Noncontact depth-resolved micro-scale optical coherence elastography of the cornea

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Abstract: High-resolution elastographic assessment of the cornea can greatly assist clinical diagnosis and treatment of various ocular diseases. Here, we report on the first noncontact depth-resolved micro-scale optical coherence elastography of the cornea achieved using shear wave imaging optical coherence tomography (SWI-OCT) combined with the spectral analysis of the corneal Lamb wave propagation. This imaging method relies on a focused air-puff device to load the cornea with highly-localized low-pressure short-duration air stream and applies phase-resolved OCT detection to capture the low-amplitude deformation with nano-scale sensitivity. The SWI-OCT system is used here to image the corneal Lamb wave propagation with the frame rate the same as the OCT A-line acquisition speed. Based on the spectral analysis of the corneal temporal deformation profiles, the phase velocity of the Lamb wave is obtained at different depths for the major frequency components, which shows the depthwise distribution of the corneal stiffness related to its structural features. Our pilot experiments on ex vivo rabbit eyes demonstrate the feasibility of this method in depth-resolved micro-scale elastography of the cornea. The assessment of the Lamb wave dispersion is also presented, suggesting the potential for the quantitative measurement of corneal viscoelasticity.

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Brillouin shift caused by the interaction between photons and acoustic phonons in ocular tissues has been proposed and utilized for the detection and mapping of tissue biomechanics. 

Current clinically-available approaches (e.g. Ocular Response Analyzer) for the detection of corneal biomechanical properties rely on large magnitude (millimeter-scale) global deformations of the eye [10], which causes nonlinear corneal response to the mechanical stimulation, leading to inaccurate measurement [11]. Also, the lack of depth-resolved detection limits the clinical usefulness of these techniques.

Elastographic methods based on ultrasonic imaging have been developed and applied to the cornea. Both the ultrasound elasticity microscope [12] and the supersonic shear imaging technique [13, 14] are used to achieve the mapping of the depth-dependent corneal mechanical properties with the scale of tens and hundreds of microns, respectively, and very recently, in vivo applications on porcine eyes have been reported [15]. However, the relatively low axial resolution of the ultrasonic imaging and the requirement of several pixels for the calculation of the displacement or strain limit the depthwise resolving ability of these two methods. Also, for an efficient detection, deformation with the amplitude of tens or hundreds of microns is required, which might limit the application of the methods for clinical research and practice in terms of the safety and convenience of the patients [16].

To overcome this resolution shortage of the acoustic imaging techniques, optical imaging approaches, such as confocal microscopy [17] and optical coherence tomography (OCT) [18] have been proposed and utilized for the detection and the mapping of tissue biomechanics. Scarcelli et al. combined the confocal configuration with Brillouin spectroscopy to probe the Brillouin shift caused by the interaction between photons and acoustic phonons in ocular...
tissues [17, 19]. Quantitative imaging of the Brillouin elastic modulus that is related to the sample Young’s modulus has been achieved with micro-scale spatial resolution in cornea [20] with the applications demonstrated in the monitoring of collagen cross-linking [21] and keratoconus [22]. This high-resolution mechanical imaging technique has also been applied in the crystalline lens for the spatially-resolved lens stiffness [23, 24]. Because the confocal imaging modality requires axial scanning for the depthwise detection, and also, due to the low amplitude (compared with the elastic scattering) of the Brillouin-scattered light for which relatively longer exposure time is usually necessary from the camera, a dense mapping of the corneal biomechanics can be time-consuming with respect to the data acquisition.

Recently, OCT has become a major clinical imaging modality that is extensively used for ophthalmology [25–27]. Relying on OCT to study tissue biomechanics, optical coherence elastography (OCE) is an emerging noninvasive biomechanical imaging technique that can provide both qualitative and quantitative tissue elasticity information [28, 29]. Benefit from the high spatial resolution of OCT [30], OCE is able to provide micro-scale mapping of the tissue elastic properties [31–33]. General OCE techniques employ a loading device to induce tissue deformation and utilize OCT-based displacement-detection technique to monitor the dynamic response of the tissue [34–36]. The feasibilities of using OCE for three-dimensional elastic imaging [37, 38], in vivo detection [39–41] and Young’s modulus measurement [42–44] have been demonstrated on tissue-mimicking phantoms and different types of biological tissues, such as skin and soft-tissue tumor.

For the assessment of corneal biomechanics, various OCE methods have been recently reported. Alonso-Caneiro et al. [45] and Dorronsoro et al. [46] studied the dynamics of the cornea during an air puff, where the temporal characteristics of the corneal response are selected to qualitatively represent the mechanical properties of the whole cornea. With static loading of the cornea through a glass window, Ford et al. [47] and Nahas et al. [38] measured the amplitude of corneal deformation and utilized the mapping of the strain to provide depth-resolved elastographic information of the cornea. Based on the detection of the elastic wave propagation inside the cornea, Li et al. [48] and Manapuram et al. [49] assessed the wave group velocity that can be used to quantitatively estimate the elasticity of the cornea.

In this study, we present the first, to the best of our knowledge, noncontact depth-resolved micro-scale OCE of the cornea in situ, which shows the depth-dependent corneal biomechanics that is associated with the structural collagen organization. Shear wave imaging OCT (SWI-OCT) [50] is utilized to image the low-amplitude corneal Lamb wave that is induced using a focused air-puff device with short-duration and low-pressure air stream. The phase velocities of the Lamb wave at the major frequency components are quantified and used to map the biomechanical properties of the cornea. The assessment of the Lamb wave dispersion suggests the potential of using this noncontact method for quantitative corneal viscoelasticity measurement.

2. Materials and methods

2.1 SWI-OCT

Our SWI-OCT system is developed with the combination of phase-sensitive OCT and a focused air-puff device. The system schematic is shown in Fig. 1. The spectral-domain OCT system employs a superluminescent diode light source with the central wavelength of ~840 nm and the bandwidth of ~49 nm, which provides the system axial resolution of ~9 μm in cornea. A high-speed spectrometer that consists of a 1200 line/mm transmission grating and a line-scanning CCD is used to resolve the interference fringes formed by the light from the reference and the sample arms. The OCT beam has the spot size of ~8 μm at the focal plane of the sample arm. The system A-line acquisition speed is set to be 25 kHz, resulting in a temporal resolution of 0.04 ms of the OCT M-mode imaging. The depthwise scale of the system is ~3 μm per pixel. The stability (standard deviation over time) of the optical phase
retrieved from the low-coherence interferometry is measured to be ~0.10 radians on the corneas in situ from the ex vivo rabbit eyes. This provides the OCT system with the sensitivity of ~7 nm to the corneal displacement, which greatly reduces the required amplitude of the corneal deformation for efficient imaging and measurements. More details of this OCT system can be found in our previous work [51, 52].

The custom-designed focused air-puff system [53] relies on an air gate and a control unit to provide a short-duration air stream with ~0.8 ms FWHM (Gaussian shape). The delivery of the air puff is through a port with flat tip and ~0.15 mm inner diameter. Our characterization of the air-puff system shows that the output air pressure for tissue loading is dependent on the air source pressure, the distance between the air-puff port and the sample surface, and the delivery angle relative to the sample surface normal. These three parameters have been used to control and estimate the stimulation pressure on the tissue of cornea. In this study, we apply ~1 Pa of the air pressure on the ex vivo rabbit eye to induce localized micro-scale corneal deformation. Compared with the corneal displacement of more than 1.5-2.0 mm that is induced by the puff of air in commercially available instruments such as Ocular Response Analyzer (ORA, Reichert Technologies, Depew, NY), our setup maximizes the preservation of the corneal structural and functional properties during the elastographic measurement.

The SWI-OCT system relies on the precise synchronization between the air-puff loading and the M-mode OCT imaging to achieve the ultra-fast equivalent frame rate for the elastic wave imaging [50]. Specifically, as shown in Fig. 1, a transistor–transistor logic (TTL) signal is generated from the computer and sent to the frame grabber (ADC) to trigger the start of the M-mode imaging. The same TTL signal is also utilized to trigger the opening of the air gate for the air-puff loading. The galvanometer-mirror is set to move one step after the completion of each M-mode imaging, which results in the transverse scanning of the laser beam on the cornea, forming a one-dimensional line. Total 415 M-mode measurement positions are conducted for each line of scanning on the cornea, covering a transverse distance of ~6.1 mm. During the data acquisition, the air-puff stimulation is kept at a constant position around the center of the scan line. Thus, relative to the mechanical loading, the depth-resolved two-dimensional imaging of the cornea is performed at an equivalent frame rate of 25 kHz, which provides sufficient sampling frequency for the spectral analysis of the elastic wave in the cornea.
2.2 Rabbit cornea

Freshly excised rabbit eyes (from Pel-Freez Arkansas, LLC) with the age of 8-12 months are overnight-shipped to our lab (chilled, but not frozen). The eyeballs are placed in a home-made holder to be kept stable with the anterior side facing up for the SWI-OCT measurement. During the experiments, 0.9% saline solution is periodically added to the cornea to avoid the dehydration. Three eyes are used in this pilot study for the feasibility demonstration.

2.3 Corneal Lamb wave and phase velocity

Because the cornea is a thin plate with the thickness of around 500-600 \( \mu \text{m} \) \[54\], the elastic wave in cornea induced by the transient air puff has different propagation characteristics from that of the more general shear wave propagation in relatively thick tissue samples \[13\]. Specifically, the elastic wave propagation in cornea is partially guided by the top and bottom surfaces with consecutive reflections from these two boundaries, which shows the features of Lamb wave \[55, 56\]. Two zero-order propagation modes usually exist for the Lamb wave in a thin plate under the low-frequency range (typically 0-2000 Hz): symmetric mode and antisymmetric mode \[57\]. In our experiment, as the direction of the air-puff delivery is set to be close to the corneal surface normal, the air-puff loading mainly generates the antisymmetric propagation mode. This can also be confirmed based on the depth-resolved visualization of the corneal elastic wave propagation from our previous work \[50\]. The guided propagation of the Lamb wave in cornea results in its highly-dispersive behavior \[13\].

The frequency-dependent phase velocity of the Lamb wave has been demonstrated to be related to the biomechanical properties of the sample through both experiments and numerical simulations. For example, under constant thickness, the sample with higher stiffness has higher phase velocity at the major frequency components \[13, 56\], which suggests that the phase velocity of the corneal Lamb wave can be utilized as an effective indicator for corneal elasticity.

2.4 Data processing

The optical phase information from the low-coherence interferometry \[58\] is retrieved over time from all the pixels of the two-dimensional depth-resolved OCT cornea image. The raw phase signal from each position is then unwrapped over time and shifted to have the start of the phase profile at the value of zero. As the interferometric phase information represents the change of the optical path-length, the displacement from the corneal surface (cornea-air interface) affects the phase profiles measured at the underlying layers \[59\]. To correct these errors and obtain the true displacement profiles inside the cornea, we have developed algorithms of using the surface deformation to compensate the extra optical path-length change \[50\]. For the corneal surface, the displacement \( d_s \) can be related to the optical phase \( p_s \) through

\[
d_s(t) = \frac{\lambda p_s(t)}{4\pi n_{\text{air}}},
\]

where \( \lambda \) is the central wavelength of the OCT laser source, and \( n_{\text{air}} \) is the refractive index of the air. Inside the cornea, the relationship between the displacement \( d_c \) and the optical phase \( p_c \) is expressed as

\[
d_c(t) = \frac{\lambda \left[ p_c(t) + \frac{(n_{\text{cornea}} - n_{\text{air}})}{n_{\text{air}}} p_s(t) \right]}{4\pi n_{\text{cornea}}},
\]

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where $n_{\text{air}}$ is the refractive index of the cornea. Because the deformation of the cornea is at the scale of micrometer, in Eq. (2), we assume that the refractive index of cornea does not change during the process of the air-puff loading and the Lamb wave propagation. We use $\lambda = 0.84$ μm, $n_{\text{air}} = 1$, and $n_{\text{cornea}} = 1.3771$ [60] in our calculation. After getting the displacement profiles for all the transverse-depthwise positions of the cornea, a binarized two-dimensional depth-resolved OCT image is used as a mask to eliminate the spatial points with random optical phase information.

Fig. 2. (a) Typical selected corneal displacement profiles over time from five locations along the Lamb wave propagation on the surface of the cornea. (b) Corresponding amplitude spectra from the fast Fourier transform of the displacement profiles in (a). The 20 dB drop cut-off frequency is indicated with dashed line in the frequency domain.

Fig. 3. Two-dimensional depth-resolved mapping of the phase of Lamb wave propagation for the typical selected frequencies of 195.3 Hz, 390.6 Hz and 585.9 Hz. The observed phase delays indicate the propagation of the Lamb wave from the center to the edges of the cornea. The transverse scale bars represent 1.0 mm and the axial ones correspond to 0.3 mm.

Because the corneal Lamb wave propagation is guided by the surface of the cornea, similar to the ultrasound elastography of the cornea [13–15], the quantification of the Lamb wave phase velocity is based on the curved propagation paths that have the same curvature as
the corneal surface. As the example to present our method for corneal elastography, Fig. 2(a) shows five typical selected corneal displacement profiles over time from the positions along the Lamb wave propagation on the surface of the cornea. Fast Fourier transform with the spectral resolution of 48.8 Hz is performed on all the available temporal displacement profiles from the two-dimensional depth-resolved field of view to obtain both the amplitude and phase spectra. The amplitude spectra, as typically shown in Fig. 2(b), are used to determine the frequency range for the phase velocity quantification. The cut-off frequency is selected based on the 20 dB drop of the maximum magnitude. For the selected frequency range, the unwrapped phase of the Lamb wave propagation can be mapped to the cornea image for each frequency component. Three examples with the frequencies of 195.3 Hz, 390.6 Hz and 585.9 Hz are shown in Fig. 3. It can be seen that from the center to the edges of the cornea, phase delays exist for all the frequencies, indicating the propagation of the corneal Lamb wave.

![Fig. 4. Illustration of the phase velocity quantification based on the (b)-(e) least square linear regression to the phase data plotted with respect to the wave propagation distance. The frequency component is ~390.6 Hz. The green curved lines in the (a) OCT corneal image indicate the propagation paths selected from four different depths inside the cornea.](image)

The quantification of the phase velocity is based on the relationship between the wavelength $\lambda_c$ and the detected phase delay $\phi$ of the Lamb wave, which can be written as

$$\frac{\lambda_c}{D} = \frac{2\pi}{\phi}, \quad (3)$$

where $D$ is the wave propagation distance corresponding to the phase delay along the curved propagation path. According to the theory of mechanical wave, the wave velocity equals the product of the wavelength and the frequency. Thus, based on Eq. (3), the phase velocity $C$ of the Lamb wave can be related to the phase delay $\phi$ through

$$C(f) = 2\pi f \times \frac{D}{\phi}, \quad (4)$$
where \( f \) is the frequency of the corneal Lamb wave. From Eq. (4), it can be seen that for a particular frequency component, the phase velocity is determined by the ratio of the propagation distance to the phase delay. Therefore, based on the two-dimensional phase map (as shown in Fig. 3), along the wave propagation path, the phase values of the Lamb wave are plotted with respect to the propagation distance, and least-square first-order polynomial regression is applied to the data to obtain the slope value, which is used to quantify the phase velocity. Prior to the quantification, an initial least-square linear fit is conducted first and thresholds of \( \pm 10\% \) of the resulted fitting line are applied to the data to further filter out the random phase values caused by the insufficient SNR of the OCT intensity.

An example for phase velocity quantification with one of the cornea samples is shown in Fig. 4, where four typical curved propagation paths (green lines) are selected from four depths inside the cornea and the quantifications are shown with one side of the cornea. The high R-square values (>0.99) of the regression indicate the good linearity of the data.

For corneal elastography, the phase velocities of the Lamb wave from all the available depths inside the cornea are quantified and mapped to the two-dimensional depth-resolved field of view. The OCT structural image and the phase velocity image are then overlapped with 50% transparency as the final corneal elastographic image. Along the depth, for each layer of the cornea, including the epithelium, the anterior and the posterior stroma, and the innermost region, depthwise averaged phase velocities are used to study the reproducibility of the results over different frequency components and also over different samples.

3. Results

A typical example of the phase velocity (at the frequency of 390.6 Hz) as a function of depth from one of the rabbit eyes (corneal thickness of \( \sim 552 \mu m \)) is shown in Fig. 5(a). For the overall trend, it can be seen that the phase velocity decreases over depth, indicating the stiffness of the cornea generally decreases from the top surface to the bottom surface, which is in accord with the results from ultrasound elastography [12] and atomic force microscopy [61]. Also, the depth-dependent velocity profile can be mainly separated into four regions based on the corresponding OCT structural image and the different variation slopes of the phase velocity. These four regions with different elastic characteristics can be associated with the structural features of the cornea, as shown in Fig. 5(b). Specifically, close to the corneal top surface, a thin layer (region I) with the thickness of \( \sim 30-40 \mu m \) has the stiffness profile starting from lower values to relatively higher values, which corresponds to the epithelium region of the cornea. The following two layers (region II and III) belong to the stroma of the cornea and have distinct stiffness values. The layer (region II) with deeper slope of the velocity change corresponds to the anterior stroma and the one (region III) with the velocity slowly decreasing corresponds to the posterior stroma. The stiffness near the bottom surface of the cornea (region IV) turns out to be the lowest, corresponding to the innermost region of the cornea. These results agree well with the observations from the studies using Brillouin optical microscopy on the intact cornea [20] and using mechanical tensile test with the stroma of the cornea [62], which demonstrates the feasibility of the proposed OCE method for depth-resolved assessment of corneal biomechanics. Based on the mapping of the Lamb wave phase velocity, Fig. 6 shows the micro-scale (\( \sim 3 \mu m \) for axial direction) elastography of the cornea, where different layers of the cornea can be visualized.

Similar results of the depth-dependent phase velocity profile have been observed for all the major frequency components. Figure 7 shows the averaged phase velocities for the four layers of cornea at different frequencies. It can be seen that for every frequency, the relative stiffness difference for the four depthwise-distributed layers in cornea is repeated. The overall decrease of the stiffness over depth is clearly indicated from Fig. 7. Besides, the change of the phase velocity over different frequencies can be observed, which shows the dispersion of the corneal Lamb wave.
Fig. 5. (a) The Lamb wave phase velocity over depth showing the depthwise distribution of the corneal stiffness which is associated with the structural features of the cornea indicated with (b) a general OCT image. Region I: epithelium. Region II: anterior stroma. Region III: posterior stroma. Region IV: innermost region.

Fig. 6. Two-dimensional depth-resolved micro-scale corneal elastography with the mapping of the Lamb wave phase velocity, showing different layers inside the cornea.
Fig. 7. Averaged phase velocities for the four depthwise-distributed corneal layers (Sample #1) at different frequencies indicate that the depth-resolved corneal elastographic result is repeated for all major frequency components. (a) and (b) are continuous plots with respect to frequency.

To study the reproducibility of the results across different samples, we performed the same imaging and measurement on two other rabbit eyes, sample #2 and sample #3, which have the corneal thickness of ~534 μm and ~596 μm, respectively. The phase velocities of the Lamb wave in these two samples also have the overall trend of decreasing from the top surface to the bottom surface in the cornea and the averaged phase velocity values for the four different corneal layers at three typical frequencies are shown in Fig. 8. It can be seen that, similar to the sample #1, the tissue of cornea is overall more elastic as it is closer to the inner side.

Fig. 8. Averaged phase velocities for the four depthwise-distributed corneal layers at three typical frequencies for the rabbit eyes sample #2 and sample #3.
4. Discussion and conclusions

This pilot study demonstrates that the proposed noncontact OCE method combining SWI-OCT with the spectral analysis of corneal Lamb wave can be used to provide the depth-resolved micro-scale elastography of the cornea. The stiffness of different layers of the cornea, including the epithelium, the anterior and posterior stroma, and the innermost region, can be assessed qualitatively through quantifying the phase velocity of the Lamb wave. The current development of this method focuses on the depth-resolving ability, and for one particular depth, all the available transverse locations along the wave propagation are used to obtain one phase velocity value. Alternatively, linear regression can be performed with a moving window along the Lamb wave propagation to have the potential transverse scale for mapping the phase velocity. However, the fixed size of the window might reduce the accuracy of the velocity measurement. Future work will be focused on the design and implementation of the adaptive window that is sensitive to the slope change of the Lamb wave phase data for accurate delineation of the transverse corneal heterogeneity induced by corneal therapies, such as collagen cross-linking.

Fig. 9. Typical corneal Lamb wave dispersion curve within the low frequency range (<750 Hz) from one of the rabbit eye samples.

The phase velocity of the Lamb wave provides the stiffness of the cornea under different frequencies, which can be considered as a relatively thorough characterization of the corneal elastic properties. Based on the frequency-dependent phase velocity, the dispersion curve of the corneal Lamb wave can be obtained. Figure 9 shows a typical plot of the Lamb wave dispersion in one of the cornea samples. The phase velocities are the averaged values from all the available depths inside different layers of the cornea. These dispersion curves indicate similar characteristics (velocity increases with frequency) with the ones from porcine corneas estimated based on ultrasound elastography [13]. The dispersion of the Lamb wave propagation in a thin plate is related to the viscoelastic properties of the material. Recently, Lamb wave dispersion ultrasound micrometry [57] has been developed and demonstrated to be able to measure the shear elasticity and viscosity based on the fitting of the Lamb wave model to the experimental data. Thus, the experimental assessment of the Lamb wave dispersion in the cornea provides the potential possibility of simultaneously quantifying both the elasticity and the viscosity of the cornea. This could significantly improve the accuracy of the corneal elasticity measurement due to taking the viscous behavior of the tissue into consideration, which is of great importance to advance the diagnosis and treatment of many corneal diseases. The existing low-frequency Lamb wave models are mainly developed for the flat plate-like samples in a fluid [57, 63] and are not applicable for the cornea that is a curved thin plate. Also, in our experimental setup, the boundary condition for the cornea is
different, as one side of the cornea is air (or can be considered as vacuum) and the other side is aqueous humor. Currently, we are actively working on the development of a more sophisticated Lamb wave model that can be adaptive to the curvature of the cornea and take into account the complex boundary conditions. The work presented in this paper introduces the experimental method to obtain the Lamb wave dispersion in the cornea with a noncontact configuration, which is of important value for the future quantitative measurement of corneal viscoelasticity.

Previous studies on corneas using ultrasound elastography did not take into account the influence of the corneal curvature on the spatial mapping of the corneal stiffness with the Lamb wave velocity [13–15]. Corneal curvature could have an effect on the depthwise distribution of the Lamb wave velocity. To quantify this effect, our future studies will include experiments on tissue-mimicking phantoms of difference curvatures, as well as the development of a refined theoretical model and adaptive numerical simulations that take into account the corneal curvature and can be used to compensate for the effect of the corneal curvature.

For the three samples at the major frequency components, within the epithelium layer, the phase velocity distribution shows similar profiles that change from lower values to relatively higher values over depth, suggesting a particular trend of stiffness variation from this region that is close to the corneal surface. Similar observations are also from the experiments with Brillouin confocal microscopy [20]. More studies with even smaller axial imaging scale combined with theoretical modeling are needed to further investigate this phenomenon.

During the SWI-OCT measurement, due to the relatively large size of the OCT scan lens, the air-puff port cannot be positioned exactly parallel to the corneal surface normal. In our experiments, we have kept the direction of the air puff perpendicular to the OCT scanning line to avoid the influence from the possible longitudinal mechanical wave inside the cornea. In our future work, a forward-scanning OCT probe [64, 65] will be incorporated with the air-puff port for free adjustment of the loading direction and also more convenient monitoring of the corneal Lamb wave propagation.

Brillouin optical microscopy [17] has been developed for noncontact mechanical imaging of the cornea with high-resolution depth-resolving capability and quantitative measurement of the Brillouin elastic modulus that can be related to the sample Young’s modulus has been achieved [20]. In comparison, the proposed noncontact micro-scale OCE method has the advantage of simultaneously providing the corneal structural image with the depthwise mapping of the corneal stiffness (as shown in Fig. 6). These two types of tissue information (the refractive index and the elasticity) can be used together in many clinical cases for better understanding of the corneal conditions. With the ultra-high resolution OCT system [66], the mechanical imaging scale (currently ~3 μm per pixel) can be further improved to single micron or even sub-micron level. Here, it is worth to mention that the scale of mapping the tissue biomechanics does not necessarily represent the axial resolution of the mechanical imaging, as the resolution is characterized as the spatial resolving ability of the mechanical contrast [67, 68]. For the resolution of the elastography that is based on the detection of mechanical waves, the spatial extent of the mechanical loading could be one of the major determinants. A thorough calibration of this proposed method will be the focus of our future work.

Compared with the existing OCE methods for corneal biomechanics [45–49], the proposed method has the feature of noncontact depth-resolved detection, which has not been achieved in cornea with OCE before. Also, the loading with a low-pressure short-duration puff of air significantly reduces the safety concerns compared with the use of pulsed laser and acoustic radiation force for the potential clinical practice. The significance of the proposed OCE method lies in that it brings the possibility of complementing the clinical widely-used OCT structural imaging of the cornea with depth-resolved micro-scale assessment of corneal biomechanics, which could provide advanced characterization of the corneal condition.
The total data acquisition time of the proposed method can be controlled within tens of seconds based on the repetition frequency of stimulation and the number of the spatial scanning positions [50], which is potentially suitable for the in vivo applications. In this particular study, during the experiments, we employed a slow repetition rate (1.25 Hz) of the air-puff stimulation which is intended for the observation of any localized corneal response caused by the Lamb wave propagation. However, based on the data analysis, this long duration of the M-mode imaging is not required, as most of the temporal points are not utilized for the spectral analysis, which is suggested in Fig. 2.

This combination of SWI-OCT and the spectral analysis of Lamb wave propagation can also be applied to other tissue samples with plate-like geometry, such as the artery wall [69], where this method can be potentially used to provide mechanical characterization of atherosclerosis. For relatively thick samples, for example, breast tumor tissue, based on the ultra-fast wave imaging with SWI-OCT, the phase velocity of the shear wave inside the tissue could be obtained with similar approach, and with the assessment of the shear wave dispersion, the elasticity and viscosity of tissue can be quantitatively measured [70].

In conclusion, we demonstrate the first, to the best of our knowledge, noncontact OCE method for micro-scale depth-resolved corneal elastography with mapping the phase velocity of the corneal Lamb wave. The monitoring of the Lamb wave in cornea is based on SWI-OCT that combines a focused air-puff device and phase-sensitive OCT. Spectral analysis is utilized to quantify the phase velocity of the Lamb wave along the curved propagation paths inside the cornea. The dispersion assessment of the corneal Lamb wave with this OCE method is potentially useful for the quantitative measurement of the corneal viscoelasticity.

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