Ultrasonic *in-vivo* measurement of ocular surface expansion

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***Abstract*—Our aim was to ascertain whether the ultrasonic measurement of longitudinal corneal apex displacements carried out in a proper headrest is a credible method of ocular pulse detection. To distinguish between longitudinal movements of the eye globe treated as a rigid body and ocular surface expansion caused by the variations of the eye-globe volume, two ultrasound distance sensors were applied to noninvasively measure displacements of cornea and sclera. The same sensors were used to examine the influence of the anterio-posterior movements of a fixed head on the registration of corneal apex pulsation. In both experiments ECG signals were synchronically recorded. Time, spectral and coherence analysis obtained for four healthy subjects showed that the ocular surface expansion due to pulsatile ocular blood flow is the main component of longitudinal corneal displacement. Ocular surface pulsation is always affected by the head movement. However, there exist some unique properties of signals, which help to distinguish between head and eye movements. A rigid headrest and a bite bar are required to stabilize the head during ocular pulse measurement. Ultrasonic technique enables noninvasive and accurate in-vivo measurement of corneal pulsation which could be of interest for indirectly estimating intraocular pressure propagation and pulsatile ocular blood flow component.**

***Index Terms*—ocular pulse, head-eye movement, ECG, spectral analysis**

INTRODUCTION

QUASI-periodic displacements normal to the corneal surface are the effect of pulsatile ocular blood flow (POBF) and intraocular pressure (IOP) variation [1]-[3]. This phenomenon, also known as the ocular pulse (OP) depends on variations in IOP, ocular hemodynamic status and biomechanical properties of the cornea. Measurement of ocular pulse amplitude was used to diagnose carotid occlusion [3]-[5] and visual field defects [6]. Examination of the ocular pulse spectral content found to be a potential diagnostic tool in glaucoma [7].

Spectral and coherence analysis of synchronically registered longitudinal corneal apex displacements and cardiac electric cycle (ECG) proved that close correlation exists between corneal surface pulsation and cardiovascular system activity [8]-[10]. Currently applied ocular hemodynamic assessment techniques are limited or uncomfortable for subjects [11]. One the other hand, the rate of pulsatile ocular blood flow can indirectly be approximated from the measurements of intraocular pressure[2],[12] so theoretically noninvasive measurement of the ocular pulse could be then viewed as a potential method of indirect POBF estimation. However, to make such an approximation several simplifications of the considered process are required.

A variety of methods have been used to measure variations of OP amplitude, including invasive [13]-[16] and noninvasive [3], [17]-[19], but only few of them considered detection of ocular surface expansions as the effect of ocular volume changes. Schmetterer et al. used an interferometric technique to show that the distance between cornea and retina changes as a result of variation in ocular blood volume [19]. Some slow but significant changes in the corneal shape were discovered by using commercially available high speed videokeratoscopy [20]. However, no clear association between the longitudinal apex movements and the corneal curvature was found. Application of custom built videokeratoscope and analysis of raw images also did not lead to discovery of any clear relationship between corneal curvature variations and cardiac activity. Spectra of variation in the radii of corneal curvature were too noisy to show any clear components related to the heart rate activity. Only in some examples the respiration frequency was noticeable [21].

Ultrasonic technique was applied successfully to measure noninvasively and accurately longitudinal corneal apex displacements (LCAD) of one or both eyes [9], [10]. However, it was suggested that observed displacement could be a superposition of the whole eye globe movements and changes in corneal curvature [20]. The aim of this work was to ascertain whether the LCAD are the effect of ocular surface expansion or they are mainly caused by the movement of the whole eye. In other words, we wanted to examine whether changes in the eye globe's volume cause the ocular surface deformation or, in contrary, the eye can be treated as a solid element moving as one piece.

Our previous study showed that the amplitude of standard ophthalmic headrest movement caused by anterio-posterior head movements is in range of ±100 μm, which means that it can be around 5 to 10 times greater than a typical range of LCAD [22]. Those observations encouraged us to examine the influence of the anterio-posterior head movements on

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measurement of corneal apex pulsation.

MATERIALS AND METHODS

A. Measurements

Custom designed and built air-coupled ultrasonic distance sensors (MediCom, Wroclaw, Poland) were used to measure ocular surface displacement as well as anterio-posterior head movements. The ultrasound system registers distance with accuracy of around 2 μm at sampling rate of 100 Hz. The hybrid sensors emit wave packets of average frequency 0.8 MHz in response to output impulses sent from a generator at repetition frequency of 100 Hz. Returned echoes are received and after low-pass filtering the analog to digital conversion is performed. In this stage signals are sampled at 50 MHz. The distance between ultrasound transducer and the measured object is calculated from the value of echo time delay estimator, indentified at the maximum of the correlation function (using a traditional time-domain based technique). The same system was used in our previous works, in which more technical details of the sensors can be found [9], [10], [22]. The system's safety was tested and no risk of corneal erosion or cavitation occurrence was found.

Two experiments were conducted during this study. Both of them were carried out in a setup, which significantly reduces the head movements. The measurement setup is composed of a rigid headrest, a bite bar and a belt strapping head to the frame of the headrest (Figures 1-2).

Fig. 1. The measurement setup for examination of longitudinal corneal apex displacement and anterio-posterior head displacements (Experiment I). Simultaneously the ECG signal was registered. The subject is placed in the rigid headrest with a bite bar. Head movement is represented by the displacements of protective glasses worn by the examined subject.

The aim of Experiment I was to distinguish between head and eye movements. Previous studies showed that even fine movements of a stabilized head are linked to cardiovascular activity [10]. This phenomenon can be explained by the presence of fine natural pulsation of blood vessels under the skin of the face. To reduce skin related pulsation effect during the measurement, subjects wore protective glasses with some foam placed underneath. A sensor was then situated in front of the protective glasses measuring their longitudinal displacement. A hole was cut on one side of the glasses, so another sensor could be placed in front of corneal apex. In this way longitudinal movement of the corneal apex as well as anterio-posterior displacements of fixed head could have been synchronically registered (Figure 1).

To detect possible ocular surface expansion, normal displacement of chosen points on the cornea and sclera of the same eye were registered (Experiment II). Figure 2 shows the position of the sensors during measurement. One transducer was placed perpendicularly at the front of corneal apex, while the other measured normal displacement of sclera around 8 mm far from limbus. The angle α between sensors axes was around 60 degrees. If the whole eye is not expanding but moving longitudinally, the amplitudes of normal displacements of the scleral surface should be lower than normal displacements of the corneal apex of the same eye. Otherwise, when normal (i.e., 90 degrees to the surface) displacements of the sclera are similar or higher to those of the corneal apex, the ocular surface expansion contributes to registered signals.

In case of all measurements, heart activity was monitored by registering ECG signals in the so called Einthoven triangle, at sampling rate of 100 Hz. In this configuration two electrodes are placed on subject's wrists and the third one on their left ankle [23].

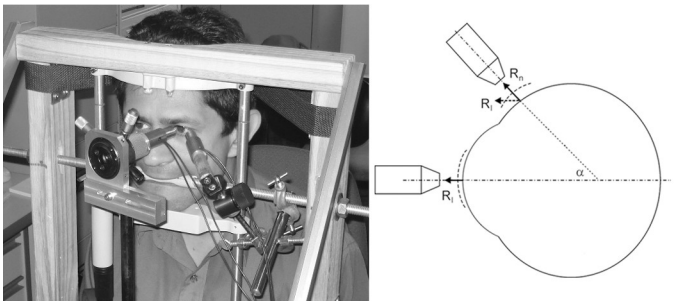

Fig. 2. Measurement of corneal and scleral normal displacements synchronized with ECG registration (Experiment II). The angle between sensors axes, α is around 60 degrees. Subject is placed in the same setup as in Experiment I. Notice the belt strapping the head to the frame of headrest.

Four subjects participated in the study; two myopes (aged 45 and 25, Subject I and Subject II), one presbyope (aged 60, Subject III) and one emmetrope (aged 23, Subject IV). All subjects had good general health and were free of any ocular or heart diseases. Only the left eyes of subjects were examined. Before the experiments, blood pressure was measured with the Blood Pressure Monitor (Omron Healthcare Co., Ltd., Kyoto, Japan). All subjects recorded normal levels of systolic (90–120 mmHg) and diastolic (60–80 mmHg) pressure. The study was conducted at Queensland University of Technology and met the requirements of the university's human ethics committee.

Each measurement performed in this study took 10 s and during this time subjects were asked to abstain from blinking and fixate on the far target to relax their accommodation demands.

B. Data analysis

Time, frequency and time-frequency analysis were performed for each of the registered signals, using Matlab (The MathWorks, Inc., Natick, MA, USA). Preliminary signals were linearly detrended. A band pass filter was applied in the range of 0.5-40Hz to remove very low frequency interference (so-called baseline wander) and respiration rate as well as high-frequency components that could not be associated with pulse harmonics. Although natural breathing frequency affects signals of ocular pulsation and ECG, in this work we were not focused on this phenomenon.

Signals of corneal and scleral normal displacements usually contain few short peaks related to saccadic movement of the eye [8]. To minimize the effect of sudden changes in the ocular surface displacements we have used a filtering procedure consisting of three steps: (i) calculating the derivative of the signal, (ii) thresholding and (iii) reintegrating.

Fast Fourier transform was applied to calculate frequency spectra of considered signals [24], [25]. Spectral characteristics of corneal, scleral and head normal displacements decay quite fast for higher frequencies [9]. For this reason, Fourier analysis was performed for the first derivatives of signals, i.e., velocity of normal displacements. Additionally, frequency characteristics were normalized so, that the height (peak) of the frequency component signifies the averaged amplitude of corneal, scleral or head velocities for a given harmonic.

Frequency spectra alone do not reveal information about signals whose frequency components vary in time [26]. Time-frequency analysis using Short Window Fourier Transform with a 2.5 second length Hamming window, was used to unravel potential nonstationarity of considered signals.

To ascertain relationships between registered signals, coherence function was calculated. With the range of values from zero to one, it indicates synergy between two signals in the frequency domain [27]. If the value of coherence function is close to one, signals are highly correlated and their phases change in the same way. A coherence value of zero indicates independence of signals components at the specified frequency.

RESULTS

In Experiment I, several measurements of corneal apex longitudinal movements and of those from protective glasses were recorded for each of the subjects. Similarly, in Experiment II measurements of corneal and scleral normal displacements were recorded. All measurements were conducted synchronically with the registration of ECG signals for each of the subjects.

Although the registered signals are unique for each subject with respect to their form and spectral characteristics, no substantial differences have been observed in their interrelationship and characteristic features regarding the context of this paper. Hence, only results obtained for Subject I and Subject IV are presented in detail.

C. Experiment I

Figure 3 shows time variations of corneal apex longitudinal position (black solid line) as well as head displacements in the same direction (represented by the movement of the protective glasses worn by a subject, grey solid line) and the ECG signals (bottom panels, black solid line), synchronically registered for Subject I (left column) and Subject IV (right column). The originally recorded signals are shown in the top panels while their filtered version (band-pass filter 0.5-40 Hz) are shown in the bottom panels. In the case of filtered signals, for both subjects the average amplitudes of the longitudinal corneal apex displacement are significantly higher than the average amplitudes of head movement (around three times). For Subject I, some low frequency variation can be seen in the signal of corneal apex movement, whereas it is absent in the head displacement. This can be attributed to the longitudinal movements of the whole eye globe, which affect measurement of corneal apex displacement but do not affect head displacements. For the rest of the subjects, signals of longitudinal protective glasses movement usually contained low frequency component (around 0.2 to 0.3 Hz) related to the natural breathing rate, as it can be seen in results obtained for Subject IV.

Frequency and time-frequency analysis were performed for filtered signals only. Representative examples of such joint representation are shown Figures 4 and 5 for Subject I and IV, respectively. Heart rate and its harmonics can be seen in frequency and time-frequency representations of all considered signals. However, frequency propagation in the corneal apex velocity spectra is significantly different to that of the head velocity. Time-frequency analysis confirms nonstationarity of the registered signals.

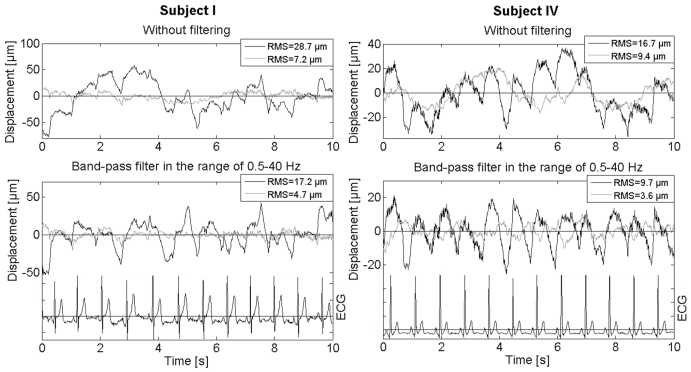

Fig. 3. Synchronically registered longitudinal corneal apex displacements (black solid lines) and anterio-posterior head displacements (grey solid lines) as well as the ECG signals (bottom plots) for Subject I (left column) and Subject IV (right column).

Spectra of corneal apex velocity obtained for Subject I contain a strong signature of the pulse and its 1st harmonic (Figure 4). Several successive harmonics can be also seen, however their amplitudes are weaker. In contrary, a characteristic feature of the spectrum obtained for the head velocity is the strong propagation of higher frequencies. The highest amplitudes are recorded for the 4th, 5th and 6th harmonic of the heart rate. This is more clearly seen in time-

frequency graphs. Similar tendency was noticed for all of the subjects participated in this study. In case of Subject IV, the strongest component in corneal apex velocity spectrum is the principal frequency of the heart rate, while in the spectrum of head velocity, the 5th and 6th harmonics have the highest amplitudes (Figure 5).

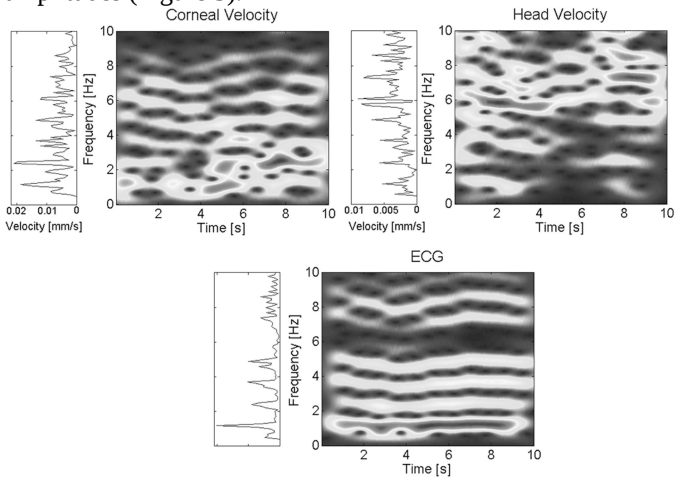

Fig. 4. Frequency and combined time-frequency representation [left plot and contour plot] of corneal apex velocity signal (top, left), anterio-posterior head velocity signal (top, right) and the ECG signal (bottom) for Subject I.

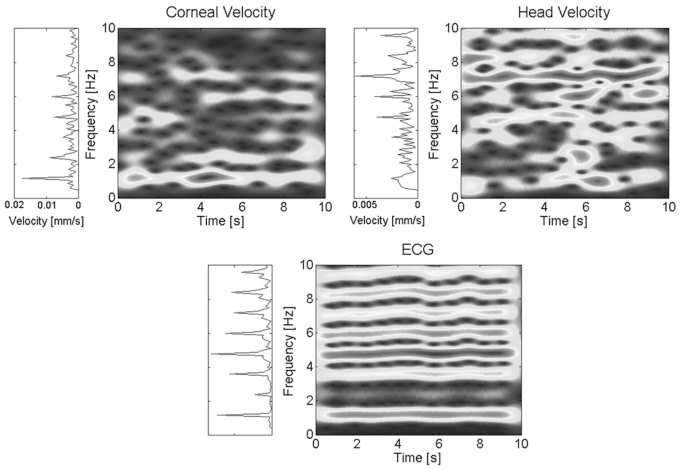

Fig. 5. Frequency and combined time-frequency representation [left plot and contour plot] of corneal apex velocity signal (top, left), anterio-posterior head velocity signal (top, right) and the ECG signal (bottom) for Subject IV.

In Figure 6, coherence functions calculated between corneal apex velocity and the ECG signal (black, solid line), head velocity and ECG (grey, solid line) and velocities of corneal apex and head (black, dashed line) are shown for Subject I and Subject IV. For both subjects, high values of coherence obtained between corneal apex velocity and ECG signal exist at the fundamental pulse frequency and its 1st harmonic (0.7<Coherence<0.9). The strongest correlation between head movement and heart activity can be seen, in contrary, in the frequency range of 5 to 10 Hz (Coherence>0.7). Corneal apex velocities are usually strongly linked to the head velocities at those frequencies which are dominant in the head movement [22]. Relative distribution of coherence functions amplitudes can be an individual feature of a subject, however mentioned tendencies are present in all of the examined cases.

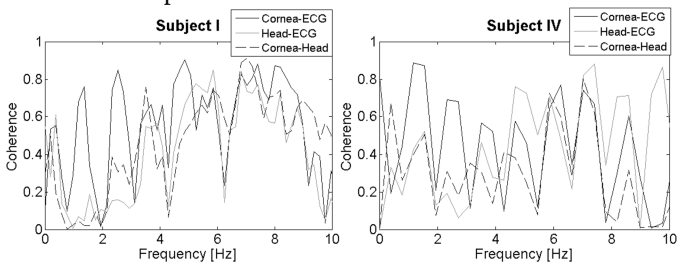

Fig. 6. Estimates of coherence functions between considered pairs of signals in Experiment I.

D. Experiment II

Figure 7 shows the radial displacements of corneal apex (black solid lines, top plots) and sclera (grey solid lines, top plots) of the left eye registered synchronically with the ECG signal (black solid lines, bottom plots) for Subject I and Subject IV. Although scleral displacements were measured around 8 mm from a limbus, it seems to be highly correlated and in phase with corneal apex longitudinal movement in both cases. A band pass filter was applied to all signals in the range of 0.5-40 Hz.

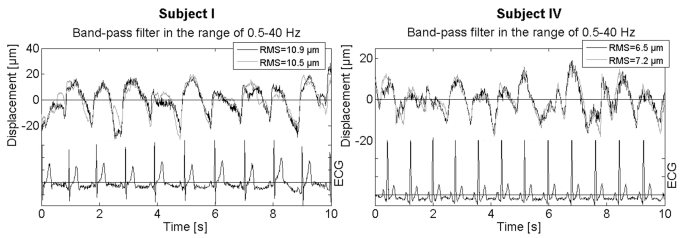

Fig. 7. Synchronically registered corneal (black solid lines) and scleral (grey solid lines) normal displacements as well as the ECG signals (bottom plots) for Subject I and Subject IV.

For a given subject the root-mean-square amplitudes of corneal and scleral displacements are almost the same. Average amplitude of corneal apex and sclera radial displacements in case of Subject I was estimated to be around 10 μm, while for Subject IV it was around 7 μm.

Frequency and time-frequency characteristics of the ECG signals as well as corneal and scleral velocities derived from cornea and sclera normal displacements are presented in Figure 8 (signals recorded for Subject I) and in Figure 9 (signals obtained for Subject IV). A strong component corresponding to the fundamental heart rate around 1 Hz (Subject I) and around 1.2 Hz (Subject IV) can be seen in all of the recordings. For both subjects the basic pulse frequency is the strongest component of the considered spectra; however frequency distribution is an individual feature.

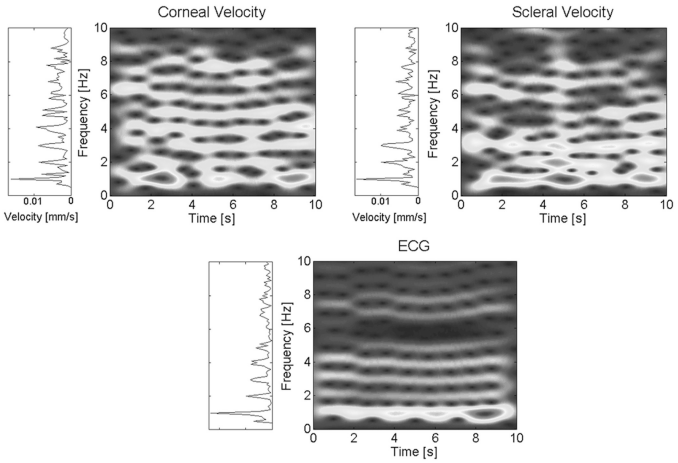

Fig. 8. Frequency and combined time-frequency representation [left plot and contour plot] of cornea and sclera normal velocity signals (top-left and top-right, respectively) and the ECG signal (bottom) for Subject I.

In all characteristics obtained for Subject I (Figure 8) up to seven harmonics of the heart rate can be noticed. Spectra of corneal and scleral velocities are comparable, however time-frequency analysis allows to see that the 2nd harmonic of blood pulsation is relatively stronger for velocity of sclera than the corneal apex.

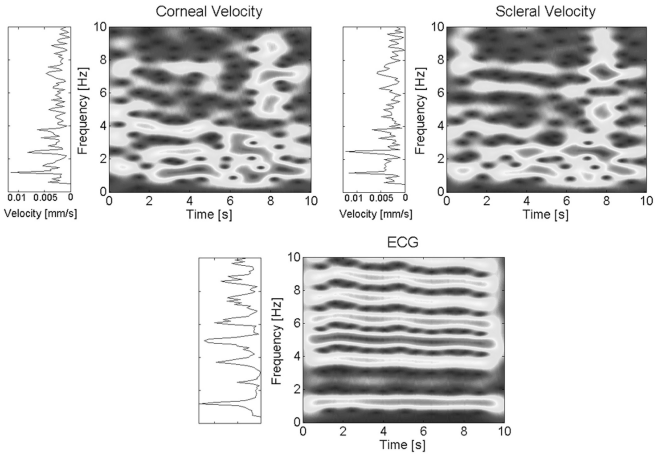

Fig. 9. Frequency and combined time-frequency representation [left plot and contour plot] of cornea and sclera normal velocity signals (top-left and top-right, respectively) and the ECG signal (bottom) for Subject IV.

Spectra and time-frequency graphs of Subject IV (Figure 9) show several harmonics of the heart rate, but in the case of signals related to the eye they are not as clear as for the Subject I. In ocular surface velocity spectra, the 1st and the 5th harmonics have relatively strong amplitudes.

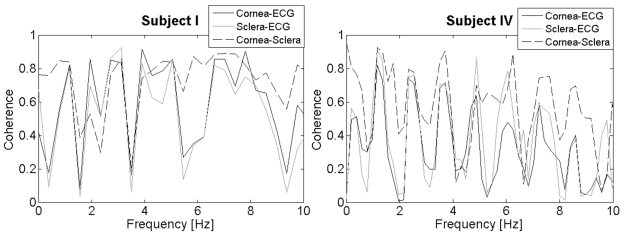

Fig. 10. Estimates of coherence functions between considered pairs of signals in Experiment II.

Figure 10 shows the estimates of coherence obtained for Subject I and Subject IV. Coherence functions were calculated between: corneal apex radial velocity and ECG signal (black, solid line), scleral radial velocity and ECG (grey, solid line) and radial velocity of cornea and sclera (black, dashed line). For both subjects considered pairs of signals are strongly correlated (at least Coherence>0.7) at pulse frequency and its harmonics. This indicates that the ocular surface pulsation is strongly related to the heart activity. High values of coherence exist between signals of corneal and scleral pulsations. Coherence functions calculated between ECG and corneal or scleral velocities are comparable in case of both subjects.

DISCUSSION AND CONCLUSIONS

The aim of experiments presented in this paper was to estimate the influence of head movement on detection of longitudinal corneal apex displacements as well as to examine if the ocular surface expands due to intraocular pressure variation and pulsatile ocular blood flow.

Using air-coupled ultrasonic sensors of high accuracy we measured normal displacements of the cornea and sclera around 8 mm from limbus and noticed that their average amplitudes are very similar. If the whole eye moves longitudinally, vector of scleral normal displacement (D_n) can be represented by its longitudinal component (D_l) using cosine relation: $D_n=D_l\cos\alpha$ (Figure 1B). During measurements, the angle between sensors was set around 60 degrees, so the longitudinal component of scleral displacements should be around 2 times lower than its normal component (assuming that the eye does not change its volume). In the case of the results presented in this work, the average normal displacements of corneal and scleral surface appeared to be of equal amplitude. However, it is not the rule and required condition to ascertain ocular surface expansion. In other cases (not presented in the paper) we sometimes observed average amplitudes of scleral normal displacements (especially in the limbus area) exceeding those of corneal apex. High values of coherence functions calculated between corneal or scleral movement and the ECG signal give evidence that measured displacements are closely linked to cardio-vascular activity.

To ascertain if difference in radii of curvature of cornea and sclera can affect distant values obtained by system based on ultrasound transducers, we tested the system using glass hemispheres of two different radii of curvature (8 mm and 12 mm) attached to micrometer gauge (similar experiment was reported earlier for flat surface in [22]). No significant differences were observed in the repeatability and accuracy of results obtained for different hemispheres and the flat surface.

It is not feasible to measure *in-vivo* ocular surface pulsation component, which is not affected by the anterio-posterior head movement. Head displacement is an indispensable part of recorded longitudinal corneal apex movement; however there exist some unique properties of head and eye movements, which help to distinguish between them. It is characteristic for all of the subjects, that the principal frequency of corneal

pulsation or its first harmonic is usually the most significant. In contrary, spectra of head velocity contain relatively stronger components of higher harmonics. This observation can help isolating those properties of the signals that are associated mainly with the eye pulsation.

To measure corneal surface displacements, a proper rigid headrest is required. In our experiments, we have used a bite bar and an ophthalmic headrest strengthened with custom designed construction (wooden frame and metal bars). In this setup the average amplitude of the head movement was usually 3 to 4 times lower than the average amplitude of corneal movement. Measuring longitudinal displacements of protective glasses instead of detecting head movement on skin surface minimized the influence of fine natural expansion of the blood vessels on the head displacement signal.

Some characteristic features of ocular surface pulsation signals such as: the number of visible harmonics, their relative amplitudes, stronger or weaker nonstationarity can be the effect of individual intraocular pressure propagation, ocular blood flow and biomechanical properties of ocular tissues. We also found some fine differences in the relative propagation of frequency in the cornea and sclera normal velocity spectra, which can be related to different mechanical properties of those tissues.

To summarize, our results indicate that either corneal surface or the scleral surface, or both of them simultaneously undergo dynamic expansions. Close correlation between signals of corneal and scleral radial displacements and cardio-vascular activity lead us to conclude that ocular surface expansion is caused by pulsatile ocular blood flow. However, the pulsatile blood flow may cause not only IOP variations but also changes in blood vessels volume in peri- and retrobulbar space. Hence, it cannot be excluded that this factor contributes to the registered signals of ocular surface expansion.

Our study tried to clarify whether ocular surface expansion and changes in ocular volume could cause some fine variation of corneal radius. However, examination of corneal curvature pulsatile changes using commercial or custom designed videokeratoscopy did not provide any clear evidence of existence of such deformations [20], [21], [28].

The role of the corneal longitudinal movement is not fully understood. Ultrasonic technique enables noninvasive and accurate measurement of corneal apex displacement and we hope that further research performed for a wider group of subjects that would include healthy as well as pathological cases (e.g., glaucoma, hypertension) could lead to the development of a noninvasive method for estimating intraocular pressure propagation and indirect assessment of pulsatile ocular blood flow.

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