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The influence of age related changes to ultrasound attenuation of human eye lens

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Introduction

The vertebrate eye lens is unique in that it is a transparent yet cellular organ. One of the prerequisites for transparency is loss of cell organelles, which scatter light. The lens of the eye is a transparent tissue due to the highly organized arrangement of structural proteins, called crystallins. The cortex of the lens contains the most recently synthesized crystallins the nucleus contains the oldest. The arrangement of these crystallins and fiber cells provides the refractive index necessary to focus images on the retina [1]. If this arrangement becomes disrupted, the lens may lose its transparency and develop the opacities known as cataract. Progressing cataract is leading to the changes in the tissue characteristics, such as light scattering and lens hardness. Lens hardness may depend on many factors such as aging, degree and extent of cataract formation, which are interlinked with changes in the nature of the lens proteins, compactness of the fibers, and other biochemical changes. Nuclear color and age have been reported as clinical markers for lens hardness. Additional evaluation using noninvasive techniques may aid further evaluation of hardness of a cataractous lens. Noninvasive tools, such as ultrasonography, that are based on tissue-density properties may provide useful information about lens hardness. Ultrasound pulses are attenuated, mainly as a result of the absorption and scattering as they propagate through the tissue. The rate of attenuation depends on the density (molecular weight and size), tissue structure, and ultrasound wave frequency. Density and hardness of the lens can be evaluated from measurements of acoustic characteristics. The attenuation of ultrasound waves by the human crystalline lens correlate with its hardness [2].

We intended to characterize cataract by using the acoustic parameters of biological tissues such as velocity and attenuation coefficient. Ultrasound examination is widely used in ophthalmology. Piezoelectric crystals generate ultrasound waves of 5 - 50 MHz. Short pulses of 2 to 3 cycles are send from transducer into the eye. These pulses propagate through the tissues of the eye with the speed that is inversely proportional to the density and elasticity of the eye. Ultrasound pulses are attenuated as the result of absorption and scattering as they propagate through the tissue. It is well known that in soft tissues, the attenuation coefficient is approximately proportional to the frequency. In other words, the high frequency components of the echo signal are attenuated more than the lower frequency components. As the result of studies, it has been shown that the proportional constant of the attenuation coefficient with regard to frequency, which is often referred to as the attenuation slope, differs with kind of tissue and the tissue condition [3]. Investigations of the acoustic velocity and the attenuation in eye tissue were performed [4]. This study has shown that acoustic parameter such as the ultrasound velocity and the attenuation coefficient differ in different eye tissues (cornea, lens, retina, choroid, sclera and vitreous body). The study of tissue characterization is based on this fact and applied to the diagnosis of intraocular tumours. As to the attenuation coefficient of the crystalline lens similar characteristics are likely to be found. Estimation of the ultrasound attenuation in a human nuclear diabetic cataract [5] has shown the possibility to use acoustic parameters as "second opinion" for physicians decision support.

Sugata Y. examined normal and cataract lenses and suggested the possibility of diagnosing cataract by measuring the attenuation characteristics of the lens [6]. The changes of ultrasound attenuation accordingly to the severity of cataract could make it possible to classify it to the stages and sound attenuation can be used as a criterion for the diagnosis of cataract. The idea about quantitative and early detection of cataract from echo signals was expressed. Therefore, further developments for the lens examination in-vivo are needed.

We measured the attenuation coefficient of the lens and to investigate of the distribution of its value in different patients groups. We used ultrasound examination and calculation of the attenuation coefficient for early stages of cataract detection.

Materials and methods

The sample consisted of 75 patients (94 eyes). The examination was performed in Eye Clinic of Kaunas University of Medicine. According to the cataract severity patients were sorted into three groups:

- healthy patients – "healthy" group (32 eyes),
- early cataract stadium – "initial cataract " group (32 eyes),
- age related cataract – "immature cataract " group (30 eyes).

Patients age varied between 24 and 35 years in the healthy patients group and between 60 and 87 years in the other two groups.

Ultrasonic signal attenuation

In order to get echoes as radio frequency (RF) signals, we used ultrasonic equipment *Mentor*^{TM} A/B ultrasonic imaging system (Mentor Advent A/B scan) with 7 MHz A-mode probe radio frequency echo-signals from a lens were digitized by the TEKTRONIX 220 oscilloscope at the sampling rate 250 MHz and 8 bit amplitude resolution, bandwidth for analog signal was 100 MHz. Manual trigger of oscilloscope was used according to sound notice from the system about the probe correct alignment to the eye axis. In-vivo examination of cataract lens was performed and the ultrasound attenuation coefficient was calculated. The echo signals from the anterior and posterior interfaces of the lens were cute down by the time windows (Fig. 1).

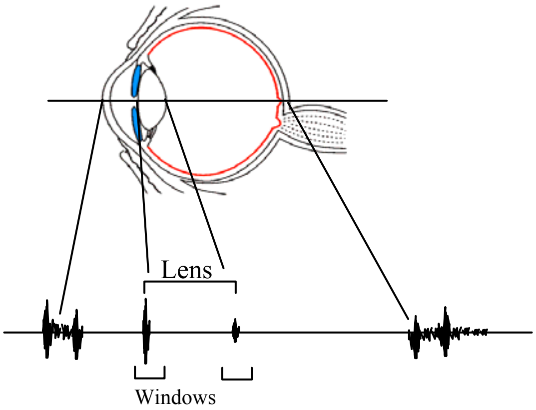

Fig. 1. **Illustration of echo signal from anterior and posterior lens interfaces**

Signal averaging was not used, but five single signals were acquired (Fig. 2). In order to get reliable results, it is important carefully to assess the quality of echo signals. We checked the amplitude of the echoes in locations, i.e., the cornea, the two interfaces of the lens, and the posterior pole by a monitor display. Echoes were stored when the amplitude of all four were greater than a certain level.

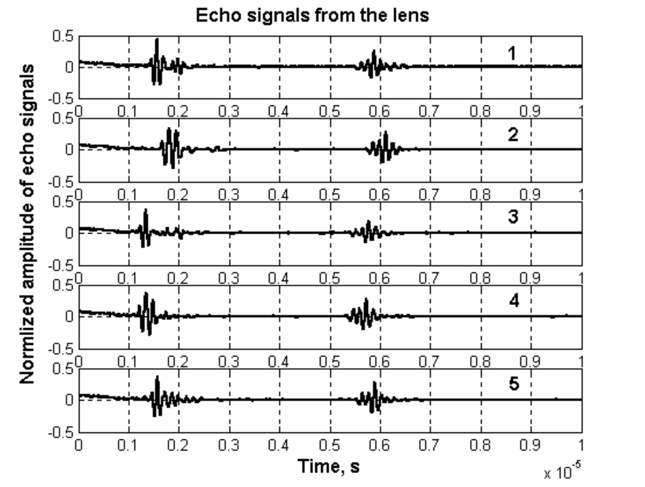

Fig. 2. **Waveforms of five echo signals received from the same lens interfaces**

The contact method is used through the open eye after blocking the blink reflex. The patient is asked to look at the red LED (light emitting diode) in the probe. The height and angle of probe is adjusted as close to the visual axis as possible. The probe is applied to the cornea. This position aids last-minute adjustments in alignment and helps to detect when the exact point of contact is achieved. When proper coupling has been achieved, the frequency of the sound rises on-axis (i.e., good), measurements are approached. When the tone changes to a higher-pitched tone, the Advent A/B system has identified the necessary ocular structures and positioned on-axis. The higher pitched third tone locks the correct reading and freezes the display. It is, however, not easy exactly to capture the axis due to unrest of the eyes. Then sequentially we selected five echo signals that satisfied the above criteria. The selected signals from the lens have been recorded. The digitized echo signals were used for off-line processing with the Matlab Numeric Computation and Visualisation software.

Each RF signal from the two interfaces is transformed to logarithmic power spectra (Fig. 3 and Fig. 4). The difference between these two spectra is obtained to eliminate the properties of the transducer and to extract attenuation characteristics. However, the spectral difference is not smooth since scattering and reflection characteristics still remain.

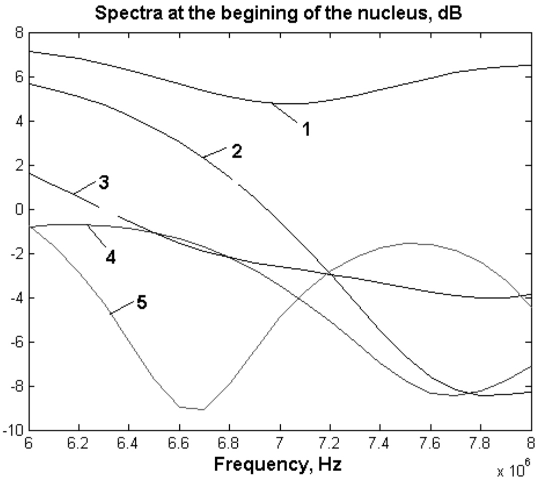

Fig. 3. **Spectra $S_{AN}(f)$ in the beginning of the analyzed lens, there power spectra numbers from 1 to 5 corresponds to the signals in Fig.2**

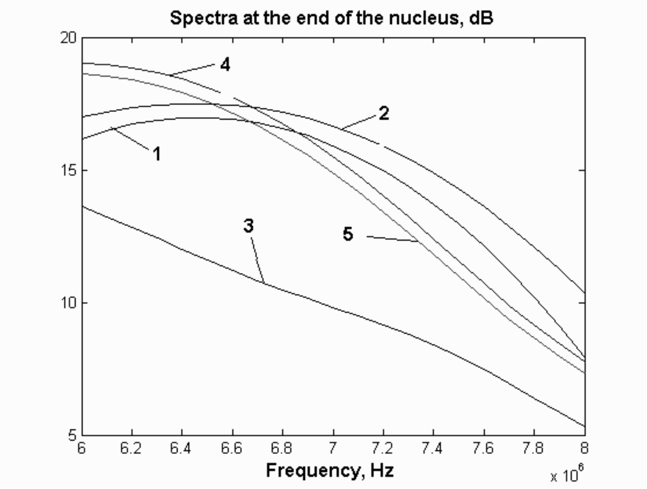

Fig.4. **Spectra $S_{PN}(f)$ in the end of the analyzed lens, there power spectra numbers from 1 to 5 corresponds to the signals in Fig.2**

The assumption that attenuation frequency function is linear $\alpha(f)=\beta \cdot f$ has been made. The attenuation coefficient β has been calculated from the logarithmic spectra difference, taking into account spectra of echo signals from anterior $S_{AN}(f)$ and posterior $S_{PN}(f)$ nucleus interfaces, the distance between interfaces d and the frequency range f_2-f_1. To the frequency function of the logarithmic spectrum difference $S_{AN}(f)$-$S_{PN}(f)$ the least-squares straight line fit $\alpha_L(f)$ was applied. The difference between the two spectra is obtained to eliminate the properties of the transducer and to extract attenuation characteristics. However, the spectral difference is not smooth since scattering and reflection characteristics still remain. Last, the attenuation coefficient β was calculated:

$$\beta=[\alpha_L(f_2)-\alpha_L(f_1)]/[2d\cdot(f_2-f_1)]$$

The attenuation coefficients β for all five stored echo signals have been calculated and the averaged value of the attenuation coefficient was obtained (Fig. 5).

The thickness of nucleus investigated was assessed taking into account the first zero-crossing instants in the echo signals and the sound velocity in cataract lens c=1620 m/s. The echo signals from anterior and posterior interfaces of the lens nucleus where selected manually with the constant time window duration of 1.024 μs.

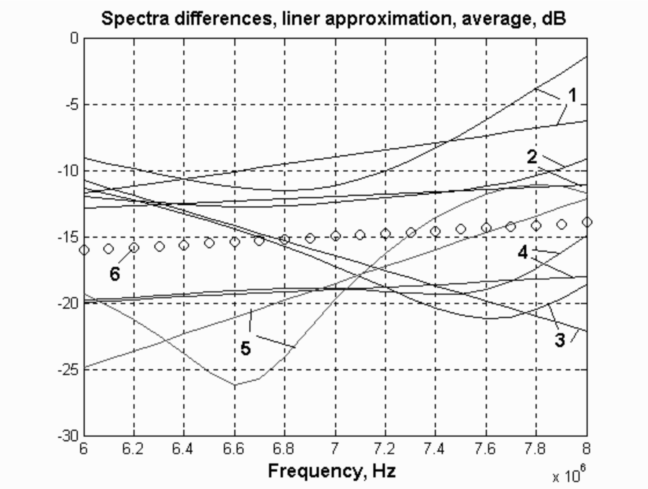

Fig. 5. **Spectra differences, linear approximation and average, there curves 1-5 – spectra (Fig. 2 and Fig. 3) differences and linear approximation of power spectra, curve 6 – average of five linear approximation curves 1-5.**

Results

The thickness of lenses and the attenuation coefficient β were calculated for all 75 patients in 3 groups using spectral difference measurement method described above. We found that the mean thickness of lenses is near the same in all groups and it changes between 4.42 mm and 3.58 mm. In Fig.6 the results of the mean thickness measurement in different groups are presented. However, we found that increase of a lens thickness is characteristic to cataract (initial and immature) groups (Fig.7). The least mean lens thickness of 3.58 mm was found in the healthy patients group. Mean lenses thickness of 4.42 mm and 4.22 mm were found in the initial cataract and the immature cataract groups respectively.

The ultrasound attenuation coefficients in all groups were measured as well. Distribution of the attenuation coefficients β in all groups is presented in Fig. 8.

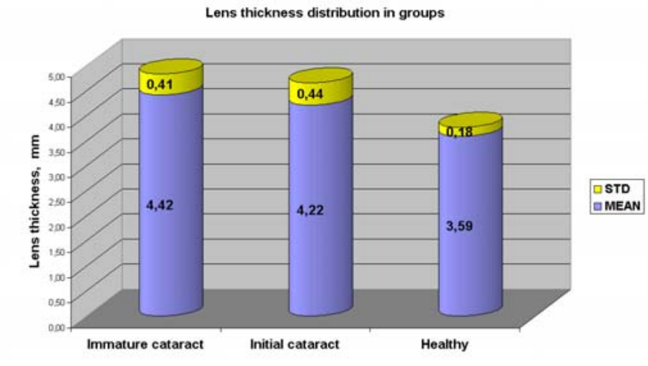

Fig.6. **Mean lens thickness distribution in all investigated groups**

It is shown that the ultrasound attenuation coefficient is significantly higher in the initial cataract and immature cataract groups, where β has been found 7.65 ± 1.33 dB/(cm MHz) and 6.94 ± 1.20 dB/(cm MHz) respectively. Significantly lower mean value of the attenuation coefficient has been found in the healthy group. In this case the mean value is 5.88 ± 1.00 dB/(cm MHz). The results of the mean ultrasound attenuation coefficient calculation are presented in Fig.8.

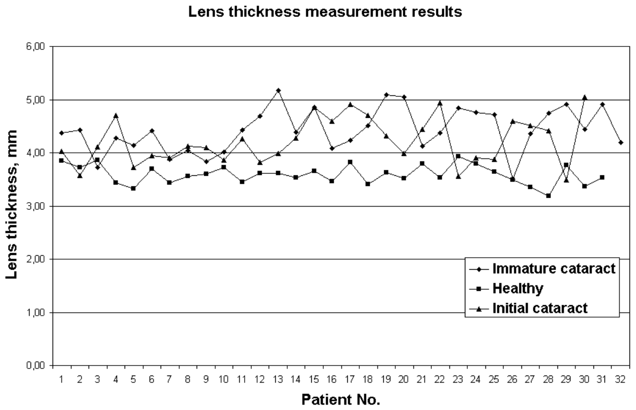

Fig.7. **Curves of lens thickness measurement distribution**

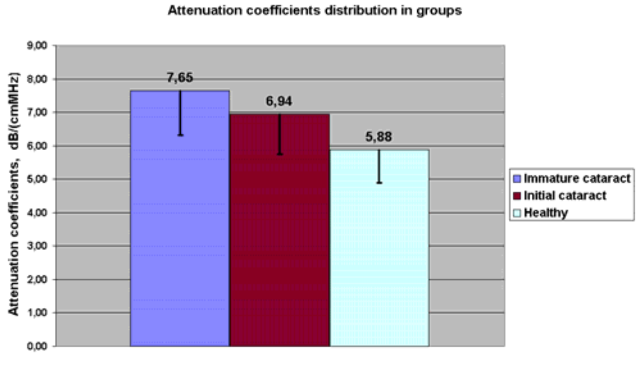

Fig.8. **Results of mean attenuation coefficients distribution in groups**

The highest value of the mean attenuation coefficient was found in the immature cataract group, but the difference in the mean coefficient value between the initial and immature cataract groups is low – 0.71 dB/(cm MHz) comparing with the standard deviation of calculations – 1.33 dB/(cm MHz). According to these results we cannot use the attenuation coefficient for differentiation of severity of cataract yet. The new improved diagnostic signal acquisition technique and introduction of more precise calculation algorithms should be done to make it possible to classify cataract lenses to the severity stages. But even now ultrasound attenuation can be used for the diagnosis of cataract.

Discussion

Cataract is a very frequent disease of a human eye and its diagnosis is not difficult. The opacities of the lens are seen with the slit lamp. But there is no any objective examination method in order to determine the degree of the intensity of cataract. Ultrasound attenuation is largely influenced by the presence of high-molecular-weight compounds and in cataract lenses increased protein aggregation contributes to the hardening of the lens and to increased ultrasound attenuation. So, the changes of the ultrasound attenuation accordingly to the severity of cataract could make it possible to classify it to the stages. The ultrasound attenuation coefficient is an indirect rate of the hardness of the lens nucleus. With the advent of modern techniques for cataract surgery, the hardness of a cataractous lens has become clinically relevant. Changes in the lens structure associated with cataract formation, aging, and lens hardening can also influence characteristics of ultrasound wave. This method could be valuable when making the prognosis of the operation term and even operation methodic. Methods for in vivo evaluation of lens hardness have clinical and research applications and must be further developed.

Lövström B. compares three methods for estimation of the ultrasonic attenuation in soft tissues [7]. The methods are called the Zero Crossing method, the Spectral Difference method and the Time Domain method. Comparisons are made for computer-generated signals as well as for signals from tissue equivalents and *in vivo* signals. For both simulated and measured signals the Time Domain method showed considerably less relative variance than the other methods. The *in vivo* measurement also showed that the Time Domain method seems to have less sensitivity to strong specular reflectors. First, the Time Domain method utilizes the entire received signal while the Spectral Difference method does not use the data between the windows in the temporal signal and also selects a pass band in the frequency domain, which may delete some information. The Zero Crossing method loses information while it is only estimating the center frequency and assuming a Gaussian shape of the power spectrum. Second reason - the Time Domain method estimates a combination of two echo signal attenuation parameters, which reduces the relative variance compared to estimating only one when the Spectral Difference and the Zero Crossing methods are used. The Time Domain method has the best accuracy of the methods.

In our study the difference between two spectra is obtained to eliminate the properties of the transducer and to extract attenuation characteristics. However, the spectral difference is not smooth, since scattering and reflection characteristics still remain.

A very important issue in lens ultrasound examination is a proper alignment of the acoustic axis of the probe with the axis of the lens. The echo signals acquired in cases of poor alignment of axes where eliminated from a further analysis. Misalignment of axes is recognized from significant changes of waveforms and high variability of the estimated attenuation coefficient. Therefore, further developments for the lens examination in-vivo are needed. To achieve better reliability of measurements the specialized triggering of acquisition of radio-frequency echo signal must be organized between the A/B imaging system and a digital oscilloscope.

Changes of ultrasound attenuation accordingly to the severity of cataract could make it possible to classify it to the stages and sound attenuation can be used as a criterion for the diagnosis of cataract. Its main objective is to aid the physician in decision making, e.g. in detecting pathological changes within an organ or following a recovery process after a disease. It is still premature to recommend this method for evaluation of cataract stages, as it is needed to investigate the association between attenuation in the lens and different cataract types analyzing many data and improving signal acquisition technique.

Conclusions

There is significant difference between ultrasound attenuation in groups with cataract (initial and immature) and healthy group. Differentiation of cataract stadium using the attenuation coefficient is complicated, because difference of the attenuation coefficient in both cases is low compared with measurement uncertainty.

The analysis of the results suggests the possibility for investigating non-invasively cataract by measuring the ultrasound attenuation characteristics of the lens.

It is important to continue investigations of the cataract differentiation trying to use for ultrasonic echo signal attenuation measurements the Time Domain method.

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Su amžiumi susijusių pokyčių įtaka ultragarso slopinimui akies lęšyje

Reziumė

Ištirtas ultragarsinio diagnostinio signalo slopinimas akies lęšyje. Įvertinta kataraktos subrendimo įtaka ultragarso slopinimui. Ištirti 94 lęšiukai žmonių, sergančių katarakta bei sveikųjų. Lęšiukas ištirtas ultragarso A-sistema, naudojant 7 MHz dažnio daviklį. Ultragarso slopinimo koeficientas lęšiuko branduolyje apskaičiuotas ultragarso signalų spektrinės analizės būdu.

Nustatyta, kad ultragarso slopinimo koeficientas didesnis katarakta sergančiųjų grupėje. Manoma, kad tai sąlygoja šia liga sergančių žmonių lęšiuko drumstumas ir senatviniai pokyčiai. Ultragarso slopinimo koeficiento vertė leidžia kokybiškai įvertinti kataraktos drumstumo laipsnį bei branduolio kietumą. Siūloma šiam tikslui naudoti tikslesnį - koreliacinį - metodą bei automatizuoti diagnostinio signalo įvedimą.

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