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Two Methods Applied to Computational Simulated A-Scan Signals for Glaucoma Diagnosis

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***Abstract*— One of the greatest impact ocular disease is the glaucoma, because it represents the main cause of non-reversible blindness. The open angle glaucoma is a silent progressive affection and patient detects it until several scotomas appear limiting the peripheral vision. Nowadays, there are techniques based on ultrasonographic images focused to support glaucoma diagnose, nevertheless these are techniques that use very high frequency ultrasound radiation, which added to the cost of hardware/software used for image formation results on a high cost technology. In this work, an initial evaluation of two methods based on A-scan modality, to support diagnose and monitoring of glaucoma, are presented. The first method is based on correlation technique and the second one on spectral analysis. To perform the analysis, ultrasonic signals were simulated, using Matlab 2016 (Mathworks Inc.) considering echoes originated by the main structures of the eye affected by glaucoma. A model to generate these signals is described. Distances between anterior surface of cornea and posterior surface of lens are estimated for different internal volumes of the eye using both methods. Results show that an error range between 0.00% to 0.02 % and between 0.05% to 0.16% were obtained for correlation and spectral methods respectively. A theoretical resolution in volume increase of 0.5 µL could be detected by means of spectral method.**

Keywords—angle closure glaucoma, open angle glaucoma, ultrasound, diagnosis, signal processing.

I. INTRODUCTION

The eyeball evaluation by means of ultrasonic radiation is an exploited technique to define its anatomical parameters and relate it to potential abnormalities caused by ocular diseases. In ophtalmology, nowadays, ultrasound is considered a standard technique to diagnose and to monitor diseases as open angle and angle closure glaucoma [1], intraocular tumors [2], vascular disorders and opaque structures [3] among others.

Ocular ultrasound is used in three modalities: 1) A-scan, better known as pachymetry. Primarily it is used to measure corneal thickness, however, this kind of clinical test gives information about other structure dimensions of the eyeball, and the lens power [4,5]. 2) B-scanning modality, which is probably the broader application of ultrasound in ophthalmology. With this modality, an ultrasonographic evaluation of the hole internal structures can be performed. One of the most common application is oriented to identify intraocular masses and to determine its position and its size. The frequency used in this imaging technique is around 10MHz, which allows to attain a penetration depth about 50 mm with a reasonable resolution. For applications that require a higher resolution, as gonioscopy and glaucoma detection, the ultrasonic microscopy is used. It achieves very high resolution images (approximately 25 µm of axial and 50 µm of lateral resolution) by using frequencies between 60 – 100 MHz, nevertheless the penetration depth can be diminished until 4 or 5 mm [3, 6]. 3) Doppler ultrasonography, mainly used to evaluate the internal vasculature; mainly the flow through the retinal artery, is used in the diagnose of open angle glaucoma and to evaluate ocular fondus too.[3].

Nevertheless, the potential use of A-scan ultrasound as a diagnosis tool of ocular diseases is a wide research field. A-scan ultrasonic inspection has the advantage to be a relative low cost tool due to the required hardware is not as expensive as other modalities more sophisticated. In this case, the relevant difficulties are overcome with specialized signal processing techniques. In this work an initial evaluation technique, based on A-scan simulated signals, to assess an early stage of open angle glaucoma or to monitor treatments of angle closure glaucoma is presented. The novelty is that with a relatively simple and low cost equipment, required to acquire an A-scan register, and with a high resolution processing techniques, it could be possible to support diagnosis and treatment of this disease. Signals simulation and processing were performed using Matlab 2016 (Mathworks Inc.).

Glaucoma is a critical disease, due to it is a frequent cause of blindness and in case of open angle type, it is a silent condition that avoid the patients perceive any symptom until several scotomas appear. There are two kinds of glaucoma: the open angle and the angle closure glaucoma (OAG and ACG, respectively). There are complex physiological and anatomical mechanisms involved in glaucoma, in general, it is caused by an increase of aqueous humor due to the partial (OAG) or complete (ACG) closure of the iridocorneal angle, which is the path where the aqueous humor is expelled through the Schlemm's canal and trabecular meshwork. In a healthy case, the normal aqueous flow is about 2 µL/min, when the angle is partially or completely obstructed, this flow diminished, and it produces an increment of ocular volume and intra-ocular pressure (IOP). The rigidity

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of the eye wall is about 0.77 mmHg/μL, then large changes in IOP can be expected with small increases of volume [1].

II. Methodology

A. Signal Simulation

The main structures of the human eye to be considered as interfaces during an ultrasonic A-scanning are: the anterior and posterior surfaces of cornea (with a typical separation of 0.5 mm between them), the anterior and posterior surface of lens (with a typical separation of 4 mm between them) and the retina. Then, it can be expected a multi-echo signal composed by two echoes originating from both cornea surfaces followed by other two echoes corresponding to both lens surfaces and finally one set of superimposed echoes reflected from the three layers that compound the eye wall at the ocular fondus.

To generate simulated signals that could be used for the objective of this work, the following assumptions were taken:

- The acumulation of aqueous humor is given in the anterior segment of the eye, which is limited between the cornea and the lens. Then, in case that the flow of aqueous humor is interrupted for the partial or complete obstruction of the iridocorneal angle, there is an increase of the volume in this segment that directly represents an increase of the total volume of the eyeball. The volume of the posterior segment (vitreous chamber contained between the lens and the retina) is constant.
- Due to volume rise in the anterior segment, the analysis will be focused in two echoes that will be displaced in time as a result of volume change: the echo due to anterior surface of the cornea (1) that will be displaced toward the time zero direction; and the echo due to posterior surface of lens (4) toward the echo produced by the retina (5). The total effect will be a separation between echoes represented with number (1) and (4) in Fig. 1.
- The initial volume of the eyeball, in the healthy condition, is of 6000 μL. To simulate the extreme case of angle closure glaucoma, increments of 2 μL will be considered.

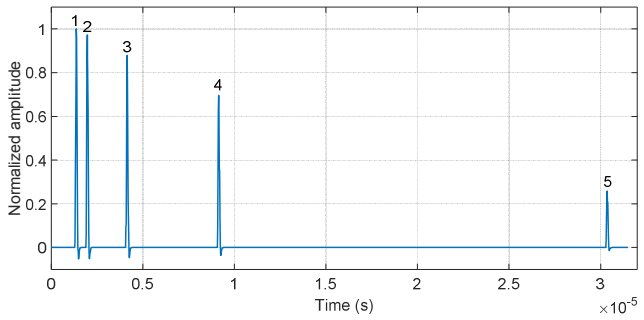

Fig. 1. Generic representation of echoes from the anterior surface of the cornea (1), posterior surface of cornea (2), anterior surface of lens (3), posterior surface of lens (4) and retina (5).

- To estimate the initial time of flight, *Tof*, between involved echoes and its variations due to volume rise, the following equation is taken:

$$Tof=[48V/(\pi c^3)]^{1/3} \quad (1)$$

where V is volume, and c is the speed of sound in the medium. This equation was deduced substituing the volume equation of a sphere in the velocity equation ($c=2*d/tof$), where d is the sphere diameter.

- The central frequency considered for the simulated ultrasonic echoes was of 10 MHz, that is a typical frequency used in A-scan imaging of eye.
- Tension of the eye wall due to the IOP and its variation resulted from volume increments were not taked into account, then the changes in the cornea thickness neither. It was supposed that the effect of this issue in the displacement of anterior surface corneal echo is negligible for the purpose of this analisys.

Once these considerations were stablished, it was necessary to define the basic waveform, ε, of the echo signal produced by the interfaces of interest. It was defined as [7,8]:

$$\varepsilon=(t)exp(-4\beta^2t^2)sin(2\pi ft) \quad (2)$$

where t is time, β is the bandwidth and f is central frequency. Considering the second assumption described above, a set of ten multi-echo signals were simulated for a volume range between 6000 μL to 6018 μL in steps of 2 μL. In Fig 2a, the set of simulated signals are graphed, where the anterior corneal echo, the posterior lens echo and the retina echo can be appreciated. An initial distance to the first interface (first echo) of 10 mm were inserted in all signals.

To appreciate the displacement between echoes 1 and 4 due to volume rise, in Fig. 2b and Fig. 2c, the signal segments containing both echoes are presented.

B. Signal processing

To obtain the time displacement between echoes 1 and 4, two methods were employed: the cross correlation and the spectral estimation.

As it is well known, the correlation sequence estimates the level of coincidence between two waveforms, giving a maximum value in a displacement (lag) where these waveforms are identical. In this work, the correlation sequences between the segment containing the first echo for the initial volume and the segments containing the first echo for the subsequent volumes were computed. The obtained results were the displacements of the first echo (it means of the anterior surface of cornea) due to volume rise. The same procedure was applied to the second echo, and displacement of the posterior surface of lens due to volume rise were obtained.

The second method is based on the spectral analysis of the signals by means of a high resolution parametric estimation of the power spectral density (PSD) [9,10]. There is a frequency related to the temporal separation between two echoes present in a signal. Considering that the time interval between echoes depends on the separation between the interfaces that produces those echoes, a relation between the frequency and this separation can be established. For the case of this work, this relation can be defined as:

$$\chi = c / (2\xi(V)) \quad (3)$$

Where χ is the frequency and ξ is the separation between the anterior surface of the cornea and the posterior surface of the lens. As it is defined in (3), ξ is a function of volume.

The power spectral density of segments containing echoes 1 and 4 were obtained by mean of the Burg algorithm [9], with a frequency resolution of 238.4 Hz and a model order equal to N/2.5 (following the criteria determined by Ulrych and Ooe), where N is the number of samples of analyzed signal.

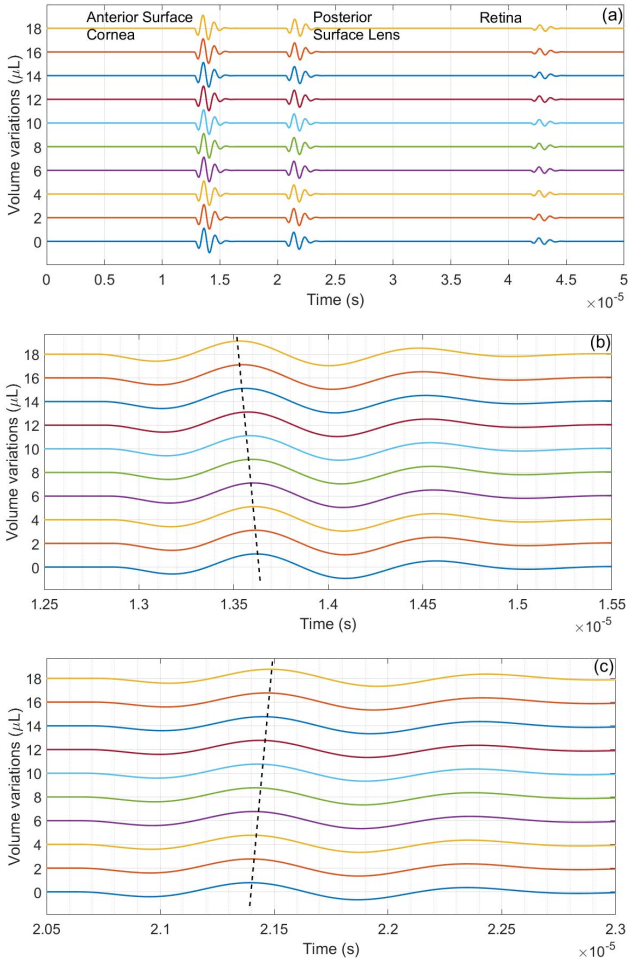

Fig. 2. (a) Simulated ultrasonic signal considering the anterior surface of cornea, the posterior surface of lens and retina echoes. A set of signal simulated for different volume increments. Zoom of the first (a) and second (c) echoes. The dotted line indicates the displacements of each echo (b), (c).

III. Results

A. Displacements obtained with cross correlation method.

In Fig. 3 and Fig 4, the first and the second normalized echo signals are showed for anterior surface of cornea and posterior surface of lens, respectively. In both cases, the first echo signal, Fig. 3a and Fig. 4a, is assumed as a reference. And these references were correlated with the other nine signals. For instance, in the Fig. 3b and Fig. 4b the second signal for each surface is showed. And, in the Fig. 3c and Fig. 4c, the correlation sequence is presented. In the case of anterior surface of cornea, the subsequent echoes from the reference echo were advanced. By this way, maximum value of correlation sequence occurs in negative times (red dot in Fig. 3c). By other hand, for the posterior surface of lens, the subsequent echoes from the reference echo were delayed. So, the maximum value of correlation sequence occurs in positive times (red dot in Fig. 4c).

Once, the temporal changes of signals were estimated from cross-correlation method, the relative displacement for each surface was obtained, Fig. 5. The anterior surface of cornea suffers a negative displacement from reference position and the posterior surface of lens presents a positive displacement. From point of view of the ultrasonic transducer it means that surface of cornea is approaching, and the surface of lens is moving away. In Fig. 6, is showed the total separation between the anterior surface of cornea and posterior surface of lens given the change of volume.

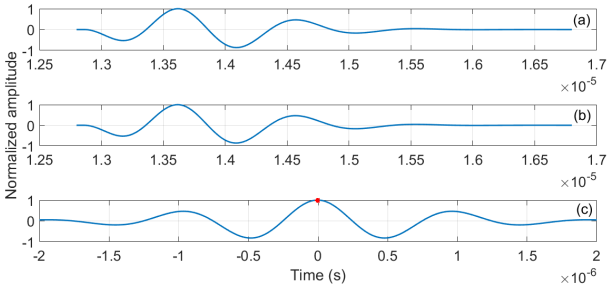

Fig. 3. Echo of anterior surface of cornea at a volume of 6000 µL (a) and at a volume of 6002 µL (b). Cross correlation sequence of both echoes (c)

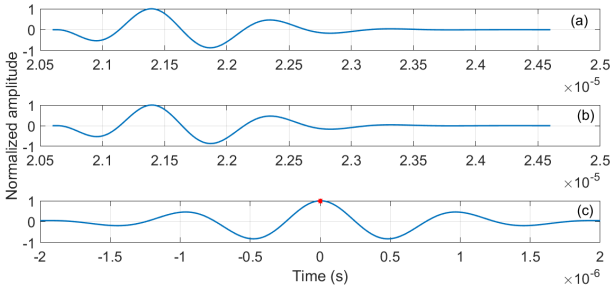

Fig. 4. Echo of posterior surface of lens at a volume of 6000 µL (a) and at a volume of 6002 µL (b). Cross correlation sequence of both echoes (c).

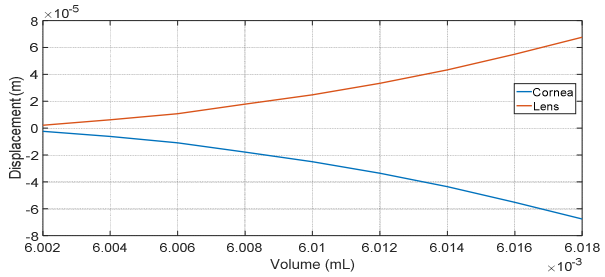

Fig. 7. Relative displacement of anterior surface of cornea (blue) and of posterior surface of lens (red) obtianed by means of correlation method.

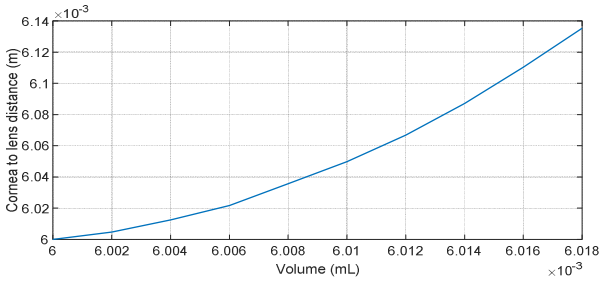

Fig. 6. Total separation between anterior surface of cornea and posterior surface of lens obtained by means of correlation method.

B. *Displacement obtained with spectral analysis method.*

Fig. 7 shows the ten PSDs obtained as a result to apply the Burg algorithm to simulated signals. Each PSD correspond to an echo signal simulated for a specific intra-ocular volume in the range between 6000 – 6018 µL. The harmonic peaks of frequency χ can be appreciated, as well as their shifts (indicated by the dotted line) related to the inter-echo separation variation.

In Fig. 8, the behavior of the 8th harmonic of χ regard with the intraocular volume is graphed. Frequency peak value diminished with the volume rise. This is due to an increase of volume produces that separation between ocular structures augments, which result on a temporal separation between echoes produced by these structures and a decrease on the frequency peak value. In Fig. 9, the separations obtained with (3) are graphed. An initial and final estimated separation of 6.047 mm and 6.173 mm respectively were detected by means of this

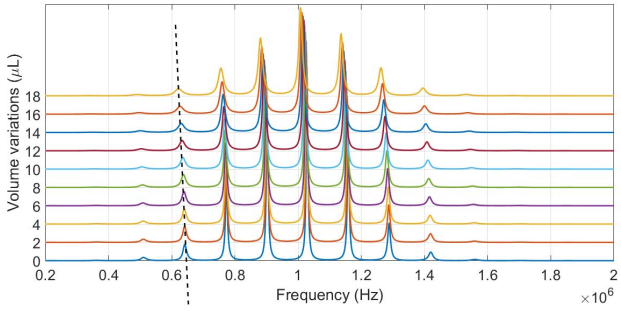

Fig. 9. PSDs obtained from spectral analysis of ten simulated signals (the segment containing cornea and lens echoes) at different volume.

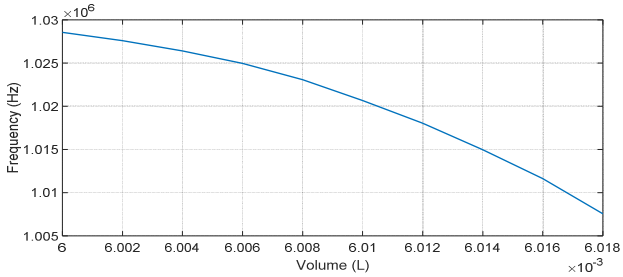

Fig. 8. 8th harmonic behavior with volume rise, obtained with spectral method.

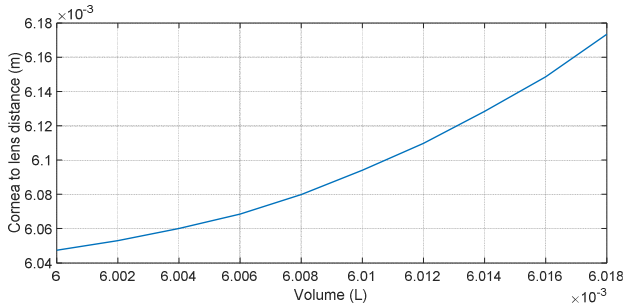

Fig. 5. Total separation between anterior surface of cornea and posterior surface of lens obtained by means of spectral method.

method. As well as the correlation method the obtained relation between volume and distance is not linear.

IV. Conclusions

Ultrasonic signals were simulated considering a constant volume rise in the range between 6000 and 6018 µL, in steps of 2 µL, to simulate a glaucoma condition. These simulated signals were processed by means of two methods: correlation technique and spectral analysis.

Both methods were implemented to obtain the distance between the anterior surface of cornea and the posterior surface of lens. With correlation method, the distance between these two structures estimated for the first volume increment (6002 µL) was 6.049 mm, while with spectral analysis the estimation was 6.053 mm; the real simulated distance at this volume was 6.050 mm. This represent an error of 0.02 % for the correlation method and 0.05% for the spectral method. These errors for the last volume evaluated (6018 µL) are 0.0 % for the correlation and 0.16 % for the spectral method.

A minimum incremental change of 953.67 Hz was detected for the 8th harmonic, and it corresponds to the increment of the first 2 µL; with the given PSD resolution (238.4 Hz) a theoretical resolution in volume increase of 0.5 µL could be detected by means of this method. This resolution could be improved taking a harmonic of higher order if it is required. The resolution of the correlation method, considering a sampling frequency of 1 GHz is 0.3 µL and it is fixed.

Both methods present a suitable resolution considering that the expected volume change is about 2 µL, which is an acceptable increment in glaucoma, taking into account that the regular aqueous outflow rate is 2 µL/min [1].

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