent years, scientists have proposed a number of new parameters. Examples include: topographic map of the dynamic corneal curvature, or parameters directly related to corneal vibrations, allowing for the classification of diseased corneas [17, 23, 24]. Despite the above examples, using advanced methods of image analysis and processing, it is possible to obtain other, new parameters describing the cornea.

A review of the literature on the analysis and processing of images from the Corvis ST tonometer revealed shortcomings in solving one of the basic problems, namely the detection of the full outer corneal contour, the determination of which is a step necessary to obtain the characteristic parameters of corneal deformation. A detailed reference to this problem and the possibilities of solving it are presented in publication [3], which is part of the doctoral dissertation. The conducted analysis of the state of knowledge also indicated that both in the Corvis ST tonometer software and in independent publications there are no parameters obtained on the basis of corneal structure analysis. Local changes in brightness in the area of the cornea and visible shifts in its structure visible in the corneal deformation images have not been analysed in the literature so far, as well as there are no tools to conduct such an analysis. In addition, a significant problem related to the difficulties in the interpretation and analysis of the obtained parameters was also noticed. The lack of standardized values of the available parameters is a fundamental limitation for ophthalmologists when it comes to their practical application. A detailed reference to the state of knowledge and deficiencies in the analysis of dynamic corneal deformation is presented in publications [1, 2, 4] which are part of the doctoral dissertation.

The above observations inspired the author to undertake detailed research in the field of dynamic analysis of the corneal deformation caused by an air puff. The use of advanced methods of image analysis and processing for this purpose creates opportunities for both the assessment of already known parameters and, even more importantly, the acquisition of new ones.

2. Research aims and theses

The main research aims included:

- development of an algorithm that uses advanced image processing methods to automatically determine the corneal edge,
- analysis of the diagnostic usefulness of parameters obtained from dynamic corneal deformation,
- analysis of changes in the corneal structure for the sequence of dynamic corneal deformation images,
- development of a method to verify the correctness of the patient's positioning during tonometry tests.

The following theses were put forward in the dissertation:

The use of image analysis and processing methods allows for the analysis of dynamic corneal deformation.

It is possible to learn how the parameters of the cornea determined during its dynamic deformation are related to corneal lesions.

The analysis of dynamic corneal deformation enables to relate it to corneal lesions.

3. Discussion of the series of scientific publications included in the doctoral dissertation

The research and literature studies carried out by the author make up a thematically coherent whole dealing with the issues of image analysis, including corneal images, aimed at improving the process of ophthalmic diagnostics as well as better understanding the processes taking place during dynamic corneal deformation during intraocular pressure measurements with a non-contact tonometer. The presented series of papers consists of three original papers, describing the research carried out by the author, and four review articles.

A schematic diagram showing the methodology of the conducted research is shown in Figure 2.

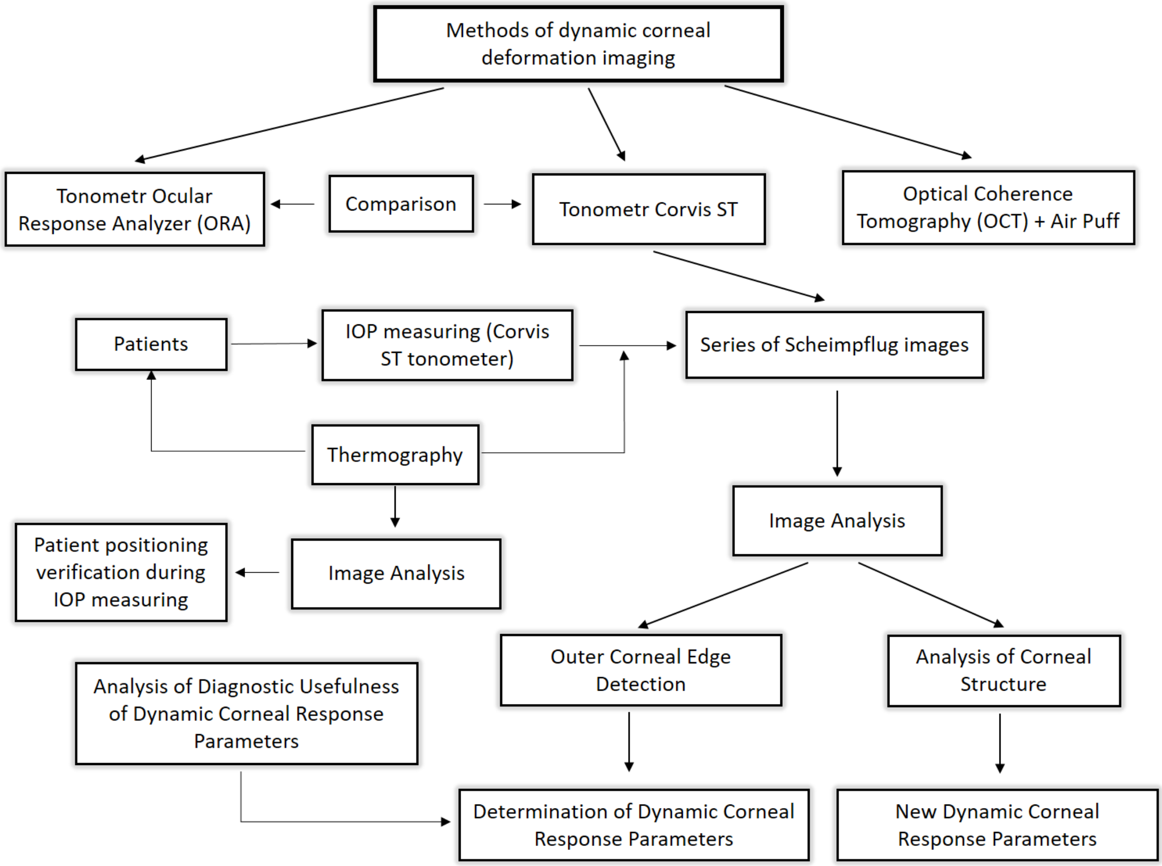

Figure 2 Diagram showing the methodology of the research carried out as part of the doctoral dissertation.

[1] Jędzierowska M., Koprowski R., Wróbel Z.: Imaging of the anterior eye segment in the evaluation of corneal dynamics. Information Technologies in Medicine 2016; 1: 63–73. (review article)

Aim: A review of the methods for imaging the anterior segment of the eye allowing for the assessment of corneal deformation caused by an air puff.

Original analysis of the presented issue: Despite the variety of existing methods and devices allowing for imaging of the anterior segment of the eye, such as a slit lamp, optical slit scanning topography (e.g. the Orbscan II device), or devices using the Scheimpflug imaging principle, e.g. Pentacam, only a few are able to assess corneal dynamics. These include non-contact tonometers: Corvis ST and Ocular Response Analyzer (ORA), and the technology combining optical coherence tomography (OCT) with the intraocular pressure measurement system using the air puff method.

The literature review shows that there is no gold standard in the analysis of corneal deformation dynamics during intraocular pressure measurements. The above-mentioned devices attempt this analysis, but they do not present the full picture of this complicated process. The presented analysis of the state of knowledge enables to specify the limitations of the devices in question, both in terms of imaging the anterior segment of the eye and the analysis of changes occurring in the anterior segment of the eye during the intraocular pressure test using the air puff method.

The Ocular Response Analyzer (ORA) analyses only the applanation signal of the corneal apex, thus the parameters available in this device refer to the point values. Therefore, it is impossible to assess the spatial differences in the properties of the cornea, both along its entire width and depth.

Extended analysis of corneal deformation is possible with the use of the Corvis ST tonometer, which, thanks to the Scheimpflug camera, allows for the registration of corneal images (cross-sections) during the examination. This solution makes it possible to use image analysis and processing methods to analyse the behaviour of the cornea and the entire eyeball during non-contact tonometer testing. One of the main problems in analysing these types of images are edge detection errors. Previous methods using, among others, polynomial approximations do not allow for full detection of corneal contours, because in order to avoid the characteristic inflection resulting from the applied method of curve approximation, the data on both sides of the corneal profile are cut off (10% cut-off). The above indicates the lack of a fully effective method for detecting the corneal edge in its full range, which would be also resistant to characteristic interferences appearing during the test with a tonometer equipped with a Scheimpflug camera.

The combination of optical coherence tomography (OCT) with an air jet stimulus provides new possibilities for imaging corneal deformation. Systems in this form are innovative solutions that provide more possibilities for imaging the cornea than the ultra-fast Scheimpflug camera, namely the possibility of registering the corneal image during its deformation in various planes as well as the imaging of the corneal vertex as a function of time, the so-called A-scan. Currently, however, such apparatuses are not available commercially, which does not allow for the use of the above advantages in the practice of ophthalmologists. The possibility of precise imaging of the cornea during its deformation during intraocular pressure measurement would be an important step towards the analysis of the dynamics of this process.

The literature review also emphasized the lack of devices that would allow for a complete analysis of the corneal deformation in relation to all corneal cross-sections, not only to the cross-section in the middle of the cornea, as in the case of a tonometer with a Scheimpflug camera. The significance of such an analysis is confirmed by, among others, currently conducted research [25] aimed at developing a device imaging dynamic corneal deformation in a three-dimensional way.

The described study shows that, regardless of the device used for the analysis of corneal deformation, there are still no methods standardizing the factors influencing its course. The indicated factors are, among others, biomechanical parameters that determine the behaviour of the cornea during non-contact tonometer testing. The theses presented in this review article, indicating the need to develop new parameters characterizing corneal biomechanics, the values of which may indicate specific disease entities or describe with high probability the possibility of their occurrence, are confirmed in more recent publications. We can mention here the studies related to the development of parameters allowing for the diagnosis and further classification of keratoconus, a disease as a result of which the corneal curvature takes a conical shape deviating from the normal one. One of such parameters is the CBI (Corvis Biomechanical Index), developed on the basis of various biomechanical parameters available in the Corvis ST tonometer. The study by Vinciguerra et al. [26] confirmed 98.4% specificity and 100% sensitivity of this parameter for the validation group. Next [27], the TBI (Tomographic Biomechanical Index) was developed, which combines the CBI index with the CT data, which provided better results in detecting the early stage of keratoconus. The latest studies [28] describe another parameter, namely CBiF (Corvis Biomechanical Factor), which is a modification of the CBI, allowing to establish a new scale characterizing the advancement level of keratoconus.

Another paper in the presented series is also a review article, which focused on the comparison of two of the above-mentioned devices: the Corvis ST tonometer and the Ocular Response Analyzer (ORA) tonometer, which, as indicated in publication [1], are the only commercially available devices allowing for the analysis of dynamic corneal deformation.

[2] Jędzierowska M., Koprowski R., Wróbel Z.: Overview of the Ocular Biomechanical Properties Measured by the Ocular Response Analyzer and the Corvis ST. Information Technologies in Biomedicine 2014; 4: 377–386. (review article)

Aim: comparison of two tonometers allowing for the measurement of biomechanical parameters of the cornea: the Corvis ST tonometer and the Ocular Response Analyzer (ORA).

Original analysis of the presented issue: As indicated in publication [1], the possibility of imaging dynamic corneal deformation caused by an air puff allows for a detailed analysis of this process. However, the very process of analysing the corneal deformation is directly related to the principle of operation of a given device, which for the tonometers described in the discussed paper is quite different.

The Ocular Response Analyzer (ORA) uses infrared light to illuminate the central part of the cornea while measuring intraocular pressure, and the detector records the intensity of the light reflected from it. The signal recorded in this way is the basis for determining specific parameters available in the ORA software. The most common parameters of this device are: corneal hysteresis (CH) and cornea resistance factor (CRF). According to the analysed literature, the hysteresis parameter is to reflect the viscoelastic properties of the cornea, and CH changes are indicated as a predictor in the assessment of, among others, glaucoma progression. The CRF parameter is to describe the "resistance" of the cornea during the deformation process, which also relates it directly to the material properties of the cornea and the CCT parameter (central corneal thickness). The values of the above parameters for healthy subjects and patients suffering from diseases such as keratoconus and glaucoma have been the subject of many studies, including those cited in the described publication. It is interesting to note that the ORA is the only device that provides a number of parameters developed on the basis of the vibration analysis of the recorded signal. Unfortunately, these parameters have not been widely used in practice so far, although the latest studies [29, 30] using artificial intelligence methods try to apply their potential in practice. It should be noted, however, that due to the fact that in the ORA we only examine the signal from the central part of the cornea, this device provides point parameters, which was also noted in [1]. This introduces quite a simplification, especially when we refer to the parameters that are to represent the material properties of the cornea, and for the calculation of which the anisotropy of the corneal material and its variable behaviour at different points of its cross-section are not taken into account. The above is the basic limitation of this device, which, as shown by the latest studies, is increasingly giving way to the Corvis ST tonometer in the analysis of biomechanical parameters of the cornea.

The principle of operation of the Corvis ST tonometer is based on the use of an ultra-fast Scheimpflug camera, which acquires a series of images showing the complete deformation of the cornea, and it is on their basis that the basic parameters are determined, i.e. the value of intraocular pressure (IOP) or the central corneal thickness (CCT), as well as those described as corneal biomechanical parameters. This review article presents individual parameters available in this device and discusses one of the first studies related to the influence of parameters obtained with the Corvis ST tonometer on IOP values. The collected research shows that the analysis of biomechanical parameters opens a new way in research on the analysis of factors influencing the behaviour of the cornea under its load conditions (an air puff stimulation).

The publications [1] and [2] are closely related to each other and on their basis it can be concluded that the biomechanical parameters of the cornea have a significant impact not only on the measurement of intraocular pressure itself, influencing its changes, but also on the results of surgical treatment, among others, on the effects of refractive operations on the cornea and the development of corneal diseases such as keratoconus. A review of the existing problems and limitations in the analysis of dynamic corneal deformation, which were summarized in the discussed papers, enabled to conclude that there is still untapped research potential to analyse this process. The greatest possibilities in this respect are offered by the Corvis ST device, as it enables the use of advanced methods of image analysis and processing to acquire new parameters.

The above papers resulted in another publication [3], which presents the basic problem related to the determination of biomechanical parameters of the cornea on the basis of images from the Corvis ST tonometer. Namely, one of the key elements in the analysis of specific features of the cornea is the correct detection of its contours, which form the basis for further calculations. Unfortunately, as described, inter alia, in [1], the image processing algorithms often used for this purpose turn out to be insufficient when confronted with real medical images. The main problem is the incorrectly detected outer corneal edge, since the detection method affects the results of the obtained parameters, which are used by ophthalmologists in the diagnosis of diseases (in particular, early detection of keratoconus [26]) and the evaluation of the cornea in candidates for refractive surgery [4]. Bearing in mind the above, in the next paper, the author dealt with the problem of outer corneal edge detection from a series of images from the Corvis ST tonometer.

[3] Jędzierowska M., Koprowski R., Wilczyński S., Krysik K.: A new method for detecting the outer corneal contour in images from an ultra-fast Scheimpflug camera. BioMedical Engineering Online 2019; 18(1): 115. (original paper)

Aim: Development of an automatic method for detecting the outer corneal edge from a series of images obtained from the Corvis ST tonometer and comparison of the new method with the known and commonly used edge detectors: Sobel, Roberts and Canny operators and others known from the literature.

Proposed solution: In order to develop a new method for detecting the outer corneal edge in the images from the Corvis ST non-contact tonometer, 15,400 2D images were analysed, constituting 110 sequences of 140 images showing the cross-section of the cornea during its deformation during intraocular pressure measurement. The developed methodology for detecting the outer edge consists of the following steps:

– image pre-processing - images were subjected to median filtering with a 7×7 pixel mask followed by normalization,
– binarization using the Sauvol and Pietkainen method - a local threshold was used selected on the basis of the mean brightness values and the standard deviation of the brightness value for a given window. To optimize the computation time of the mean brightness values and standard deviations in a given window, integral images were used,
– morphological opening - a disk-shaped structural element with a radius of 3 pixels was used,
– detection of the corneal image in a binary image - two methods were proposed: the first one based on the labelling of binary areas and selecting the object with the longest diagonal, and the method using the convolutional neural network (CNN), consisting of 15 layers, including 3 convolutional layers, which allowed for both detection and classification (recognition of the corneal image),
– marking the outer corneal edge.

The obtained values of the position of the outer corneal edge were compared with the position of the outer edge marked by an expert, determining the measurement error (δ_k). The error value for the author's method was compared with the measurement error values calculated for the known edge detection methods: the Sobel, Roberts and Canny operators.

The individual stages of data processing for the known and for the newly proposed method are presented in the block diagram (Figure 3).

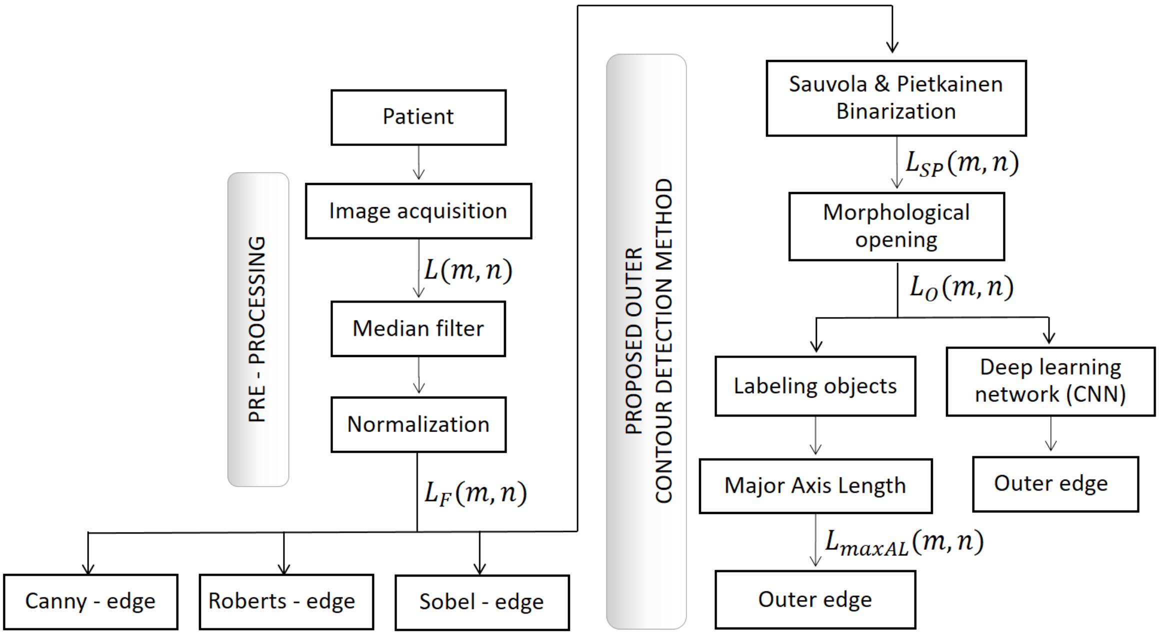

Figure 3 Block diagram showing the various stages of analysis. During image pre-processing, the data were prepared to allow for outer corneal edge detection. In the next stages of data processing, the known methods of edge detection were used and a new method for outer corneal contour detection in images from the Corvis ST tonometer was presented [3].

Original elements of the presented method:

- development of the concept of a new method for detecting the outer corneal edge, selection and optimization of the parameters of each stage of analysis;
- development of a method for quantifying the accuracy of outer corneal edge detection using the outer corneal contour determined by an expert;
- implementation of the proposed methods of cornea detection and assessment of its accuracy against an Expert in Matlab;
- verification of the practical usefulness of the obtained results.

Results achieved: Correctness of the algorithms for detecting the outer corneal edge was determined on the basis of the measurement error δ_k, designed on the basis of the difference between the position of the corneal edge obtained by a given method and the position of the outer corneal contour determined by an expert. The measurement error was calculated for each of the four methods analysed separately for all 15,400 images. The mean values of the obtained errors along with their minimum and maximum values and the standard deviation for each method are presented in Table 1.

Table 1 Summary of the mean values of δ_k as well as the minimum, maximum and standard deviation of δ_k obtained for all the compared methods: Sobel, Roberts, Canny and the author's method of outer corneal edge detection in the images from the Corvis tonometer [3].

Method	$\boldsymbol{\delta_k}$	$\boldsymbol{\delta_{k(min)}}$	$\boldsymbol{\delta_{k(max)}}$	***std***
Proposed	**0,16%**	**0,09%**	**3,62%**	**0,19%**
Sobel	3,43%	0,25%	42,12%	6,21%
Roberts	5,78%	0,17%	61,67%	9,19%
Canny	1,26%	0,53%	50,70%	3,11%

The author's method showed the lowest mean error value (0.16%), stability (standard deviation 0.19%) and resistance to disturbances characteristic of the Corvis ST tonometry test compared to the methods known from the literature. For the other methods, the error was: $5.78 \pm 9.19\%$ for the Roberts method, $3.43 \pm 6.21\%$ for the Sobel method, and $1.26 \pm 3.11\%$ for the Canny method.

The proposed method of edge detection is also more resistant to disturbances characteristic of images obtained from the Corvis ST tonometer than the built-in method (available in the tonometer software), which enables to increase the accuracy of intraocular pressure measurements. What is more, it works better than the known edge detectors commonly used in the analysis of medical images, namely Sobel, Roberts and Canny, and thus can be another precise diagnostic tool for patients with eye surface disorders. The proposed method can be used to obtain corneal parameters. Due to the above, in order to search for new diagnostic parameters, the author, in the next paper [4], reviewed the latest parameters determined on the basis of the analysis of dynamic corneal deformation images, focusing on the analysis of their usefulness in clinical practice.

[4] Jędzierowska M., Koprowski R.: Novel dynamic corneal response parameters in a practice use: a critical review. BioMedical Engineering Online 2019; 18(1): 17. (review article)

Aim: Presentation of the practical application and the diagnostic reliability of the parameters of the dynamic corneal response indicated in the literature

Original analysis of the presented issue: Analysis of the literature cited in the discussed paper allowed to draw the following conclusions:

- in clinical practice, the parameters related to the deformation amplitude ratio as well as the stiffness parameters (SP-A1 and SP-HC) are of the greatest importance. The aforementioned parameters may constitute early indicators of the assessment of the effects of corneal refractive procedures. Table 2 presents a summary of changes in the above parameters depending on the procedure performed,
- the parameter of biomechanically corrected intraocular pressure (bIOP) is a parameter independent of the corneal biomechanics. This is confirmed by studies conducted both in subjects with a healthy cornea and patients after various refractive procedures. bIOP can also be classified as a parameter independent of the central corneal thickness and age. On the basis of the analysis of the cited literature, it was also noticed that the measurements of this parameter (bIOP) should be as precise as possible, because the change in the pressure value is also influenced by factors, which were not included in the correction algorithm, such as, inter alia, pressure fluctuations depending on the time of day, its dependence on blood pressure, as well as the number of repetitions and the time interval between subsequent tests.
- on the basis of the reviewed literature, the Corvis Biomechanical Index (CBI) parameter was found to be an effective indicator in detecting patients with keratoconus, but its effectiveness in detecting other corneal pathologies was not confirmed. It was also noticed that CBI is more sensitive than the Tomography and Biomechanical Index (TBI) parameter available in the integrated system of the Scheimpflug camera and Pentacam tomograph. Thanks to the literature studies, it was observed that the most effective classification in terms of the early detection of keratoconus in patients can be obtained by combining the data obtained from the CBI and TBI parameters.

The above conclusions are confirmed by the most recent studies [28, 36] (already cited above in this summary), where a new scale was used to obtain the best results for the classification of keratoconus severity, based on the combination of the CBI parameter and tomographic data. The parameters of dynamic corneal response can therefore be used to support ophthalmic diagnostics and to evaluate the parameters of the cornea, not only to correct intraocular pressure measurements.

Table 2 Summary of the changes in DCR (dynamic corneal response) after corneal surgery [4]

Parameter	**Lee et al.** [31]		**Lee et al.** [32]		**Fernandez et al.** [33]	**Hirasawa et al.** [34]	**Vinciguerra et al.** [35]
	PKR (n = 35)	**PRK+LASIK (n = 34)**	**LASIK (n = 64)**	**PRK (n =65)**	**SMILE (n = 43)**	**CATARACT (n = 39)**	**CLX (n = 34)**
DA Ratio (1 mm)	↑	↑	–	–	↑	↑	↓
DA Ratio (2 mm)	↑	↑	↑	↑	↑	–	–
SP-A1	↓	↓	↓	↓	↓	↓	↑
SP-HC	↓	↓	–	–	–	–	↑
IntInvRad	↑	↑	↑	↑	↑	↑	↓
bIOP	No significant difference	No significant difference	No significant difference	No significant difference	↓	↓	↑
ARTh	–	–	↓	↓	–	↓	–

PRK *= photorefractive keratectomy;* ***LASIK*** *= laser-assisted laser in situ keratomileusis;* ***SMILE*** *= small-incision lenticule extraction;* ***CATARACT*** *= cataract surgery;* ***CLX*** *= corneal cross-linking;* ***DA Ratio (1 mm)*** *= Deformation Amplitude Ratio at 1 mm;* ***DA Ratio (2 mm)*** *= Deformation Amplitude Ratio at 2 mm;* ***SP-A1*** *= Stiffness Parameter A1;* ***SP-HC*** *= Stiffness Parameter HC;* ***IntInvRad*** *= Integrated Inverse Radius;* ***bIOP*** *= biomechanically corrected IOP;* ***ARTh*** *= Ambrosio Relational Thickness to the horizontal profile.*
The up arrow (↑) indicates a significant increase in the given parameter; down arrow (↓) indicates a significant decrease in a given parameter; horizontal lines (-) indicate the lack of analysis of a given parameter.

In the next paper, the author dealt with the problem of analysing the corneal structure during a tonometry examination. As confirmed by the author's previous studies [1, 2, 4], none of the available parameters based on the analysis of dynamic corneal deformation provided information about changes in the structure of the observed cross-sections. Which is why, in the next study [5], the author focused on the analysis of images from the Corvis ST tonometer in terms of looking for a relationship in the observed changes in the corneal structure.

[5] Jędzierowska M., Koprowski R., Wilczyński S.: Analysis of changes in corneal structure during intraocular pressure measurement by air-puff method. Information Technology in Biomedicine 2022; 155-167. (original paper)

***Aim**:* Development of a methodology enabling the analysis of the corneal structure during intraocular pressure measurements using the non-contact method.

Proposed solution: For the analysis of the corneal structure, the authors proposed a method of analysing images from a tonometer equipped with a Scheimpflug camera in terms of looking for a relationship in the observed changes in the corneal structure. An algorithm was developed to enable fully automatic tracking of changes visible in the images of corneal cross-sections obtained during intraocular pressure measurements. The method was divided into two main stages:

1. Separation of corneal cross-sections from an image sequence - at this stage, the method of detecting the outer corneal edge described in [3] was used.
2. Analysis of changes in the corneal structure in successive images in a sequence (over time).

The key step was to track specific areas of the cornea in its 140 successive images. Tracking was based on finding the areas with the highest correlation to the originally selected fragment.

An illustrative block diagram showing the subsequent stages of the analysis is shown in Figure 4.

Original elements of the presented method:

- development of the subsequent steps of the method for analysing the sequence of corneal images, including the selection of the main criterion (correlation) allowing for the identification of the searched fragments in subsequent images in a sequence,
- development of a method of quantitative analysis of tracked displacements - proposing two parameters determined on the basis of the obtained displacement values;
- implementation of the proposed methods of image analysis in Matlab;
- analysis of the obtained results.

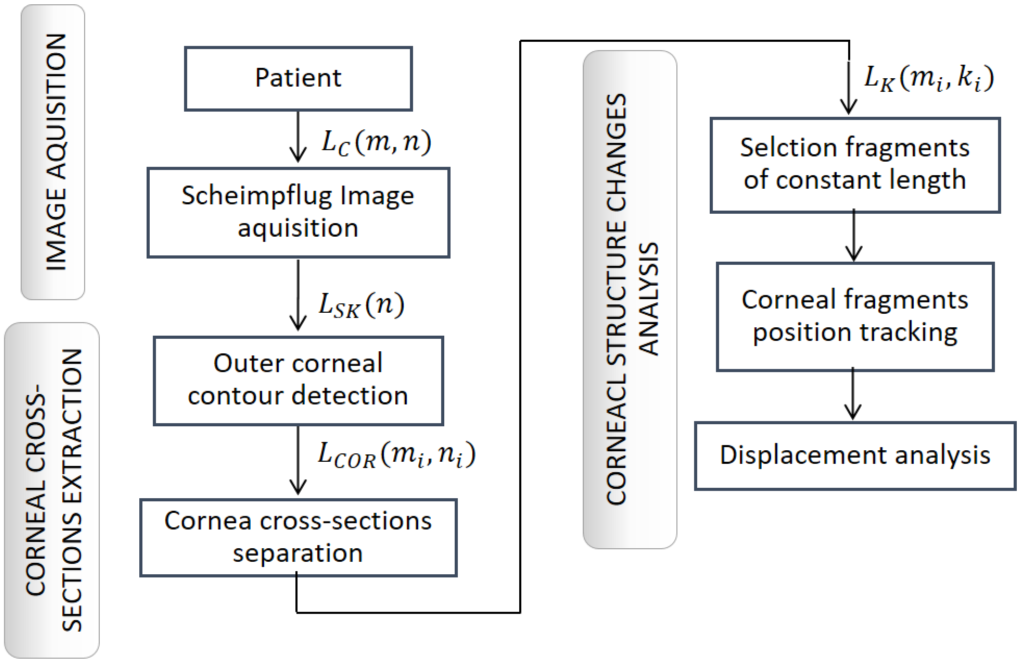

Figure 4 Block diagram showing the individual stages of corneal structure analysis. The diagram was divided into three stages: 1- image acquisition, 2 - separation of corneal cross-sections, where the determination of the outer corneal edge using the authors' method described in [3] is most essential, and stage 3 - analysis of corneal structure changes in subsequent images in a sequence [5].

Results achieved: The obtained results allowed for fully automatic time tracking of specific areas of the cornea, the displacements of which, according to preliminary studies, are characterized by asymmetry. The two parameters, proposed in the study, for the assessment of changes in the corneal structure over time, i.e. the absolute displacement of the studied area ($|\Delta n|$) and the value of its maximum deviation (d) allow for the quantitative assessment of the analysed changes. For all subjects (group of 20 healthy subjects), the parameter d indicated an increase in the value of the maximum deviation of the monitored areas in the central part of the cornea and was characterized by lower values of the standard deviation than the parameter $|\Delta n|$. The obtained results of the preliminary studies of the analysis of corneal structure changes described in the paper allow us to conclude that the parameter d seems to be the most appropriate parameter for the assessment of this problem, which also indicates its potential use in the assessment of the parameters of corneal biomechanics. It is worth emphasizing that none of the available parameters based on the analysis of the dynamic corneal deformation process analysed changes in the structure of the observed cross-sections.

Although the changes in the structure presented in this paper can be analysed using image processing methods, these methods we are not able to explain their origin and connect them with possible changes in the corneal material during its deformation. Therefore, although the subject of the author's research is not directly related to the corneal biomechanics, important in the context of the significance of the theses presented in this doctoral dissertation summary, there is another paper [6], in which the author analysed the practical limitations and problems related to modelling the biomechanical properties of the eyeball during intraocular pressure measurements.

[6] Jędzierowska M., Koprowski R., Wróbel Z.: Limitations of Corneal Deformation Modelling During IOP Measurement : a Review. Information Technologies in Biomedicine 2019; 469–480. (review article)

Aim: Analysis of problems and limitations related to the modelling of the human eyeball during intraocular pressure measurement.

Original analysis of the presented issue: Basically, the greatest controversy and problems related to the modelling of the human eyeball arise in the context of analysing the behaviour of this complex structure in response to an external stimulus, such as an air puff. A biomechanical eyeball model, which would be applicable to simulating the behaviour of the eye during the intraocular pressure measurement should primarily include the geometry, materials of individual tissues and the optics of the model. The analysis of literature allowed to identify the main problems in the description of such a model, namely:

– determination of the type of corneal material. On the one hand, the literature presents the cornea as a linear viscoelastic material, on the other hand, some authors [37–39] support the hypothesis that during tonometry tests it is not possible to activate the viscous properties of the cornea, which is related to the fact that the time when the force causing the observed deformations is applied is too short [38]. However, in the light of the latest publications, it is indicated that they can be assessed on the basis of data from the Corvis ST non-contact tonometer [40, 41],
– model geometry determination - simulations were carried out both on two-dimensional axial-symmetrical models as well as on 3D models,
– taking into account or ignoring the presence of fluids inside the eyeball

- simulations of corneal vibrations - although it is known that they are present during corneal deformation forced by air, their modelling still presents many difficulties. The conducted analysis of the literature showed that that there are no models to separate the vibrations of the entire eyeball from the vibrations of the cornea itself (high-frequency vibrations, above 100Hz),
- describing the boundary conditions of the model, which essentially affect the operation of the model tested under dynamic conditions. The literature review showed that so far there are no mechanical parameters describing the action of the muscles surrounding the eyeball.

To sum up, it should be noted that the possibility of analysing corneal deformation images from the tonometer equipped with the Scheimpflug camera is an additional tool that allows for the verification and comparison of the values obtained for the tested models in numerical experiments with those obtained through image analysis. Development of a coherent model, which would provide the possibility of a realistic simulation of the eyeball response to an impulse in the form of an air puff, as well as allow for the correction of its geometry, would lead to the creation of a valuable tool for ophthalmologists.

The aspect of repeatability of measurements is often neglected in the literature on the measurement of biomechanical parameters of the cornea. The measurement methods used and the parameters obtained described in the above publications [1, 2, 4] as well as those proposed in the paper [5] should be independent of the operator, individual variability of patients, and above all, reproducible for the same patient. The author discussed these aspects in another publication [7] which does not deal directly with the analysis of corneal parameters, but focuses on the problem of assessing the correctness of the intraocular pressure measurement process itself.

[7] Jędzierowska M., Koprowski R., Wilczyński S., Tarnawska D.: The use of infrared thermal imaging in tonometry with a Scheimpflug camera. J. Therm. Biol 2021; 96:102823 (original paper)

Aim: Development of a method for assessing the correctness of measuring intraocular pressure depending on the position of the patient's head during non-contact tonometer testing with the use of a thermal imaging camera.

Proposed solution: Thermographic measurements of the patients' faces were performed before and after the intraocular pressure test using the non-contact method. Then, in order to obtain information on temperature changes in the places where the patient's face meets the tonometer frame (forehead and chin), an original, semi-automatic method of analysing the acquired images was developed. The presented method consists of the following stages: 1) automatic image stabilization before and after the IOP examination, 2) selection of regions of interest (places where the patient's face meets the tonometer supports), 3) determination of the mean temperature and analysis of its changes before and after the tonometer test for selected areas. Figure 5 shows a block diagram presenting the various stages of the analysis of thermal images.

Original elements of the developed method:

- development of the concept of the measuring station and the method of using thermal imaging to assess the position of the patient's head in the tonometer supports,
- development of a method for automatic correction of image position (image stabilization in terms of vertical and horizontal displacements and angular stabilization of images),
- implementation of the proposed image analysis method in Matlab;
- analysis of the obtained results.

Results achieved: The proposed semi-automatic method of thermal image analysis allows for:

- obtaining the mean temperature values for the same areas in a semi-automatic way for thermal images of the face before and after the tonometry test,
- automatic correction of the position of thermal images with regard to shifts in the horizontal and vertical planes as well as rotation correction.

The tests performed in a group of 10 patients provided a qualitative assessment of temperature changes in the places of contact of the patient's face with the tonometer before and after the intraocular pressure measurement. The obtained results indicate a decrease in temperature in selected areas for thermal images after a tonometry test. Based on the obtained values of the mean temperature difference for all measurements in both regions of interest, as well as the theory of heat exchange between the surface of the facial skin and the surface of the touched object with a lower temperature, a reference value of $-0{,}2\ °C$ was established (i.e. a threshold value of mean temperature difference (Δt) in selected areas of thermal images). Due to the above, the change threshold allowing to determine whether the patient correctly placed the head in the tonometer supports is a temperature change of at least −0,2 °C. In addition, it is noteworthy that the temperature changes in the thermal images before and after the test can be related to the force with which the patient rested their head on the tonometer supports, e.g. a greater temperature change may indicate incorrect patient positioning in the tonometer supports.

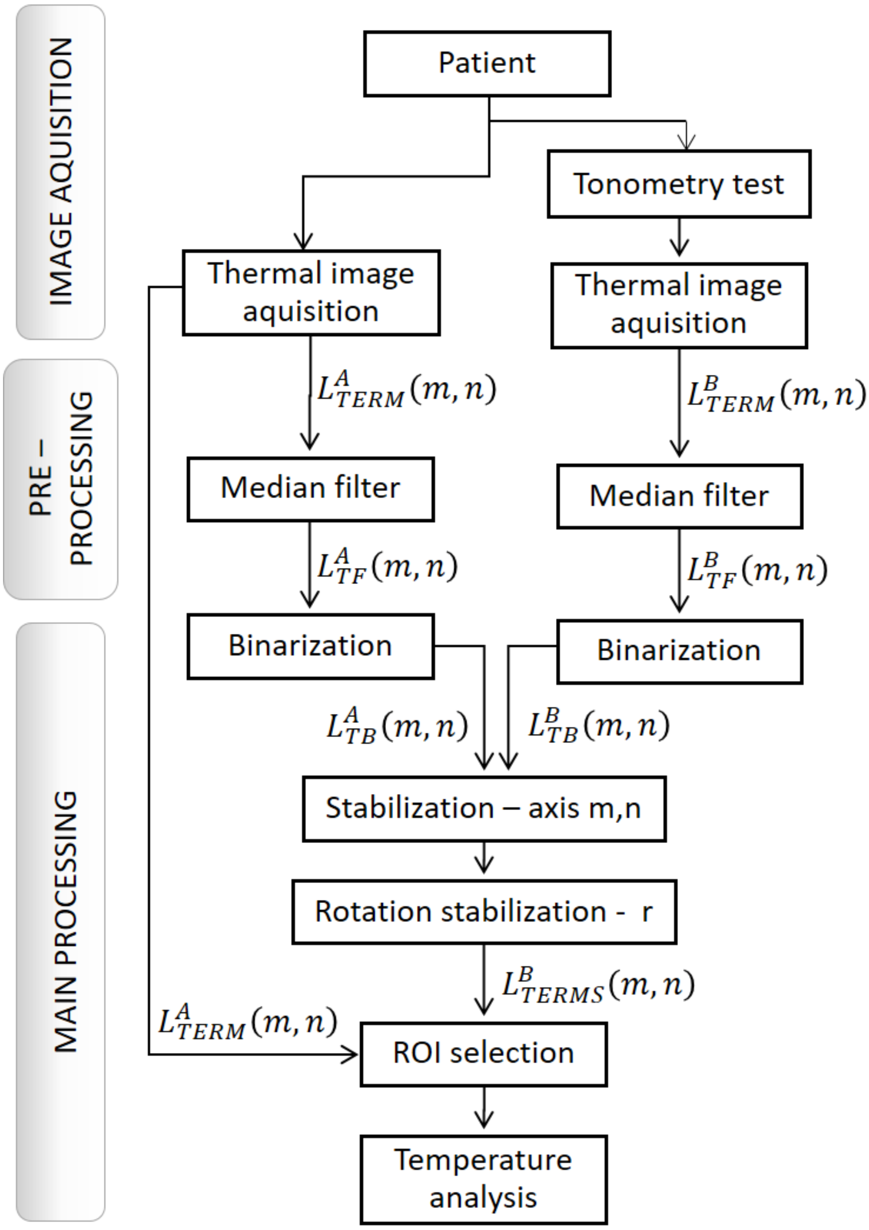

Figure 5 Block diagram showing the various stages of the analysis of the obtained thermal images. The diagram has been divided into three steps: image acquisition, image pre-processing, and main image processing [7].

The proposed method of analysing changes in the temperature of the patient's face, both before and after the test with a non-contact tonometer, is a tool that helps ophthalmologists in assessing the correctness of the intraocular pressure measurement process, because, as shown in the literature, the positioning of the face in the tonometer supports may have an influence on the intraocular pressure value, e.g. excessive bending or unnatural position of the neck cause an increase in intraocular pressure. The obtained knowledge can also be used in the standardization of the measurement procedure with a non-contact tonometer, by improving the repeatability of the measurements taken (control of the correct and repeatable positioning of the patient's head in the device supports). The proposed method thus contributes to the optimization and development of intraocular pressure measurement procedures.

4. Summary and conclusions

The doctoral dissertation summary discusses a series of seven single-topic scientific articles, which include the author's own research in the field of biomedical engineering related to the analysis of dynamic corneal deformation resulting from an air puff.

The research presented in this paper made it possible to achieve the objectives of the study proposed at the beginning, which are considered to be the author's contribution to the field of biomedical engineering:

- A method of automatic determination of the outer corneal edge has been developed, allowing for the detection of its full contour, resistant to the disturbances characteristic for the method of acquiring dynamic corneal deformation images. The proposed method is the most effective (ensuring the most accurate detection of the outer corneal edge) of all the tested algorithms;
- A detailed analysis of the diagnostic usefulness of the available parameters of dynamic corneal deformation has been performed, presenting the relationships between the characteristic parameters and corneal lesions. The parameters influencing the change in the value of the intraocular pressure have been listed;
- A method for analysing the corneal structure has been developed, allowing to track characteristic changes in its structure. Two new parameters of dynamic corneal deformation related to changes in its structure during intraocular pressure tests using the non-contact method have been developed;
- A non-invasive method of verifying the correctness of the patient's positioning during tonometry examinations using thermal imaging has been developed.

Based on the above, it should be stated that the conducted research confirms the correctness of the theses formulated at the beginning of the study according to which the use of image analysis and processing methods allows for the analysis of dynamic corneal deformation. It is also possible to learn how the corneal parameters determined during its dynamic deformation are related to the corneal pathological changes, and the analysis of dynamic corneal deformation allows for its comparison with corneal lesions.

The image processing methods presented in the articles have been verified based on real images obtained from the Corvis ST tonometer. The images were obtained in cooperation with the Ophthalmology Department of the Regional Railway Hospital in Katowice and a specialist from OCULUS. The innovation of the proposed methods of analysis and processing of images from the Corvis ST tonometer is based on an innovative approach to the presented problems of detecting the outer corneal edge based on the analysis of the structure of an image sequence showing the corneal deformation and the use of thermal image analysis of patients' faces to improve the quality of tonometry examinations, which has not been carried out so far. The proposed solutions can be used in:

- analysis of the course and diagnosis of eye diseases (changes in the corneal dynamics are associated with lesions),
- three-dimensional presentation of corneal deformation,
- improvement in the quality of intraocular pressure measurements with the Corvis ST tonometer,
- correction of the intraocular pressure value (by linking biomechanical parameters with IOP),
- classification of patients with corneal diseases based on the newly proposed corneal structure parameters.

The author’s research described in this summary expands the range of available methods of computer image analysis. Moreover, it allows for the measurement of new parameters of the cornea. It also broadens the knowledge about the use of corneal biomechanical parameters in intraocular pressure correction, evaluation and prediction of the results of eye surgery, in particular in patients with keratoconus, and refractive surgery.

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