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Mohammed Al-Kalbani
St. James's Hospital

Emilia Mihaylova
Technological University Dublin, emilia.mihaylova@tudublin.ie

Niamh Collins
Royal Victoria Eye and Ear Hospital

David Coakley
St. James's Hospital

Gerard Boyle
St. James's Hospital

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Mohammed Ali Al-Kalbani
St. James's Hospital

Emilia Mitkova Mihaylova
Dublin Institute of Technology, emilia.mihaylova@dit.ie

Niamh Collins
Royal Victoria Eye and Ear Hospital

Vincent Toal
Dublin Institute of Technology, vincent.toal@dit.ie

Davis Coakley
St. James's Hospital

See next page for additional authors

Authors
Mohammed Ali Al-Kalbani, Emilia Mitkova Mihaylova, Niamh Collins, Vincent Toal, Davis Coakley, and Gerard Boyle

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M. Al-Kalbani[*a,c], E. Mihaylova[b], N. Collin[c,d], T. Vincent[b], D. Coakley[c], G. Boyle[a]
[a]Department of Medical Physics and Bioengineering, St.James's Hospital, Dublin;
[b]Center for Industrial and Engineering Optics, DIT, Dublin;
[c]The Mercer's Institute for Research on Ageing in St. James's Hospital Dublin;
[d]Royal Victoria Eye and Ear Hospital, Dublin

ABSTRACT

Ocular Microtremor (OMT) is a continual, high frequency physiological tremor of the eye present in all subjects even when the eye is apparently at rest. OMT causes a peak to peak displacement of around 150nm-2500nm with a broadband frequency spectrum between 30Hz to 120Hz; with a peak at about 83Hz. OMT carries useful clinical information on depth of consciousness and on some neurological disorders. Nearly all quantitative clinical investigations have been based on OMT measurements using an eye contacting piezoelectric probe which has low clinical acceptability. Laser speckle metrology is a candidate for a high resolution, non-contacting, compact, portable OMT measurement technique. However, tear flow and biospeckle might be expected to interfere with the displacement information carried by the speckle. The paper investigates the properties of the scattered speckle of laser light (λ = 632.8nm) from the eye sclera to assess the feasibility of using speckle techniques to measure OMT such as the speckle correlation. The investigation is carried using a high speed CMOS video camera adequate to capture the high frequency of the tremor. The investigation is supported by studies using an eye movement simulator (a bovine sclera driven by piezoelectric bimorphs). The speckle contrast and the frame to frame spatiotemporal variations are analyzed to determine if the OMT characteristics are detectable within speckle changes induced by the biospeckle or other movements.

Keywords: Ocular Microtremor, biospeckle and speckle correlation.

1 INTRODUCTION

During visual fixation there are three main types of eye movement, OMT, slow drifting of the eye and rapid flicks of the eye called microsaccades. Ocular Microtremor is a continual, high frequency physiological tremor of the eye present in all subjects even when the eye is apparently at rest. OMT causes a peak to peak displacement of a round 150nm-2500nm with a broadband frequency spectrum between 30Hz to 120Hz, with mean peak a round 83Hz for normal healthy subjects [2,3].

The OMT signal provides an indication of the functional activity of the brainstem[4] and OMT frequency is reduced in patients with neurologic disorders involving the brainstem [5,6]. The OMT signal has potential prognostic value in coma [4,7]. The OMT signal diminishes with increasing depth of anesthesia [8,9]. Joint time-frequency analysis of OMT signal has shown to accurately determine depth of anesthesia[10].

2 OMT MEASUREMENT TECHNIQUES

A number of techniques are reported in the literature for measuring OMT. The original method used in measuring OMT was a light reflection based method, which relied on the detection of changes in the angle of a reflected beam from a mirror mounted on the eye [11, 12]. Other methods reported include corneal reflection [13 14], open/closed eyelid piezoelectric

technique (PZT system) [15] [16], IRIS system [17] [18], sclera search coil [19] [20], in-plane speckle interferometry [1], [21]. Nearly all quantitative clinical investigation of OMT have been carried out using the PZT system.

Although the reflection mirror, corneal reflection, IRIS system, sclera search coil methods have been reported in the literature of OMT, none have satisfied the resolution required to measure OMT [2]. On the other hand the capacitance gauge method does meet these requirements as reported by Bengi and Thomas [15]. However it requires skill to position the moving plate and requires a number of voluntary microsaccades of a known size to calibrate the instrument for each setting. Also it not easy to isolate the vertical and horizontal components of the OMT (in clinical investigation we are only interested in the horizontal component).

The open eyelid PZT system has a number of advantages over other methods including its high level of accuracy. This has lead to it being accepted as the current method of choice for OMT clinical investigations. However it does not come without its disadvantages. Prior to measurement anesthetic eye drops must be administered to avoid patient discomfort. Furthermore the recording duration is limited acceptability, since it is minimized to prevent drying and irritation of the eye. Also to accuracy of the OMT amplitude as determined by the PZT system is open to debate owing to the unknown loading effect on the eyeball [22].

In-plane speckle interferometry technique has proven feasible in OMT measurement, and overcomes a number of the current limitations of other techniques. This paper further investigates OMT speckle metrology as a means to enhance the build of an optical speckle technique in measuring the OMT signal.

3 OMT AND SPECKLE METROLOGY

Optical metrology techniques in general have an a number of important advantages over current methodologies: i.e. sensitive, noncontact and non-invasive [23].

As mentioned earlier, Boyle [1] was the first to introduce the speckle interferometry technique in the measurement of the OMT signal. The optical configuration shown in Figure 1 shows an in-plane, phase modulating speckle interferometry using a photodiode to measure OMT by using the eye sclera (the white of the eye) as the target. The laser beam used was supplied by He.Ne laser (λ=632.8nm).

Boyle (2001) [1]

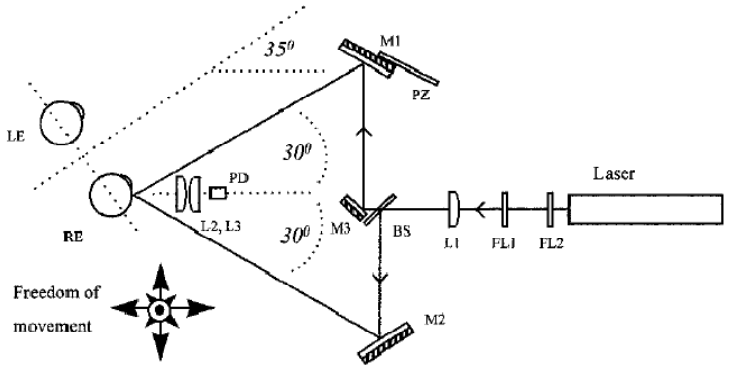

Figure 1. shows an in-plane, phase modulating speckle interferometry using a photodiode to measure the OMT by using the eye sclera (the white of the eye) as the target. FL1, FL2, filters; L1, focusing lens; BS, beam splitter; M1, phase-modulating mirror; PZ, piezoelectric element; M2, M3, fixed mirrors; RE, right eye; L2, L3, collecting lenses; PD, photodiode.

The resolution of the system was 100nm which is about 4 times less than the ideal resolution for the OMT measurement[2], but sufficient enough to capture it. The setup was tested using a calibrated piezoelectric driven OMT simulator with white plastic surface to represent the eye sclera. Further testing was performed using a small bovine scaleral sample to take into account the effect of the biospeckle in the measurement of the simulated signal. Boyle et al [17] noted that there were a number of distinctive low frequency noisy phases during the signal simulation measurements which were not noted with the plastic target[24]. It was concluded that they arose from biospeckle fluctuations. He concluded that the sclera surface allow the generation of the interference which is fundamental for speckle interferometry. However these tests did not include simulation of head movements, tear flow and sclera blood flow.

To further confirm the feasibility of this approach a third test was also performed, whereby a 140Hz sinusoidal signal was superimposed on the measurement of the in-vivo eye. The spectrum of the measured signal showed a spike at 140Hz, which concluded that the system operates correctly in-vivo.

The setup was further developed using a laser diode (λ=638nm) coupled by phase maintaining fibers with integrated phase modulation that allowed construction of a compact portable device [21], [25]. The system has not yet been tested in-vivo. Additional simulation tests were performed [26] using eye drop solution (Brolene Propamidine) to simulate eye tears by applying it to the plastic surface during the OMT recording. This resulted in an error in the displacement measurement of 1.9%. The author concludes that there is no apparent effect of tear flow on the measurement results. The test of the tear flow does not simulate the effect of having biological sclera as the target, which could cause a higher level of disagreement between the measured and the simulated signal.

The work by Boyle was based on a photodiode system. This system configuration limits the measurement to one dimension and monitoring of speckle pattern changes is lost. Using a high frame rate CCD camera will resolve the issue.

The introduction of the second dimension will also allow the study of the time-varying speckle, also enabling the study of the bio-speckle of the eye and speckle contrast. The effects of boiling speckle and multiple scattering phenomena which observed in most biological tissues could be more quantified and analyzed. The speckle contrast measurement analysis will allow the study of the blurring effect and the results may suggest the possibility of using speckle correlation technique to measure the OMT signal. To introduce the speckle correlation to OMT will allow for a compact and simpler method than the interferometry technique. This is due to that fact the correlation method is based in single beam illumination, while the speckle interferometry requires that two beams aligned to one spot with same angle to the surface normal of the target and also requires to apply a phase modulation and demodulation during the measurement process. Also the speckle correlation technique is less sensitive to room vibrations making it more favorable for clinical use.

4 STATISTICS OF LASER SPECKLE

As the laser speckle is a random phenomenon it can only be described statistically. A detailed explanation of the speckle statistics theory is described by Goodman[27]. In this work we will be interested into two parameters, speckle contrast and speckle size. The speckle size statistics will be used to design the optical configuration of the imaging lens used in the speckle correlation for the OMT measurement. Also the study of the speckle size will be useful in improving the speckle interferometry and investigates the possibility of replacing the photodiode with CCD camera (with no requirement of phase modulation) in the current setup introduced by Boyle. The speckle contrast will be useful in looking at the effects of the biospeckle of the eye sclera and the tear flow.

4.1 Speckle contrast

If the motion of the object is faster than the exposure time of the CCD camera, this causes rapid intensity fluctuations of the speckle pattern resulting in a blurred image. To quantify the blurring effect of the speckle a first-order statistical measure known as the local speckle contrast (C). The local speckle contrast is defined as the ratio of the standard deviation to the mean intensity.

$$C = \frac{\sigma_I}{\tilde{I}} \qquad \textbf{Equation 1}$$

The following are the properties of the local speckle contrast:

- The speckle contrast lies between the value of 0 and 1 for Gaussian statistics.
- Contrast of a value one demonstrates that there is no blurring and contrast of a value of zero indicates that the object is moving fast enough to average all the speckles.
- The higher the velocity of the object the smaller the contrast. Lower contrast decreases the signal to noise ratio.

4.2 Speckle size

The second-order statistics, speckle size is an important measure in the speckle metrology. This is an important parameter in the motion measurements using speckle techniques in the design, simulation and analyzing of the optical setup. In the speckle interferometry, the speckle motion must be much smaller than the speckle size, while the opposite is true for the speckle photography[28].

The radius of the smallest spot is estimated as follows [29]:

$$r = 1.22\lambda\frac{d_I}{D} \qquad \textbf{Equation 2}$$

where the d_I and D are the image distance from the lens and the aperture of the lens, respectively. The above equation is used to determine the minimum pixel size required to capture a single speckle. For optical configuration shown in Figure 2, the equation above could be further modified to help to determine the minimum pixel size using the lens equation.

$$\frac{1}{d_o} + \frac{1}{d_I} = \frac{1}{f} \qquad \textbf{Equation 3}$$

Where d_o and f are the object distance from the lens and the focal length, respectively. The magnification (M) is:

$M = {}^{d_I}\!/_{d_o}$ Therefore Equation 3 becomes:

$$d_I = f(M+1) \qquad \textbf{Equation 4}$$

Then we can introduce magnification factor to Equation 2.

$$r = 1.22(1+M)\lambda\frac{f}{D} \qquad \textbf{Equation 5}$$

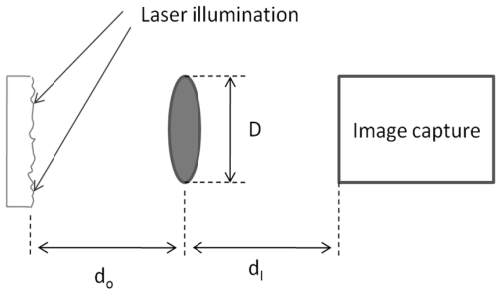

Figure 2. Schematic diagram of the speckle correlation.

5 SPECKLE CORRELATION

The speckle correlation technique has not been reported in OMT measurement literature. The technique is based in capturing the speckle fluctuations using a CCD camera at a frame rate higher than the object motion displacement speed [30]. As the speckle from a rough object has a unique pattern (like a finger print), the displacement of the object would a shift in the speckle pattern by the same amount. The motion is obtained by correlation process as follows:

1. From the captured data a frame (f2) and the preceding frame (f1) are selected.
2. Next a sub-image (f1s) is formed from the middle of speckle pattern of f1.
3. Then a 2D cross-correlation map [31] obtained between f1s and f2 with a step size of one pixel (setup size is the number of pixels over which f1s is shifted in x-direction and y-direction to calculate the next correlation coefficient) .
4. Finally the x-y displacement of the object during the period from f1 and f2 is found by comparing the correlation peak to the middle of the correlation map.

6 EYE SCLERA AND BIOSPECKLE

In the literature the anterior part of the sclera and the cornea were the mediums used to measure the OMT signal. In the in-plane speckle informatory system in measuring OMT, the sclera (also called the white of the eye) is used as the target [1, 21]. The same applies for the contacting piezoelectric technique [16] as the cornea could be damaged by the probe loading. In addition with the speckle technique the sclera provides a better reflection medium and also limits the eye laser exposure hazards.

The sclera is a high scattering medium [32] but due to the blood vessels (unlike the cornea) and the bulbar conjunctiva (a transparent membrane covering anterior part of the sclera) biospeckle is expected when reflecting a laser beam from it. Due to the constant flow of eye tear, this may cause a source of error in speckle techniques implemented in measuring OMT (increasing moisture level has been shown to increase biospeckle activity [33]).

7 OMT SIMULATOR

The OMT simulator used in this experiment is based on the scaleral surface simulator used by Sheahan's [22], which was further developed by Boyle [24]. The simulator is made of a white plastic disc to model the eye sclera, mounted to three piezoelectric bimorphs as shown in Figure 3. The three bimorph length is twice the average radius of human eyeball to give close approximation for the OMT simulator [22]. The outer bimorphs are used to drive the mounted disc and the third is used as a reference for the calibration of the simulator.

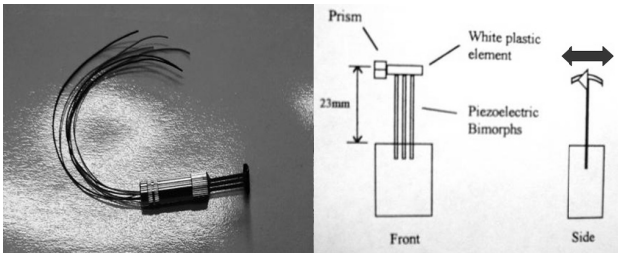

Figure 3. The simulator is made of a white plastic disc to model the eye sclera, mounted to three piezoelectric bimorphs .

A small prism is used to calibrate the simulator using a He-Ne laser Michelson interferometer. The phase and the frequency response is flat to within 0.3 dB over the OMT range (20Hz-150Hz).

8 EXPERIMENTAL ARRANGEMENT

The experimental arrangement for recording is shown in Figure 4. A speckle pattern was formed by projecting the laser beam on to the specimen surface using a He-Ne laser (5mW, λ=632.8nm). Then the beam is spatially filtered to give a smooth Gaussian intensity profile. A collimating lens is used to control the size of the illuminated spot. The spot size used in the experiments approximately 1mm. The laser power was controlled by adjustment of the spatial filter with collimated lens and monitored using PD300 thermal head with Nova 2 display. The laser power was set to 250μW. For the case for in-vivo speckle investigation a power filter is used with 5% transmission for the optical setup alignment.

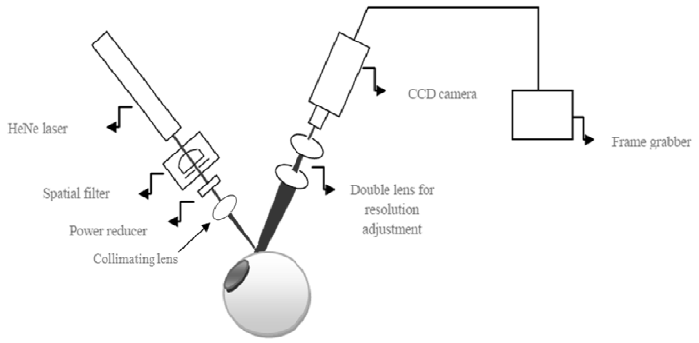

Figure 4. The experiment arrangement for the eye sclera speckle investigation.

The emerging speckle was focused using a double lens combination. The real image formed was projected to a CCD camera. The resolution of the system is controlled by the adjusting the double lens with the aid of Equation 5 to calculate the speckle size. For the initial experiments a CCD color camera with 576 x 720 pixels (pixel size 10μm square), RGB and acquisition rate of 25 frames per second is used. For the ground experiment were recorded by a high speed digital video camera (Motion Scope PCI 8000S, Redlake Inc) with a frame rate of 500Hz (500Hz frame rate acquisition speed is sufficient to track the speckle pattern changes in the presence of the OMT movement) ,280 x 320 pixels and pixel size 7.4μm square.

8.1 Eye laser safety

The Maximum Permissible Exposure (MPE) level of the eye to laser radiation depends on the wavelength of the laser used and the exposure time. The higher the wavelength the lower the MPE as the energy is lower. Also the longer exposure time the higher the level of radiation applied to the eye.

There are two standards that give guide lines for the MPE levels of the laser radiation, the International Electrotechnical Commission (825-1) [34] and the American National Standards Institute (Z136.1)[35]. The two standards agree in the same MPE level of the eye.

Following the guidelines of the two standards to calculate the safe eye laser levels, the MPE limit for the He-Ne laser (λ=632.8nm) laser in Wm^{-2} are calculated as follows:

$$MPE = \begin{matrix} 10^2 C_3 C_6 & if\ t > T_2 \\ 18t^{0.75} C_6 & if\ t < T_2 \end{matrix} \qquad \textbf{Equation 6}$$

Where

$$T_2 = 10 \times 10^{0.02(\lambda - 550)} \qquad \textbf{Equation 7}$$

With λ=632.8, T_2=453s. Since the experiment setup does required to excide T_2, therefore the MPE is:

$$MPE = 18t^{-0.25} \qquad \textbf{Equation 8}$$

With C_6=1, implying a direct beam viewing of the laser, although the beam is directed to the sclera of the eye, but for safety we assume the worst case scenario. Using Equation 8 to calculate the MPE for 10 seconds recording period with CCD camera, MPE_{10s}=10.1Wm^{-2}.

The beam intensity is averaged over a pupil area of 38.48μm^2. This will give us MPE_{10s}=388.7μW. The limit to the speckle investigation is set to 250μW for 10s exposure (64% of the MPE).

8.2 Experimental testing

The experimental testing is divided into two experimental setups:

8.2.1 Static target

In this experiment a static target with different surfaces is used. The first one is based on having the plastic disc on the simulator (not driven) as the target. The second target is based on having a small sclera flap with the conjunctiva from a recently deceased animal. The third condition is based on adding a simulated tear flow to the sclera flap.

8.2.2 OMT simulation

In the OMT simulation testing the scaleral surface simulator is used. The simulator plastic disc was used as a target for the speckle investigation. The simulator was driven by a signal generator with frequencies from 20Hz-150Hz and amplitudes from 100nm-3500nm.

8.2.3 Data analysis

The captured data from the cameras are stored in video (avi file format), for further analysis. The data were first denoised using 2D Daubechies wavelet (db02) with Undecimated Wavelet Transform (UWT), for noise reduction due to the low laser power in the investigation. Next the speckle contrast and the 2D cross-correlation was calculated for the denoised data by using sub-image size of 15x15 pixels and a step size of a pixel in calculating the 2D correlation map .

The analysis has been carried on computational platform Intel(k) Core(TM)2 CPU T7200@2.00 GHz with 2.00 GB of Ram. All the analysis has been done in MATLAB [36] and LabVIEW [37].

9 RESULTS

Figure 5 shows (a, b or c) five subsequently acquired images from the CMOS camera running at 500Hz frame rate and the simulator driven by 80Hz at amplitude of 1µm peak to peak. The targets in the three conditions are a) Simulator plastic disc as the target. b) Eye sclera flap attached to the simulator. c) Eye sclera flap attached to the simulator and stimulated eye tear flow.

Figure 6 shows the local speckle contrast of the three target conditions of 100 consecutive frames, but with static condition (no simulator driving signal). The plastic target has the highest local speckle contrast (the top plot in Figure 6) with mean of 0.467 and standard deviation of 0.001. In the case where the eye sclera flap is used (the middle plot in Figure 6) the mean is 0.450 and standard deviation of 0.003. In the third case eye sclera flap target with stimulated eye tear flow (the bottom plot in Figure 6), have the lowest local speckle contrast with the mean of 0.425 and a standard deviation of 0.007.

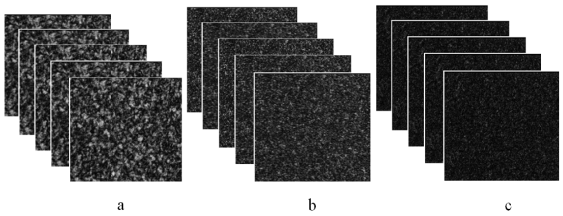

Figure 5. Shows consecutive frames acquired with camera set at 500Hz frame rate and the target driven by 80Hz sinusoidal signal of 1µm peak to peak amplitude. a) With the simulator plastic disc as the target. b) With the eye sclera flap attached to the simulator. c) With the eye sclera flap attached to the simulator and stimulated eye tear flow.

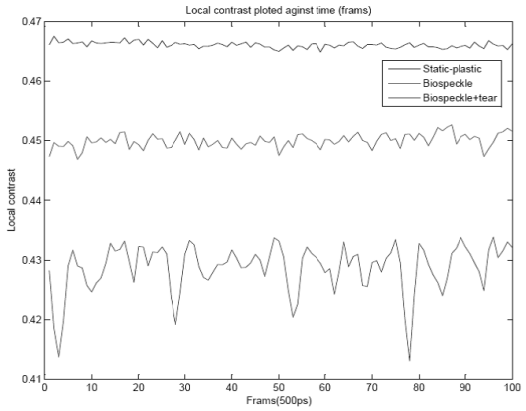

Figure 6 shows the local speckle contrast of the frames captured by the camera from a static objects.

Figure 6 shows a typical a 2D cross-correlation of consecutive speckle frames (500Hz frame rate) of sclera flap with stimulated tear and simulator driven with 80 Hz at 1μm peak to peak amplitude.

Using the simulator with sclera flap attached and simulated tear flow the capability of using the speckle correlation was tested. By driving the simulator at frequencies of OMT range (20Hz and 150Hz), the speckle correlation was apple to reconstruct the signals with echoes of noise due to the surrounding environment. Figure 7 shows reconstructed 80Hz sinusoidal signal by the speckle correlation of sclera flap and simulated eye tear attached to the simulator and driven by 80Hz with displacement of 1μm. In the case of system resolution, 300nm was achieved.

Also an OMT signal (obtained by the contacting piezoelectric technique) was used to drive the simulator. The speckle correlation technique was able to reconstruct the signal with 0.99 correlation factor (see Figure 9).

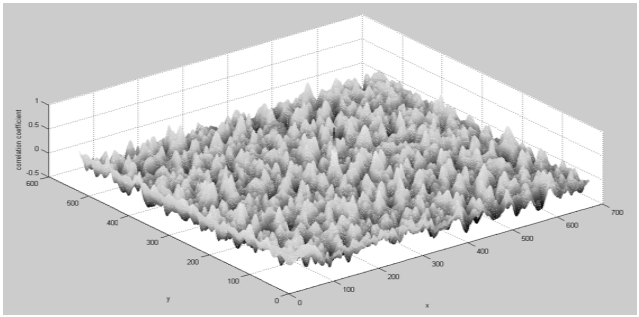

Figure 7. Shows a typical cross-correlation of two subsequently acquired images with sclera flap and stimulated eye tear.

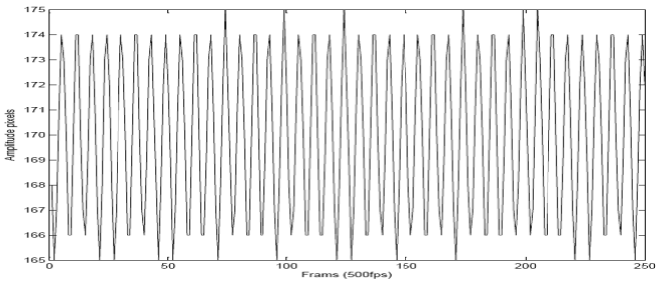

Figure 8. Shows a sine wave (80Hz) simulated signal captured by the speckle correlation technique.

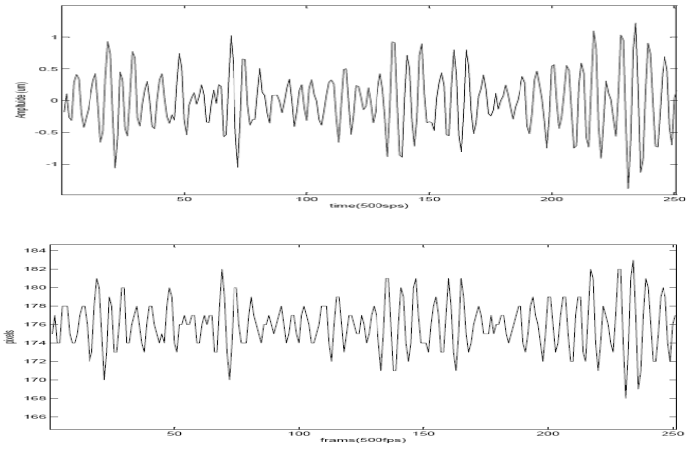

Figure 9. Shows in top graph a simulated OMT signal applied to the simulator. In the bottom is the reconstruction of the signal using the speckle correlation technique.

10 DISCUSSION

10.1 Static target

Biospeckle phenomena have been shown in previous studies to be produced when speckle techniques have been used with living organisms. Due to the characteristics of the eye sclera anatomy, we accept the presence of the biospeckle due to blood flow, bulbar conjunctive transparency and eye tear flow. This was confirmed by the current study using a high speed camera.

The presence of the biospeckle activity will cause an increase in the noise level when used to measure OMT measurement by speckle metrology techniques (such as speckle interferometry). This was quantified by measuring the local speckle contrast of speckle from rough object (plastic disc) compared to the one with eye sclera flap. Also tear flow was introduced to the sclera flap as a third comparison for simulating real OMT measurement case.

The results show that there is a drop of 4% of the local speckle contrast from eye sclera compared with the rough surface. The simulation of tear flow caused a drop of 9% to the local speckle contrast compared to the rough surface. This implies that a high production of tear flow (such as in the case of eye dryness) will increase the noise level in the OMT measurement by speckle methods as lower speckle contrast leads a decrease in the signal to noise ratio [38].

10.2 OMT simulation

The speckle correlation technique is a candidate for OMT measurement. The possibility of measuring the OMT signal with this technique will provide a simple, portable non-contacting method. The technique would allow an x-y direction measurement of OMT signal, which was not achieved by the other OMT measurement techniques. Also the system should be less sensitive to environmental noise in clinical scenarios compared to the speckle interferometry technique, which is the case in OMT clinical studies.

The current setup with speckle correlation was able to reconstruct the simulated signal generated by the OMT simulator with frequencies comparable to the OMT case (20Hz-150 Hz) using high speed CMOS camera. Also the technique was

able to reconstruct the simulated OMT signal as shown in Figure 9. The system was tested with more realistic simulation by having sclera flap attached to the OMT simulator with simulated tear flow.

On the other hand the current method achieved a resolution of 300nm which is about 6 times less than the ideal resolution for the OMT measurement [1]. This due to the low power (250μW) used in the speckle investigation to meet eye safe laser exposure levels and the specification of the camera used. The enhancement of the resolution will require a higher magnification factor of the speckle size projected to the camera detector which limited to the speckle light power. Having a high speed camera with higher sensitivity to lower power level measurements and a wider detector window (current 280 x 320 pixels and pixel size 7.4μm square) will improve the resolution of the system.

11 CONCLUSION

This paper investigates in general the possibility of using speckle metrology techniques in measuring OMT. The results conclude that noise addition due to the biospeckle activity of the eye sclera and tear flow does not affect the displacement information of the OMT.

Also the paper investigates the possibility of using speckle correlation technique in particular in measuring OMT. The experiment is based in using OMT simulator. The results show the possibility of measuring displacement from 300nm to 4500nm with frequencies ranging from 20Hz to 150 Hz. The speckle correlation technique has a potential application as a clinical portable tool in the measurement of OMT and overcoming the current difficulties in using other measurement techniques. However, further modification in the optical setup will be required to achieve the ideal resolution to measure the OMT activity (50nm).

12 Acknowledgment

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