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Cataract measurement by estimating the ultrasonic statistical parameter using an ultrasound needle transducer: an *in vitro* study

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Abstract

A cataract is a clouding of the crystalline lens that reduces the amount of incoming light and impairs visual perception. Phacoemulsification is the most common surgical method for treating advanced cataracts, and the optimal phacoemulsification energy is determined by the lens hardness. A previous study proposed using the ultrasonic Nakagami image to complement the B-scan for distinguishing different degrees of lens hardening. However, it is difficult to implement the use of an imaging probe to detect the lens during phacoemulsification surgery in a clinical situation. To resolve this problem, this study applied an ultrasonic needle transducer to estimate the Nakagami parameter as an alternative for characterizing the cataract lens. Cataracts of porcine lenses were artificially induced *in vitro*, and the Young's modulus, backscattering intensities, and the Nakagami parameters were measured. The results showed that the backscattering intensity was not correlated with Young's modulus. In contrast, the average Nakagami parameter increased from 0.34 to 0.95 with increasing Young's modulus of the lens from 1.71 to 101 kPa. The above findings showed that the Nakagami parameter estimated with a needle transducer may be useful in differentiating different degrees of lens hardening, and implied that determining the optimal ultrasonic energy during clinical cataract surgery is possible if the needle transducer can be combined with the phacoemulsification probe to estimate the Nakagami parameter.

Keywords

ultrasound; needle transducer; cataract; Nakagami parameter

1. Introduction

A cataract is a clouding of the normally transparent crystalline lens of the eye due to factors such as aging, lens damage and heredity. The formation of a lens cataract can be treated as a process of fibrosis, whereby both protein aggregation and fiber coemption occur inside the lens (Tabandeh *et al* 2000, Kanski 2006). The lens fibrosis not only results in blurred vision

but also increases the hardness of the lens. Phacoemulsification is typically applied to advanced cataracts to replace the turbid lens of the patient with an artificial one so as to recover the vision. The lens hardness influences the optimal ultrasonic energy in phacoemulsification, where optimizing the energy improves the efficiency of the surgery and reduces the injury to the lens capsule and corneal endothelium. For these reasons, evaluating the lens hardness is critical for a successful phacoemulsification surgery.

Ultrasound is an effective approach to objective evaluation of the hardness of the cataract lenses. The frequently applied methods are based on measuring ultrasonic attenuation and sound speed, which tend to increase with the hardness of the cataract lens (Tabandeh *et al* 2000, Huang *et al* 2007a, 2007b, 2009). High-frequency ultrasound B-mode imaging can also be used to locally monitor cataract formation. In general, the echo intensity of the cataract lens differs from that of the normal lens, for optical opacities produce acoustic inhomogeneity, with the cataract area exhibiting high echogenicity (Coleman *et al* 2006). However, the echo intensity may not be a reliable indicator, due to inadequate reproducibility for the grading and staging of lens hardening. For instance, our previous study, which investigated cataracts of porcine eyes *in vitro* using high-frequency ultrasound, showed that the B-mode image merely revealed the structures of the cataract lens, and it was difficult to determine the lens hardness (Tsui *et al* 2007). Compared to the B-scan which shows the backscattered intensity, we found that the Nakagami parametric image based on the statistical distribution of the backscattered envelope has a different performance in visualizing the degree of lens hardening. Recall that the Nakagami image is a complementary image for the B-scan, providing information associated with the scatterer arrangements and concentrations in tissues (Tsui and Chang 2007). It has been shown that high-frequency Nakagami imaging could distinguish both global and local variations in lens hardness (Tsui *et al* 2007).

Recently, we encountered problems when we attempted to utilize the Nakagami image in a clinical situation. First, the signal-to-noise ratio (SNR) of the ultrasonic backscattered echoes from a lens *in vivo* is not as good as that *in vitro*, because the existence of some eyeball tissues (e.g., iris, cornea and anterior chamber) will cause the acoustic attenuation effect. The poor signal quality is unfavorable to an accurate estimation of the Nakagami parameter (Tsui *et al* 2005, 2008). Although the SNR can be improved by enhancing the transmitting acoustic power and the transducer focusing, the safety considerations prohibit such an approach, and the resolution in the far-field of the transducer may further degrade due to the diffraction effect. Second, imaging the lens *in vivo* requires placing a transducer outside the eyeball to scan. Although the high-frequency transducer is small in size, transducer scanning for imaging would interrupt the surgery. Such an operation is difficult to combine with phacoemulsification for simultaneously performing surgery and evaluating the lens hardness to allow an automatic adjustment of the surgery energy.

To resolve the above problems, using an ultrasonic needle transducer instead of using an imaging transducer to estimate the Nakagami parameter for measuring the lens hardness may be a better solution for clinical purposes. This proposed approach could have three advantages. First, a needle transducer has a much smaller diameter (typically < 1 mm). This smaller diameter makes possible the combination of the ultrasonic transducer with the invasive phacoemulsification probe for simultaneously treating and measuring the lens hardness. In particular, the lens hardness may be locally different. The combination of the needle transducer and the phacoemulsification probe for real-time feedback to optimize the phacoemulsification energy by continuously estimating local lens hardness may provide better treatment efficiency. Second, the needle transducer with a smaller size is favorable to a higher-frequency design. In a condition of using the same transducer element and backing materials, increasing the frequency by reducing the thickness of the element can shorten the

pulselength to enhance the axial resolution, making the Nakagami parameter sensitive to the variation in scatterer properties (Tsui and Wang 2004). Third, using a needle transducer to invasively measure the lens can reduce the loss of acoustic energy due to wave propagation. This may improve the performance of the backscattered intensity to detect the hardness of cataract lens. For the above reasons, this study explored the feasibility and performance of using an ultrasonic needle transducer to measure the backscattered intensity and the Nakagami parameter for quantifying the hardness of a cataract lens.

2. Materials and methods

2.1. Lens sample

Porcine eyes collected from a local slaughterhouse were used as experimental samples. A surgical knife was used to separate the lenses from the eyes. Each lens was then washed carefully with a saline buffer solution to remove the iris remnants and adhering vitreous. To induce the cataract, the lenses were immersed in a mixture solution of ethanol, 2-propanol, and formalin at a ratio of 3:3:4. With increased immersion time, the lens hardness increased accordingly (Sugiura *et al* 1999). We used a total of 28 independent lens samples for seven groups, comprising a control group and six groups with immersion times of 20, 40, 60, 80, 120 and 160 min, respectively. Each group was composed of four samples.

2.2. Experimental procedure

Prior to ultrasonic experiments, the hardness of each cataract lens was estimated by measuring the Young's modulus using a commercial mechanical device (ElectroForce 3100 Test Instrument, Bose Corporation, MN). The lens, placed on a flat holder, was compressed by a circular metal disk, which was driven by a linear motor. Then the compression force and resulting deformation of the lens were measured using the built-in sensors in the device. The strain rate of measurement system was 0.02 s^{-1} . The relationship between the stress and strain was calculated, with the strain defined as the ratio of the total deformation to the initial thickness. Young's modulus was computed from the slope of the stress-strain curve.

Subsequently, the lens sample was placed on a rectangular polyurethane holder. The high-frequency ultrasonic needle transducer was mounted on a different holder. The transducer, with a central frequency of 47 MHz, has a -6 dB bandwidth of 53% and a pulselength of about $0.15 \mu\text{s}$. The -6 dB beam width is about 0.1 mm, which is calculated by wavelength F-number. The transducer specifications are summarized in table 1, and the details for the transducer design and test were described in the previous study (Zhou *et al* 2007). Both the needle transducer and the lens samples were immersed in the saline buffer solution at room temperature, as shown in figure 1. The distance between the needle transducer and lens was about 1.2 mm. The tip of the needle transducer was aimed at the center of the lens. The experimental setup is shown in figure 2. An ultrasonic pulser/receiver (Model 5900PR, Olympus NDT, Waltham, MA, USA) was used for driving the transducer and receiving the ultrasound backscattered signals from the lens. The signals were amplified to 40 dB by the built-in amplifier in the pulser/receiver, and digitized using a 14 bit analog-to-digital converter (ADC) (CS14200, Gage Applied Technologies, Inc., Lachine, QC, Canada) with a sampling rate of 400 MHz. Note that an electronic limiter (Matec Instruments Company, Northborough, MA) was placed in front of the ADC for protection purposes. The backscattering signals were also monitored on-line by a digital oscilloscope (9350AL, LeCeoy, Chestnut Ridge, NY).

Please refer to figure 3 for a typical ultrasonic backscattered echo from a cataract lens. For each lens, the acquisition of the backscattered signals ranged in the region of interest (ROI) after the reflection echo contributed by the lens surface was repeated 500 times for signal

averaging. The signal datalength corresponding to three times the pulselength is a requirement for correct estimation of the Nakagami parameter (Tsui and Chang 2007), and thus the ROI had a length of $0.45 \mu\text{s}$. Subsequently, the averaged signal was used to estimate the backscattering intensity and the Nakagami parameter. Five independent measurements were carried out to obtain the averages and standard deviations of the parameters. The beam width was used as the interval between each acquired backscattered signal to ensure that the five measurements were independent.

2.3. Parameter analysis

The estimations of both the backscattered intensity and the Nakagami parameter were based on the Nakagami distribution model. The Nakagami distribution $f(r)$ of ultrasonic backscattered envelope R is given by

$$f(r) = \frac{2m^m r^{2m-1}}{\Gamma(m)\Omega^m} \exp\left(-\frac{m}{\Omega} r^2\right) U(r), \quad (1)$$

where $\Gamma(\cdot)$ and $U(\cdot)$ are the gamma function and the unit step function, respectively. $E(\cdot)$ denotes the statistical mean, and the scaling parameter Ω and the Nakagami parameter m associated with the Nakagami distribution can be obtained from

$$\Omega = E(R)^2 \quad (2)$$

and

$$m = \frac{[E(R^2)]^2}{E[R^2 - E(R^2)]^2}. \quad (3)$$

The scaling parameter means the average power of the backscattered envelope. The Nakagami parameter is a shape parameter estimated from the second and fourth statistical moments of the backscattered envelopes to reflect the backscattered statistics. The backscattered statistics changes from a pre-Rayleigh distribution to a Rayleigh distribution as m varies from 0 to 1, and is a post-Rayleigh distribution when m is larger than 1 (Shankar 2000). The backscattered intensity and the Nakagami parameter were estimated by equations (2) and (3), respectively.

3. Results

The scaling parameter as a function of immersion time is shown in figure 4(a), to describe how the backscattering intensities of the ultrasonic echoes differed with the stage of the cataract. The results showed that the scaling parameter did not significantly change when the immersion time was increased from 20 to 160 min, indicating that the backscattered intensity may be weak to differentiate the hardness of the cataract lens. This can be further demonstrated by comparison of the scaling parameter and Young's modulus, as shown in figure 4(b). This result showed that the scaling parameter did not vary when Young's modulus was increased from 1.71 to 101 kPa, suggesting that the backscattering intensity measured by the 47 MHz needle transducer could not be used to discern variations in the lens hardness.

The average Nakagami parameter is plotted as a function of immersion time in figure 4(c), revealing that the Nakagami parameter increased from about 0.34 to 0.95 as the immersion time increased from 20 to 160 min, corresponding to a rate of increase of 0.0044 min^{-1} . This indicated that the statistics of the backscattered envelope varied from a pre-Rayleigh distribution to roughly a Rayleigh distribution as the immersion time increased. Based on the observations of the experimental data, the exponential increasing function was used to fit the Nakagami parameter as a function of immersion time. The correlation coefficient was 0.81, implying that the Nakagami parameter may be a good indicator of the lens hardness. To confirm this point, the Nakagami parameter versus Young's modulus of the cataract lens for different immersion times was plotted, as shown in figure 4(d). That plot showed that the Nakagami parameter increased from 0.34 to 0.95 as Young's modulus increased from 1.71 to 101 kPa, corresponding to a rate of increase of 0.0061 kPa^{-1} . The exponential fitting of the experimental data showed a correlation coefficient of 0.81, demonstrating that the Nakagami parameter estimated using the needle transducer performed better than the backscattering intensity in distinguishing variations in the hardness of the cataract lens.

4. Discussion

The real-time hardness detection of a cataract lens during phacoemulsification surgery for better cataract treatment is a challenging problem we want to resolve. In the phacoemulsification operation, a surgeon makes a small incision on the cornea and inserts a needle-thin probe into the cataract lens after removal of the anterior portion of the lens capsule. Lens emulsification is then achieved by linear or torsional vibrations of the tip of the probe, created by ultrasound waves, and the lens fragments are aspirated. In order to prevent problems that could be encountered during imaging of the lens during phacoemulsification surgery, this study explored the performance of the ultrasonic needle transducer in estimating the backscattered intensity and the Nakagami parameter for characterizing the cataract lens.

It has been shown that the backscattered intensity measured by a 35 MHz transducer cannot effectively differentiate each stage of lens cataract (Tsui *et al* 2007). This study used a 47 MHz needle transducer. In theory, the scattering cross section is approximately proportional to the fourth power of the ultrasonic frequency (Shung *et al* 1992), and therefore increasing the ultrasonic frequency should be able to improve the performance of the backscattered intensity in detecting variations in the lens hardness. However, the experimental results in figures 4(a) and (b) still showed that the intensity estimation is useless in cataract characterization. The increase in tissue hardness indicates that the tissue tends to be incompressible. However, this does not mean that the scatterers have the ability to produce stronger echoes. Indeed, some previous studies have demonstrated that the tissue hardness is difficult to differentiate by the intensity of the B-mode image (Ophir *et al* 1991, 2000, Righetti *et al* 1999). The same phenomenon was also found in the current results. The possible reason may be that even though the fiber coemption in the lens is strong, it is not sufficient to produce a significant change in lens echogenicity. Although a significant change in the backscattered intensity may be obtained by increasing both the ultrasound frequency and the transducer bandwidth (i.e. shortening the pulselength), the attenuation effect would become stronger at a higher frequency, making the backscattered intensity unreliable in the assessment of the lens hardness.

The current results showed that the Nakagami parameter has a better performance than the backscattering intensity in identifying lens hardness. The reason why the Nakagami parameter could differentiate the lens hardness has been discussed in our previous study (Tsui *et al* 2007). In brief, the process of cataract formation is associated with increases in the hardness and opacity of the lens due to increases in both protein aggregation and inner

fiber compaction (Tabandeh *et al* 2000). Thus, cataract formation may be treated as a process of change in the spatial arrangement and concentration of the scatterers corresponding to protein and fibers, and therefore we can indirectly estimate the scatterer concentrations in tissues by estimating the Nakagami parameter (Shankar 2000, Tsui and Wang 2004). The results in figures 4(c) and (d) indicated that the backscattered statistics with a short immersion time have a pre-Rayleigh distribution (i.e. $m \leq 1$), implying that little protein aggregation and fiber coemption are present in the initial stage of cataract formation. For cataracts induced by the long immersion, the backscattered statistics gradually approached a Rayleigh distribution (i.e. $m = 1$), representing a stronger protein aggregation and fiber coemption.

It is interesting that the needle transducer can also be used to calculate other acoustic parameters for evaluating the mechanical properties of the cataract lens. For example, a needle transducer with a metal reflector, which is attached to the side of the needle transducer as a reference target, can be used to measure regional acoustic attenuation in the lens (Huang *et al* 2007b). A needle transducer without a reflector can also be used to estimate the attenuation coefficient using the spectral-shift measurement approach (Huang *et al* 2009). While this paper may seem similar to the above previous studies, the spirit and possible contributions are different. The increase in the attenuation coefficient could be due to a change in acoustic absorption caused by biochemical interactions among the lens constituents (Huang *et al* 2007a). The increase in attenuation is also dependent on a combination of an increase in elastic properties and other frictional factors that consume energy, which is lost as heat (Shung 2006). However, as discussed earlier, the Nakagami parameter reflects the changes in the arrangement, distribution and concentration of scatterers in the cataract lens. More importantly, the Nakagami parameter may have some advantages over the attenuation coefficient when combined with the needle transducer for detecting the lens hardness.

First, in a condition of using the needle transducer without a reflector in front of the transducer surface, backscattered signals with a long acquired datalength are necessary for the use of the spectral-shift method to calculate the attenuation coefficient. A long signal length allows better data fitting to obtain the slope of frequency downshift versus depth for an accurate estimation of the attenuation coefficient. Compared to the previous study, which used backscattered signals with a datalength of $3.9 \mu\text{s}$ to estimate the attenuation coefficient (Huang *et al* 2009), the Nakagami parameter needs a length of only $0.45 \mu\text{s}$ (i.e. three times the pulselength) to successfully detect the lens hardness. This also means that the Nakagami parameter has the potential to be applied to very high-frequency measurements of cataract lenses for sensitivity enhancement. Second, compared to the algorithm based on the spectrum analysis for the attenuation estimation, the calculation of the Nakagami parameter is very simple. The simplicity of the Nakagami parameter allows evaluation of the hardness of the cataract lens with less computational complexity. Third, the outer diameter of the used needle transducer is 0.91 mm. This transducer design makes the combination of the needle transducer with the phacoemulsification probe feasible. Currently, we are trying to find an appropriate method to integrate the needle transducer and the phacoemulsification probe into one device. In theory, the needle transducer should be parallel to the phacoemulsification probe, and both of them should be confocally arranged such that the needle transducer can receive the backscattered echoes from the insonified areas of the phacoemulsification probe to determine the hardness of the treated lens. In the near future, we hope that the needle transducer can be combined with the phacoemulsification probe for the estimation of the Nakagami parameter to realize real-time ultrasound power adjustment during phacoemulsification surgery.

Finally, we would like to emphasize that clinical validation needs to be further performed before the Nakagami parameter based on the ultrasonic needle transducer is used as a reliable tool for detecting the cataract lens. The reason is that actual cataracts in the clinic may involve only part of the lens (e.g., cortical, nuclear, etc) and may have a variety of contributing abnormalities (swollen cells, calcium deposition, epithelial cell migration, globular bodies, etc).

5. Concluding remarks

In this study, we explored the performance of an ultrasonic needle transducer in measuring the backscattered intensity and the Nakagami parameter for quantifying the hardness of the cataract lens in order to avoid problems that could be encountered during imaging of the lens during phacoemulsification surgery. It was found that, with the use of the needle transducer, the backscattered intensity did not yield useful information as to the lens hardness, whereas the Nakagami parameter could effectively distinguish variations in the lens hardness. Compared to the acoustic parameters, using the Nakagami parameter for characterizing the cataract has some advantages including a shorter data length for analysis, less computational complexity, and a potential for very high-frequency measurements. According to the current results and discussion, it seems quite possible to realize real-time feedback and the optimization of the ultrasonic energy during phacoemulsification surgery by integrating the needle transducer and the phacoemulsification probe to estimate the Nakagami parameter and thereby determine the lens hardness. Our next goal is to develop an integrated phacoemulsification probe with a high-frequency needle transducer for animal experiments and preclinical studies.

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Figure 1.
Measurement of the cataract lens by the needle transducer.

Figure 2.
Experimental setup.

Figure 3.
A typical ultrasonic echo signal from a cataract lens.

Figure 4.

(a) Average scaling parameter as a function of immersion time. (b) Average scaling parameter as a function of Young's modulus. (c) Average Nakagami parameter as a function of immersion time. (d) Average local Nakagami parameter as a function of Young's modulus.

Table 1

Characteristics of the ultrasonic needle transducer

Piezoelectric material	PMN-33%PT
Center frequency	47 MHz
F-number	3
Focal length	1.2 mm (nature focus)
Size	0.4 mm × 0.4 mm (rectangular shape)
Pulselength	0.15 μ s