Ultra-wideband optical coherence elastography from acoustic to ultrasonic frequencies

Xu Feng1,3, Guo-Yang Li1,3 & Seok-Hyun Yun1,2

Visualizing viscoelastic waves in materials and tissues through noninvasive imaging is valuable for analyzing their mechanical properties and detecting internal anomalies. However, traditional elastography techniques have been limited by a maximum wave frequency below 1-10 kHz, which hampers temporal and spatial resolution. Here, we introduce an optical coherence elastography technique that overcomes the limitation by extending the frequency range to MHz. Our system can measure the stiffness of hard materials including bones and extract viscoelastic shear moduli for polymers and hydrogels in conventionally inaccessible ranges between 100 Hz and 1 MHz. The dispersion of Rayleigh surface waves across the ultrawide band allowed us to profile depth-dependent shear modulus in cartilages ex vivo and human skin in vivo with sub-mm anatomical resolution. This technique holds immense potential as a noninvasive measurement tool for material sciences, tissue engineering, and medical diagnostics.

Measurement of the mechanical properties of materials is routinely performed in many places in sciences, engineering, and industries, as well as hospitals. Widely used tools include strain–stress testing and dynamic mechanical analysis for measuring bulk properties, and atomic force microscopy (AFM) and microrheology for local measurements. In clinical medicine, elastography has been adopted for disease diagnosis. Elastography allows to noninvasively measure the elasticity of tissues in normal and abnormal states using medical imaging modalities, such as ultrasound and magnetic resonance imaging (MRI). In all these tools, samples under test are deformed by some force, their responses are measured, and the mechanical properties are calculated from the data. The timescale or frequency range of the measurement spans from quasi static (as slow as 10^{-5} Hz) to acoustic (as fast as 10^3 Hz) ranges. Higher speeds up to a few tens of kHz have been used in AFM and in our recent work on dynamic optical coherence elastography (OCE). In the latter, elastic waves of short impulse or continuous-wave monotones are generated, their propagation within a tissue is visualized, and from the data the wave velocities are determined and related to the elastic moduli of the tissue. While the material analysis thus far has been focused on the quasi-static to acoustic ranges, we hypothesized that a higher frequency range beyond 10 kHz can offer a window of opportunity that was previously underappreciated especially for elastography. First, the higher frequency data can reveal the viscoelastic characteristics of materials in the shorter time scale. Dynamic mechanical analysis (DMA) is widely used to characterize viscoelasticity, but it has a limited frequency range (1–100 Hz). The time-temperature superposition technique can mimic the high-frequency responses of simple, homogeneous materials but is not applicable to composite materials and living matters. Ultrasound non-destructive testing is an established technique using ultrasound waves, typically at 500 kHz–20 MHz, to measure the time of flight across a material or structure with well-defined boundaries to determine bulk elastic properties, but this technique is not directly applicable to elastography and especially for complex materials such as tissues. Second, since the spatial resolution of elastography is approximately given by the wavelength of elastic waves, the higher frequency can lead to the higher resolution. Third, wave velocity dispersion over an extended frequency range is useful to...
extract more detailed mechanical information such as the depth-dependent variation of elasticity and internal stress. The depth information is not accessible using laser Doppler vibrometry or AFM-based rheology that only probes the surface\(^{4,25}\).

Despite all these anticipated benefits mentioned above, it is technically challenging to extend the upper frequency limit. Because the wave energy is proportional to \(A_f^2\) (\(A\), amplitude; \(f\), frequency) and the viscosity tends to grow with \(f\), the energy dissipation or damping of a wave increases with \(A_f^2\). So, with increasing frequency, the wave amplitude must be reduced by \(f^{-3/2}\) to avoid excessive sample heating or damage. Detecting the reduced amplitude requires improved sensitivity, for example, by a factor of a thousand when comparing 100 kHz–1 kHz. To analyze waves with submicron amplitudes, a nanometer-scale sensitivity is required to an instrument. OCE is an emerging elastography technique\(^{25,27}\) built on optical coherence tomography (OCT)\(^{28}\). OCE has been developed with a variety of different system architectures and applied to various tissue types, such as cornea\(^{28,29}\), sclera\(^{30}\), breast\(^{31}\), brain\(^{32}\), and skin\(^{33}\). As OCE uses optical interferometry, it offers superior detection sensitivity in the order of nanometers, compared to micrometers for ultrasound and millimeters for MRI. The high sensitivity of OCE makes it a good candidate for elastography beyond the acoustic range.

Here, we demonstrate an OCE system capable of visualizing elastic waves from the acoustic to ultrasonic frequencies up to a few MHz. We developed a novel aliasing technique, demodulation algorithm, and jitter-correction method to handle such high frequencies far beyond the typical axial line-scan (A-line) rates of OCT. After verifying the system with homogeneous materials, we apply it to dynamic shear analysis of soft materials, and stiffness mapping of complex tissues in a the typical axial line-scan (A-line) rates of OCT. After verifying the jitter-correction method to handle such high frequencies far beyond the typical axial line-scan (A-line) rates of OCT. After verifying the system with homogeneous materials, we apply it to dynamic shear analysis of soft materials, and stiffness mapping of complex tissues in a

\[2k\delta_{1}(T)\]

and \(\delta_{0}T\) are assumed to be multiples of \(2\pi\) for convenience. Figure 1b illustrates \(R(\delta)\) for \(\delta=\lambda\). For the typical case of \(k_{f}T=5\), we get \(R(\delta)=r(2k\delta_{0})+\omega_{m}T+2k\delta\cos(\omega_{m}T)\), where \(\omega_{m}=2k\delta_{0}\) is the carrier frequency. In the frequency domain, it consists of an amplitude \(\delta_{0}(2k\delta_{0})=r(0)\) and two first harmonic sidebands at \(\omega_{m}\pm\omega_{m}\) with an amplitude of \(\delta(2k\delta_{0})=r(0)\delta_{0}\). This is depicted in Fig. 1c. In OCT, the frequency-domain analysis is performed by discrete Fourier transform \(F(\omega)=\mathcal{F}(\{\ell\})\) for each A-line data. The frequency resolution is about equal to the half of the A-line rate \(f_{A}=1/T\). OCE has been operated with relatively low modulation frequencies less than the A-line rate: that is, \(f_{m} \approx 0.5f_{A}\). This ensures that the first harmonic sidebands overlap with the main peak. The carrier and modulated components interfere with each other in the pixel at \(\omega_{m}\) with a phase \(\phi_{m}=2k_{f}\delta_{0}+2k\delta\cos(\omega_{m}T)\). From the amplitude of the phase variation, \(\delta_{m}\) is readily measured.

It is possible to extend OCE to ultrasonic frequencies simply by employing ultrafast OCT systems with MHz A-line rates\(^{30,37}\) while satisfying \(f_{m} \approx 0.5f_{A}\). Then, the same data processing method as described above is applicable. However, since most OCT systems, including commercial products, use A-line rates less than 100 kHz, it should be worthwhile to develop a general method for OCE that works even when \(f_{m} > f_{A}/2\). Below we describe such a method, which takes advantage of signal aliasing.

General demodulation algorithm for high frequency OCE

When \(f_{m} > f_{A}/2\), the modulation sidebands separate from the carrier (Fig. 1d). In this case, one cannot directly apply the conventional method. We rewrite \(R(\delta)\to \mathcal{F}(\{\ell\})\) for \(r(2k\delta_{0})+\omega_{m}T+2k\delta\cos(\omega_{m}T)\). Now, that the modulation component is separated from the carrier, the vibration amplitude \(k_{f}\delta_{0}\) manifest itself in the amplitude of the Fourier component at \(\omega_{m}\pm\omega_{m}\). In this case, \(\delta_{m}\) can be measured from the amplitude, not the phase. However, this is only possible for the mirror-like sample when there is no other signal (background) present at \(\omega_{m}\pm\omega_{m}\).

Consider a tissue-like sample that has continuous scattering points along its depth with \(r(z)\). The problem of retrieving \(\delta\) from the scatterer at \(z_{0}\) becomes more complicated. We used simulated data to demonstrate this problem (Fig. 2). As shown in Fig. 2a, the Fourier component \(r(\omega_{m}-\omega_{m})\) contains three signals: First, the vibration signal \(r(\omega_{m}-\omega_{m})\) (negative sideband) originated from the scatterer at \(\omega_{m}\) (Scatterer 1). Second, the time-independent reflection signal from a different scatterer at \(z_{m}=z_{m}(\omega_{m})\) (Scatterer 2), where \(z_{m}=\omega_{m}(k_{f})\). Depending on whether \(r(\omega_{m}-\omega_{m})>r(\omega_{m}-\omega_{m})k_{f}\) or not, the phasor circle may or may not exclude the origin, and \(\delta_{m}\) is embedded differently in the phase and amplitude of \(F(\omega_{m})\). Third, the vibration signal (positive
The vibration amplitudes of Scatterers 1 and 3 can be retrieved from the demodulation algorithm is provided in Methods. The situation of Fig.1e (ii). Second, we normalize the signal from the carrier DC time average. This brings the phasor circles to the origin as depicted in Fig. 1 (Supplementary Fig. S1). We used phase-sensitive interferometric detection38,39 to obtain sub-wavelength vibration amplitudes. The fundamental limit of 43.2 kHz, and maximum average optical power of 12 mW on samples was attenuated to generate a signal-to-noise (SNR) of 40 dB at the air-glass interface.

The OCT system (Supplementary Fig. S2). To generate mirror-like reflection, a flat glass plate was attached to the PZT. The laser power on the sample was attenuated to generate a signal-to-noise (SNR) of 40 dB at the air-glass interface.

Figure 3a shows a typical A-line profile in the Fourier domain when $f_m$ was 679.6 kHz. The signal appeared at the 107th pixel. The interval between pixels is 21.5 μm in depth or 52.7 kHz. Two first harmonic sidebands emerged at about 12 pixels away from the main peak. The side lobes were lower by 20 dB in signal power (10 dB in amplitude) than the main lobe. Since the ratio of the sidelobe to the carrier is equal to $k_0 g$, we obtain $g = 20.4$ nm. To verify its accuracy, we characterized the same PZT using a laser Doppler vibrometer. The vibration amplitudes measured by OCE were consistent with those measured by the Doppler vibrometer (see Supplementary Fig. S3). Furthermore, we measured the sideband position over a broad range of excitation frequencies. Our result showed that the sideband position increased linearly with the vibration frequency, with the expected slope of 0.019 pixel/kHz (Fig. 3b).

### Noises and time jitter correction for ultrasonic frequencies

Various noises ultimately limit the system’s sensitivity to vibration and the accuracy of wave velocity measurement. The fundamental limit comes from optical SNR, $X$, in A-lines. The length of the modulation-induced phasor is $r(z_0) k_0 \delta(z_0)$. The minimum detectable amplitude $\delta_{min}$ is then given by $r(z_0) k_0 \delta_{min}(z_0) = r_{min}(z_0) k_0$. The minimum detectable reflection coefficient by definition is $k_0 \delta_{min} = X^{0.5}$. So, $k_0 \delta_{min} = X^{0.5}$, same for non-aliased and aliased regimes. We note that although $\delta(z_0)$ is obtained from sidebands at $z_0 \pm z_m$, its error is governed by the SNR of the main peak at $z_0$. In OCE, $\delta$ is typically extracted from a set of M-mode data consisting of N A-lines. Then, the sensitivity is improved by $\sqrt{N}$, and $k_0$.
δmin = X−0.5 N−0.2. For the above experiment, where N = 108 and X = 104, we find δmin = 195 pm. Another fundamental noise source is 1/f electrical noise. SNR at low frequencies may be limited by the 1/f noise rather than the reflectivity-limited phase noise. Mechanical vibrations of optical components add noises. In our system, the mechanical jitters of beam scanners and rotating polygon were corrected using the phase of the stimulus waveform. We found the time-jitter over sweep period T follows a Gaussian distribution with a standard deviation σT of 4.9 ns in our system (Supplementary Fig. S5).

Next, we derive the theoretical time jitter induced phase error σT. Let τi denote the position of the jitter in the i-th sweep, where ⟨τi − ⟨τi⟩⟩ = σT. The timing of the m-th A-line is given by tm = mT + \sum_{i=1}^{m} τi. The output from the m-th A-line is Fm = k0δe^{iωmt}. δ is determined from the inverse discrete Fourier transform of Fm at ωm. The result is k0δ(1 + iωm\sum_{i=1}^{N} τi/N). The standard variation of the second term is σT = \sqrt{ωm/3\sigmaT}. The total phase noise Δφ is a square sum of the SNR- and jitter-induced noises: Δφ = 1/NX^2 + 0.58N(ωmσT)^2.

Finally, the phase noise causes uncertainty in determining the wave velocity, v, from the phase variation along the propagation distance. The error Δv in velocity is given by Δv/v = Δφ/2π(L/L), where L is the effective measurement length. In soft materials, elastic waves are attenuated, and L is typically a couple of wavelengths. Therefore, Δφ/v = 0.01 yields a high accuracy of Δv/v < 1%.

Ultrasonic OCE of hard materials

To verify our system at ultra-high frequencies, we measured various hard materials. Mechanical waves were excited on the surface by using a custom-made contact probe with the piezoelectric actuator (see Methods). For a 5 mm-thick acrylate plastic block, we obtained a flat dispersion curve over 1–2 MHz (Fig. 4a). Since the wavelength (<1.4 mm) is smaller than the thickness, the excited wave is the Rayleigh surface wave with a velocity cR = (0.862 + 1.14v)(1 + v)c0, where c0 is the pure (bulk) shear wave speed and v denotes the Poisson’s ratio. The shear elastic modulus μ is given by μ = ρc0^2, where ρ is the density. From the measured cR = 1285 ± 16 m/s and known ρ = 1.2 g/cm^3 and v = 0.37, we obtained μ = 2.26 ± 0.06 GPa. This value at MHz is slightly higher than the literature value of 1.7 GPa measured by quasi-static mechanical tools. The difference is presumably due to the viscoelasticity of the material. Next, we measured a 1 mm-thick polystyrene plate. Figure 4b shows a representative k-domain plot measured at 787.6 kHz. The dispersion relations for the A0 and S0 waves were fitted using the Lamb wave model. The result was μ = 1.64 ± 0.05 GPa, in comparison to quasi-static shear modulus of ~1.3 GPa reported in literature. We also performed OCE on glass and metal (Supplementary Fig. S6). We obtained μ = 24.0 ± 0.61 GPa for borosilicate glass and 45.7 ± 1.79 GPa for copper (Fig. 4c). These values were consistent with their quasi-static shear moduli, indicating their near-pure elasticity. We also performed OCE on the cortical surface of a bovine tibia bone specimen (μ = 1.6 g/cm^3 and v = 0.3) and found μ to vary from 2.36 ± 0.04 GPa at 485 kHz to 3.60 ± 0.12 GPa at 2 MHz (Fig. 4d). This frequency dependence is in part due to the viscoelasticity of the bone but also contributed by its depth-dependent variation of modulus. Later we will show how the wave velocity dispersion can be used to measure depth-dependent elasticity.
slopes across the frequency range. For the rubber, wave attenuation (elasticity, which and the coefﬁcient of attenuation (Supplementary Fig. S8). The measured speed (surface waves47,48, which is evidenced by the two separated peaks in the proﬁles contain not only the Rayleigh waves but also supershear surface waves47,48, which is evidenced by the two separated peaks in the wavenumber domain (Supplementary Fig. S7). We isolated the Rayleigh surface wave pattern. The measured surface displacement at 1 MHz is displayed. 

The measured storage and loss shear moduli are plotted in Fig.5c, fitting result (dashed lines). Wavenumber domain plot displayed at 787.6 kHz resolves the two wave modes. c Comparison of shear moduli measured by MHz OCE and literature values obtained from static mechanical testing.

Dynamic shear analysis of uniform soft materials
Next, we measured soft polymer samples using surface waves excitation in a frequency range of 0.1 kHz–100 kHz. Figure 5 displays the experimental and analysis data from a rubber (Ecoﬂex 00–50), polydimethylsiloxane (PDMS), and a tough hydrogel47,48, respectively. Figure 5a, d, g show measured surface displacement proﬁles at 40 kHz. The proﬁles contain not only the Rayleigh waves but also supershear surface waves47,48, which is evidenced by the two separated peaks in the wavenumber domain (Supplementary Fig. S7). We isolated the Rayleigh wave and derived the complex wave number  and the coefﬁcient of attenuation ( ) are shown in Fig. 5b, e, h. The complex shear modulus,  , is related to the complex wave numbers via:

\[
\mu' = \rho \omega_n^2 \left( k_f^2 - k_i^2 \right) \left( k_f^2 + k_i^2 \right)^{-2}
\]

(1)

\[
\mu'' = 2 \rho \omega_n^2 k_f k_i \left( k_f^2 + k_i^2 \right)^{-2}
\]

(2)

The measured storage and loss shear moduli are plotted in Fig. 5c, f, i. They show characteristic frequency dependencies due to viscoelasticity, which ﬁt well into a power law model with a single or two slopes across the frequency range. For the rubber,  and  increase from 50 to 160 kPa and from 9 to 323 kPa, respectively, over 0.2 kHz–50 kHz. grows at a faster rate above 10 kHz and becomes greater than  above 40 kHz. The crossover of  and  causes strong wave attenuation ( ). When , waves become overdamped, and their velocities cannot be determined. Our data agreed with previous measurements over 0.2–7.8 kHz by MRI elastography49,50, but high-frequency data above 10 kHz could not be found. For the PDMS, our data up to 130 kHz show no crossover between  and . The low frequency data agree with previously reported storage modulus values of 1.0–2.6 MPa and loss tangents of 0.2–1.0 MPa49,50, which were measured by time-temperature superposition using DMA below 100 Hz.52. The tough hydrogel sample showed the lowest viscosity among the three materials. The low viscosity is due to the water that lubricates highly-entangled polymer chains and reduces energy dissipation53, as previously suggested from DMA results up to 100 Hz46. Our data reveals the unusually low  over the entire acoustic range, suggesting that this material is good at transmitting sounds and even ultrasounds.

Depth-resolved stiffness mapping of cartilage
We applied OCE to bovine cartilage in the knee joint ex vivo (Fig. 6a). The firm, connective tissue consists of three layers with different mechanical properties: the noncalcified cartilage (NCC), calcified cartilage (CC) and the bone (Fig. 6b). In our three-layer model, the thicknesses and shear moduli of NCC, CC and bone layer are denoted by  and  (i=1, 2, 3), respectively. The NCC layer is readily distinguishable in the OCT image, from which we determined . Unfortunately, the lower part of the CC layer and the underlying bone are not visible due to the limited optical penetration depth. We estimated the thickness of the CC layer to be mm from cross-sectional cuts of equivalent samples (see Methods) and assumed . We measured the elastic wave motions over 10–500 kHz. Figure 6c shows the dispersion of the Rayleigh waves, which shows several features. Besides a dramatic transition between 20 and 40 kHz, there appears to be a weak transition between 80 and 100 kHz. The Rayleigh surface wave has a 1/e amplitude decay depth equal to, approximately, a half wavelength. Therefore, as the frequency increases, the wave is increasingly conﬁned near the surface, and its speed reﬂects the average stiffness of the region. The high speed below 20 kHz is due to the hard bone ( ), see Fig. 6d). The first downward transition from 20 to 40 kHz is related to the bone–CC interface as the Rayleigh wave moves away from the bone. And the downward transition from 80 to 100 kHz is attributed to the CC-NCC interface and indicates that . Using a three-layer theoretical model15, we ﬁtted the experimental data and plotted the best-ﬁt result in Fig. 6c, from which we determined  and . These shear elastic moduli are within the range of previously reported values between –2.3 MPa by MRI elastography15 and 27.4 MPa by laser scanning vibrometer15.

Fig. 4 | Ultrasonic OCE of hard materials. a Measured Rayleigh wave speeds (circles) at ultrasonic frequencies on an acrylate plastic block. Inset, a theoretical Rayleigh surface wave pattern. The measured surface displacement at 1 MHz is displayed. b Measured asymmetric (AO) and symmetric (S0) Lamb wave modes on a 1 mm thick polystyrene bottom plate (AO: magenta circles, S0: blue circles) and the ﬁtting result (dashed lines). Wavenumber domain plot displayed at 0.1 MHz.
Our demodulation method allowed us to generate subsurface wave maps (Supplementary Fig. S9). Figure 6d shows cross-sectional displacement images obtained at 100, 140, and 500 kHz, respectively. It is apparent that the wavelength is longer in NCC than CC. We performed finite element analysis (FEA) using the geometrical and elastic parameters obtained from the curve fitting to generate displacement maps. The simulation reproduces the measured displacement fields quite well. The optical SNR from the deep CC region is low,
and light penetrates poorly into bones because of strong light scattering. Nonetheless, substantial energy of elastic waves reaches the bone, partially reflected from and partially transmitting into the bone. This boundary effect of elastic waves affects the wavelength of the wave along the surface and is reflected on the wave dispersion curve.

**Depth-resolved stiffness mapping of in vivo human skin**

We next examined the stiffness of human fingertip skin in vivo over 100 Hz–500 kHz. We have previously measured the moduli of the epidermis, dermis, and hypodermis in the forearm skin by OCE at acoustic frequencies. With ultrasonic frequencies, we were interested in resolving the stratum corneum and the viable epidermis layers within the epidermis (Fig. 7a). Figure 7b shows cross-sectional displacement images at different frequencies. At 20 kHz, the Rayleigh wave is confined predominantly in the SC and VE layers. Above 300 kHz, the majority of the elastic energy resides in the SC layer.

The wave velocity dispersion curve has a strong frequency dependence in the normal skin condition (Fig. 7c, red circles). The wave speed increases dramatically with frequency, an opposite trend to the cartilage. This is consistent with the elastic waves profile of the skin, which tends to decrease with depth. As the frequency increases, the surface elastic waves are increasingly more localized in the upper stiffer region (see Supplementary Fig. S10). Because the elastic modulus of epidermis is greater than dermis and hypodermis, the surface waves are leaky waves, and this anti-waveguiding loss makes it difficult to extract the intrinsic material absorption from measured wave profiles. Therefore, we approximated the skin layers as pure elastic materials. To relate the dispersion to shear modulus, we consider a depth-profile of elastic shear modulus, $\mu(z)$. There are no analytic solutions for wave propagation for arbitrary nonuniform modulus. For small nonuniformity, the wavenumber can be estimated from $k^2 = \frac{\mu z}{\rho c^2}$, where $\psi(z)$ is the wave function in a uniform medium with a space-averaged modulus: $\psi(z)^2 = 2k_c c^{-2k_c z^2}$, where $k_c = 0.31 k$. We may extend the perturbation theory to large variation with a simplified form:

$$k^2 = \frac{\partial \omega^2}{\partial z} \int_0^{L_z} \frac{1}{\mu(z)} dz$$

where $L_z$ denotes the penetration depth of the Rayleigh wave. We may choose $L_z = 1/2k_c = 0.25 \lambda$ or more generally, $L_z = \alpha L_2 = \alpha\lambda^2$; where $\alpha$ is a fitting constant. By differentiating both sides of Eq. (3) with respect to $\omega$, we obtain

$$\mu(z) = \rho \omega^2 (\omega - \omega')/(\omega + \omega')$$

where $z = \omega\lambda/\nu_0$, $\nu_0 = 1.048 \nu_0$ is bulk shear velocity obtained from the measured Rayleigh wave velocity $\nu_0(\lambda)$, and $\nu' = -d\omega/df$. Notice that in bulk isotropic materials, where $\nu' = 0$, Eq. (4) is reduced to $\mu = \rho \omega^2$. Figure 7d shows $\mu(z)$ obtained from the experimental data. Also shown are depth profiles calculated using Eq. (4) using an empirical best-fit function to the data in Fig. 7c. We find $\mu(z)$ to decay rapidly from 56 MPa at the surface to 100 kPa at the asymptotic depth (using $\alpha = 0.25$). This finding is consistent with the fact that water content decreases exponentially from the VE to the surface of SC and that the elastic modulus decreases exponentially with depth in SC.

We measured the same skin immediately after the fingertip was immersed in warm water for 20 min. The thickness of the SC layer increased from 0.31 mm to 0.41 mm due to swelling (Fig. 7e). The wave velocity at high frequencies decreased significantly (Fig. 7c, green squares), indicating a softening of the SC layer. The Rayleigh waves became overdamped at frequencies above 50 kHz due to high viscous damping. Using Eq. (4), we obtained $\mu = 2.6$ MPa at the surface of the hydrated SC.

To verify, we performed FEA simulation by modeling the skin as a four-layer structure. We measured the shear moduli of the dermis ($\mu_d = 9–17$ kPa) and hypodermis ($\mu_h = 2–3$ kPa) layers from wave dispersion below 1 kHz. The shear modulus in the SC layer at the pre-
hydrated condition was assumed to have an exponentially decreasing function from $\mu_0 = 50 \text{ MPa}$ at the surface to $\mu_t = 2 \text{ MPa}$ at the interface between the SC and VE layers (Supplementary Fig. S11). In the hydrated condition, the stiffness of the swollen SC layer was assumed to be uniform and the same as the VE layer ($\mu_0 = \mu_t = 2 \text{ MPa}$). In Fig. 7c we plot the dispersion relations obtained by the FEA simulation, which captures the salient features of the dispersion relations.

Discussion

We have demonstrated an OCE system capable of visualizing elastic waves within various materials and tissues over a wide range of shear modulus from 1 kPa to 10 GPa and across an unprecedented frequency range from static to a few MHz. The fundamental reflectivity-limited performance of the system provided sufficient SNR to determine wave velocities with high accuracy. The measured speed dispersion over the wide frequency range was critical to extract depth-dependent stiffness from multi-layered tissues commonly found in various tissues. The contact area of the PZT probe was optimized to be less than half the wavelength to maximize acoustic impedance matching from the actuator motion to the elastic waves. Throughout the experiments, the peak wave amplitude ranged from several hundreds of nm at acoustic frequencies to as small as 10 nm at ultrasonic frequencies.

The demodulation scheme was highly effective and allowed the upper frequency limit to be no longer limited by the A-line rate. This relaxes the system requirement. The demodulation scheme should be applicable to any swept source OCT systems regardless of their A-line rates. Ultra-high speed OCT systems with ultrahigh A-line rate up to several MHz are available using laser techniques such as Fourier domain mode locking\textsuperscript{36} and stretched-pulse active mode locking\textsuperscript{37}, and they will be well suited to build into MHz-range OCE systems without aliasing. In both aliased and non-aliased schemes, all the acquired data points are used for signal processing. Therefore, in principle the same SNR is expected for the same data acquisition time, and we expect shot noise-limited performance in both schemes as long as practical noises, such as the phase noise of laser sweep, are minimized. Ultimately, the maximum frequency for the wave based OCE technique is limited by viscous damping in samples, which can make waves overdamped. The critical frequency seems to be at a few hundreds of kHz for soft materials.

It should be noted that the aliasing scheme does not work for spectra-domain OCT because signal modulation during the A-line acquisition period is averaged out due to the integrating nature of the OCT interferometry from a point scatter located at $z_0$ can be expressed as

$$I(t) = r(P(t) \cos(2k_0z_0 + 2k_1t\Delta z_0)),$$  \hspace{1cm} (5)

where $r$ denotes the reflectance amplitude, $P(t)$ denotes the optical power profile, $k = k_0 + k_1 t$ denotes the wavenumber of the swept source. The Fourier transformation of the photocurrent acquired during time interval $-T/2 \leq t \leq T/2$ with respect to $k = 2k_1t$, denoted by $F(z)$, is given by

$$F(z_0; z) = \frac{r}{2} \int_{k_1 T}^{k_1 T} \exp \left[-4n_2 \frac{k^2}{(2nk_1 T)^2} \right] e^{i k z_0} dk,$$  \hspace{1cm} (6)

where $T$ is the period of wavelength sweep (A line period). We assume that the optical power profile has a Gaussian shape with a full width at half maximum (FWHM) $\sigma T$, i.e., $P(t) = \exp \left[-4n_2 \frac{t^2}{(\sigma T)^2} \right]$. Then we get

$$F(z_0; z) = \frac{r}{2} \left( \frac{\pi}{\ln 2} k_1 T \right) \{ F_0(z) + \text{c.c.} \}.$$  \hspace{1cm} (7)

where we introduce $F_0(z)$ that is defined as

$$F_0(z) = e^{-4n_2 z_0^2 / (\ln 2)^2 \sigma^2} e^{-2k_0z_0}.$$  \hspace{1cm} (9)

Without loss of generality, the displacement of the scatter along the laser beam can be expressed as $\Delta z(t) = \delta g(t)$, where $\delta$ is a constant and $g(t)$ is a dimensionless function of time. Then the location of the scatter is $z_0 + \Delta z$. Since the laser is periodically tuned, we introduce $t = t - mT$ for the $m$-th A line acquired during $mT - T/2 \leq t \leq mT + T/2$, and $g_m(t) = g(t + mT)$. Substitution of $z_0$ and $P(t)$ in Eq. (5) with $z_0 + \delta g_m(t)$ and $P(t)$, we can get

$$I_m(t) = rP(t) \cos(2k_0z_0 + 2k_1t\Delta z_0 + 2k_0 A_2 \delta g_m(t) + 2k_1t \delta g_m(t)).$$  \hspace{1cm} (10)

We make assumption that the wavelength tuning range is a small fraction of the mean wavelength, $k_1 t \ll k_0$, to get

$$I_m(t) = rP(t) \cos(2k_0z_0 + 2k_1t\Delta z_0 + 2k_0 \delta g_m(t)) = rP(t) e^{i (2k_0z_0 + 2k_1t\Delta z_0 + 2k_0 \delta g_m(t))} + \text{c.c.}$$

$$= rP(t) e^{i (2k_0z_0 + 2k_1t\Delta z_0) \left[ 1 + (-2ik_0 \delta) g_m(t) + \frac{1}{2} (-2ik_0 \delta)^2 g_m^2(t) + \ldots \right] + \text{c.c.}}.$$  \hspace{1cm} (11)

Knowledge of material properties\textsuperscript{68}. Finally, the emergence of deep learning offers a new approach to apply the information-rich elastography data to multi-parameter inverse problems\textsuperscript{69}.

Methods

Swept-source OCT signal

The photodetector current $I(t)$ of the OCT interferometry from a point scatter located at $z_0$ can be expressed as

$$I(t) = rP(t) \cos(2k_0z_0 + 2k_1t\Delta z_0),$$  \hspace{1cm} (5)

where $r$ denotes the reflectance amplitude, $P(t)$ denotes the optical power profile, $k = k_0 + k_1 t$ denotes the wavenumber of the swept source. The Fourier transformation of the photocurrent acquired during time interval $-T/2 \leq t \leq T/2$ with respect to $k = 2k_1t$, denoted by $F(z)$, is given by

$$F(z_0; z) = \frac{r}{2} \int_{k_1 T}^{k_1 T} \exp \left[-4n_2 \frac{k^2}{(2nk_1 T)^2} \right] e^{i k z_0} dk,$$  \hspace{1cm} (6)

where $T$ is the period of wavelength sweep (A line period). We assume that the optical power profile has a Gaussian shape with a full width at half maximum (FWHM) $\sigma T$, i.e., $P(t) = \exp \left[-4n_2 \frac{t^2}{(\sigma T)^2} \right]$. Then we get

$$F(z_0; z) = \frac{r}{2} \left( \frac{\pi}{\ln 2} k_1 T \right) \{ F_0(z) + \text{c.c.} \}.$$  \hspace{1cm} (7)

where we introduce $F_0(z)$ that is defined as

$$F_0(z) = e^{-4n_2 z_0^2 / (\ln 2)^2 \sigma^2} e^{-2k_0z_0}.$$  \hspace{1cm} (9)

Without loss of generality, the displacement of the scatter along the laser beam can be expressed as $\Delta z(t) = \delta g(t)$, where $\delta$ is a constant and $g(t)$ is a dimensionless function of time. Then the location of the scatter is $z_0 + \Delta z$. Since the laser is periodically tuned, we introduce $t = t - mT$ for the $m$-th A line acquired during $mT - T/2 \leq t \leq mT + T/2$, and $g_m(t) = g(t + mT)$. Substitution of $z_0$ and $P(t)$ in Eq. (5) with $z_0 + \delta g_m(t)$ and $P(t)$, we can get

$$I_m(t) = rP(t) \cos(2k_0z_0 + 2k_1t\Delta z_0 + 2k_0 A_2 \delta g_m(t) + 2k_1t \delta g_m(t)).$$  \hspace{1cm} (10)

We make assumption that the wavelength tuning range is a small fraction of the mean wavelength, $k_1 t \ll k_0$, to get

$$I_m(t) = rP(t) \cos(2k_0z_0 + 2k_1t\Delta z_0 + 2k_0 \delta g_m(t)) = rP(t) e^{i (2k_0z_0 + 2k_1t\Delta z_0 + 2k_0 \delta g_m(t))} + \text{c.c.}$$

$$= rP(t) e^{i (2k_0z_0 + 2k_1t\Delta z_0) \left[ 1 + (-2ik_0 \delta) g_m(t) + \frac{1}{2} (-2ik_0 \delta)^2 g_m^2(t) + \ldots \right] + \text{c.c.}}.$$  \hspace{1cm} (11)
We define
\[ G_{m}^{(1)}(z) = \int_{-\infty}^{\infty} I_m(k) e^{i2\pi k z} dk, \]
\[ G_{m}^{(2)}(z) = \int_{-\infty}^{\infty} I_m(k) e^{i2\pi k z} dk. \]  

The Fourier transform of the photocurrent \( I(\ell) \) is
\[ F_m(z_0; z) = \frac{1}{2} \left\{ \left[ F_0(z) + (-2i\kappa_0 \delta F_0(z) \right] G_{m}^{(1)}(z) + \frac{1}{2} \left(-2i\kappa_0 \delta^2 F_0(z) \right) G_{m}^{(2)}(z) + \cdots \right\} + \text{c.c.}, \]

where \( z \) denotes the convolution.

For harmonic vibration studied here, \( \Delta z = \delta \sin(\omega_0 t + \phi) \), where \( \delta \), \( \phi \), and \( \omega_0 \) denote the vibration amplitude, initial phase, and angular frequency, respectively. Then have \( G_m(\ell) = \sin(\omega_0 \ell + \omega_1 \ell + \phi) \), and
\[ G_{m}^{(1)}(z) = \frac{1}{2} \left( e^{i(\omega_0 m \tau + \phi)} \delta(z + \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) - e^{-i(\omega_0 m \tau + \phi)} \delta(z - \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) \right), \]
\[ G_{m}^{(2)}(z) = \frac{1}{2} \left( \delta(z - \frac{\omega_0 m \delta m T}{C_0} + e^{-i(\omega_0 m \tau + \phi)} \delta(z - \omega_0 \frac{mT}{C_1} - \omega_1 \frac{mT}{C_2}) \right), \]

where \( \delta(z) \) is the Dirac delta function. Inserting Eq. (13) we get
\[ F_m(z_0; z) = \frac{1}{2} \left\{ \left[ F_0(z) - \delta_0 \delta(z - \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) \right] e^{i(\omega_0 m \tau + \phi)} F_0(z + \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) \right. \]
\[ - e^{-i(\omega_0 m \tau + \phi)} F_0(z + \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) + \frac{1}{2} \left( \delta_0 \delta(z - \omega_0 \frac{mT}{C_1} - \omega_1 \frac{mT}{C_2}) \right) e^{-i(\omega_0 m \tau + \phi)} F_0(z - \omega_0 \frac{mT}{C_1} - \omega_1 \frac{mT}{C_2}) \right\} + \text{c.c.} \]

Taking the first order approximation, we have
\[ F_m(z_0; z) = \frac{1}{2} \left\{ \left[ F_0(z) - \delta_0 \delta(z - \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) \right] e^{i(\omega_0 m \tau + \phi)} F_0(z + \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) \right. \]
\[ - e^{-i(\omega_0 m \tau + \phi)} F_0(z + \omega_0 \frac{mT}{C_0} - \omega_1 \frac{mT}{C_1}) + \frac{1}{2} \left( \delta_0 \delta(z - \omega_0 \frac{mT}{C_1} - \omega_1 \frac{mT}{C_2}) \right) e^{-i(\omega_0 m \tau + \phi)} F_0(z - \omega_0 \frac{mT}{C_1} - \omega_1 \frac{mT}{C_2}) \right\} + \text{c.c.} \]

Demodulation of vibrations from internal scatters
Given the axial coordinate \( z_0 \), without loss of generality, the Fourier transform of the photocurrent for the \( m \)-th scan, denoted by \( F_m(z_0) \), is
\[ F_m(z_0) = F_m(z_0 + \omega_0 m T + \omega_1 m T) + F_m(z_0 - \omega_0 m T - \omega_1 m T). \]

where \( m \) is an integer, where \( N \) is the number of A lines. We have
\[ \sum_{m=1}^{N} F_m(z_0 + m T) = F_m(z_0), \]

Note that the sum \( \sum_{m=1}^{N} F_m(z_0 + m T) = 0 \), given that \( n \) is an integer, where \( N \) is the number of A lines. We have
\[ \sum_{m=1}^{N} F_m(z_0 + m T) = F_m(z_0 + z_m + z_m) - F_m(z_0 + z_m - z_m). \]

The left side of Eq. (21) contains the left side lobes of the scatter \( S^L \) and the right side lobes of scatter \( S^R \). Here we show the extraction of the vibration for \( S^R \) as an example. Note that \( \sum_{m=1}^{N} f_m(z_0 + z_m) = f_m(z_0 + z_m + z_m) - f_m(z_0 + z_m - z_m). \]

Experimental setup
Our experimental setup (Supplementary Fig. S1) is based on a home-built, swept source OCT system. The system uses a rotating-polygon mirror wavelength-swept laser with a central wavelength of 1307 nm and a 3-dB bandwidth of 80 nm at an A-line rate of 43.2 kHz. The axial resolution is 16 μm. The optical beam is scanned by a pair of galvanometer mirror scanners and focused by a wide-aperture scan lens (Thorlabs, LSM54–1310) yielding a long working distance of 64 mm and a transverse resolution of ~30 μm. The average optical power on the sample is 12 mW. A fiber Bragg grating (FGB) and photodiode (PD) produce a pulse signal synchronized to each wavelength sweep cycle of the laser output. This FPGA-based clock ensures time synchronization among the modulation waveform to PZT, OCT beam position scan, and OCT data acquisition. The signal from a dual-balanced detector (Thorlabs, PDB110C, 100 MHz) was digitized by a data acquisition board (Signatec, PXI4400, 14 bit) at a sampling rate of 108 MHz. A total 2048 data points were acquired from a dual-balanced detector (Thorlabs, PDB110C, 100 MHz).
beam is then moved to the next position, and the stimulus waveform is repeated. A total of 96 positions are acquired. Typical, we set N to be in the range of 100–250. For N = 108, a single M-scan at each transverse location takes 2.5 ms, and the total measurement time per frequency is 0.24 s.

The harmonic waveforms are sent to a wideband PZT via an amplifier (PiezoDrive, PDM2008B for frequencies below 200 kHz, and E&I 1020L above 200 kHz). For the ultrasonic OCE of hard materials, the PZT was in direct contact with the sample with a contact area of 2 mm×2 mm to generate sufficient push force. For the dynamic shear analysis of soft uniform materials, a custom mechanical actuator comprising of a PZT and a 3D-printed cylindrical tip with 0.6 mm radius was used. The tip was designed to facilitate the theoretical model of near-field surface wave. For the depth-resolved stiffness mapping of the joint and skin, a 3D-printed prism-shape tip with a line contact of 2 mm is used to reduce wave attenuation and suppress supershear surface wave.

Displacement field analysis
All algorithms were developed in MATLAB (MathWorks Inc., MATLAB 2019). The raw data collected from the M-B scan was processed using the standard sweep-source phase-stabilized algorithm to obtain the complex-valued OCT tomogram. When \( f_m > f_A/2 \), the correct vibrations occurred at two side lobes. We typically selected the left side lobe, and then applied the demodulated algorithm to extract the surface displacement profiles. Next, we performed a 1-dimensional Fourier transform to move the data from time domain to frequency domain. The frequency domain data was filtered at the driven frequency (when \( f_m < f_A/2 \)) or the aliased frequency (when \( f_m > f_A/2 \)) to obtain lower noise waveforms. After we obtained the displacement profiles over the x coordinate, we performed another 1-dimensional Fourier transform to move the data from the spatial x domain to the wavenumber k domain. The wavenumber \( k \) of the surface wave was then determined from the plot by selecting the peak corresponding to the Rayleigh surface wave. This filtering in the k-x domain is critical to remove other higher-order modes especially at high frequencies. The phase velocity is then given by \( v = 2\pi/k \). To obtain the cross-sectional displacement image, the same method used for obtaining the surface wave displacement was applied throughout the entire pixels along the depth z. In addition, the motion artifact caused by the surface wave motion was corrected within the sample.

** Laser Doppler vibrometer experiment**
We measured the vibration amplitude on a PZT using a laser Doppler vibrometer (Polytec, HLV 1000). The experimental setup is shown in Fig. S3. The drive waveform was generated by a National Instrument board and amplified by a power amplifier (Crest Audio, 1001A) before feeding to the PZT. The stimulus waveform and data acquisition are time synchronized. A retro-reflective adhesive tape was adhered to the surface of the PZT to enhance the vibrometer signal. The laser Doppler vibrometer can reliably measure vibration frequencies up to 80 kHz. The stimulus frequency was varied from 50 to 80 kHz with a 10 kHz increment. Data were averaged 100 times to improve SNR. After finishing the laser vibrometer experiment, the same PZT was measured under the OCE setup. The linear slope efficiency of the PZT at 80 kHz was measured for a voltage range from 0 to 5 V. The measured slope efficiencies (in nm/V) were compared between the vibrometer and the OCE system.

** Measure complex wave number from surface waves**
For soft materials, the near-field displacement is primarily dominated by the Rayleigh and supershear surface waves in high frequency regime. An analytical approximation solution for the surface waves excited by a cylindrical probe can be obtained. The surface displacement at lateral coordinate \( x \) is

\[
    u(x) = \text{in} \left( \frac{a_0 K^4}{\rho_0 a_0} \right) \left\{ J_1 \left( \frac{K a_0}{R} \right) \frac{H_0^{(1)}}{J_0^{(1)} (K a_0)} \left( -K a_0 x \right) + \frac{J_1 \left( \frac{K a_0}{R} \right) K a_0}{J_0^{(1)} (K a_0)} \frac{H_0^{(1)}}{J_0^{(1)} (K a_0)} \left( -K a_0 x \right) \right\},
\]

where \( J_1 \) is the Bessel function of the first kind of order 1, \( H_0^{(1)} \) is the Hankel function of the first kind, \( a_0 \) is the radius of the cylindrical probe, \( \rho_0 \) is the pressure amplitude exerted to the sample by harmonic vibrations of the probe, \( a_0 \) is the vibration frequency, \( K \), \( K a_0 \), and \( K a_0 x \) are wavenumbers of the shear, Rayleigh surface, and supershear surface waves, respectively. \( K \) and \( K a_0 \) are roots of the secular equation \( F(k) = 4K^2 - 4K^2e^{-2K} \) or \( F(k) = 4K^2 \sqrt{k^2(K^2 - K^2)} \). To derive \( K \) from the experiments, we fit the real and imaginary displacements simultaneously with Eq. (23) using the least-squares method. Representative fitting results can be found in Supplementary Figure S9.

** Finite element analysis**
FEA was performed with Abaqus 6.12 (Dassault Systèmes). We used plane strain models and performed time domain simulations. A localized harmonic surface pressure was applied to excite elastic waves, simulating the PZT actuator in the experiments. Other sides of the model were completely constrained. The geometry and total time of the model was scaled according to the wave wavelength and stimulus frequency, respectively. The time increment and total time were 0.1 and 20/fm, respectively. The width and height of the model were about 16 folds of the maximum wavelength to avoid reflection from the boundaries. The model was divided into uniform layers. For the simulation of the knee joint, the thickness of each layer was determined from the OCT images. The top layer thickness was 300 μm, the middle layer thickness was 2.5 mm, and the thickness of the bottom layer was set to about 16 times the maximum wavelength (for the lowest frequency) minus the thickness of the first two layers. The shear modulus values of the three layers from top to bottom were 5.6 MPa, 13.2 MPa, and 3.27 GPa, respectively. The Poisson’s ratios for the top, middle, and bottom layers were 0.4999, 0.499, and 0.3, respectively. A gradient mesh was adopted to reduce computational costs. At the surface the mesh size was smaller than one tenth of the wavelength and at the bottom the mesh size was about half of the wavelength. The element type used in this study was 8-node biquadratic element (CPESR). The convergence of the model was checked by making sure the results independent of the mesh size.

** Preparation of hard materials**
The acrylic block plastic (McMaster-Carr) presented in Fig. 4a had a thickness of 5 mm and an area of 50 mm×50 mm. The polystyrene petri dish (Fisher Scientific) presented in Fig. 4b had a bottom thickness of 1 mm and a diameter of 150 mm. The borosilicate glass coverslip (Fisher Scientific) measured in Supplementary Fig. S6a had a thickness of 0.15 mm and an area of 24 mm×50 mm. The copper foil (All Foils Inc.) measured in Supplementary Fig. S6b had a thickness of 0.3 mm and an area of 15 mm×40 mm. The glass coverslip and the copper foil were placed on a lens holder so that the sample was bounded by the air on two sides.

** Preparation of soft materials**
The bulk silicone rubber has a diameter and height of 60 mm and 12 mm, respectively. It was prepared from Ecoflex 0050 material (Smooth-On Inc) by mixing the Ecoflex 1A and 1B at 1:1 ratio by weight. The mixture was poured into a mold and cured at room temperature overnight. The material was then post-cured in an oven at 80 °C for 2 h. The bulk PDMS sample has a diameter and height of 120 mm and
50 mm, respectively. It was prepared by using a 2:1 mixing ratio of base elastomer and curing agent (Sylgard 184, Dow Corning) and cured for 45 min at 85 °C. The hydrogel sheet had a size of 40 mm × 40 mm and a thickness of 1.3 mm under fully swollen, highly entangled condition. All soft materials were assumed to have a mass density of ρ = 1000 kg/m³.

**Cartilage tissues**

Two fresh bovine tibia bones from two juvenile calves were obtained 1 h post-mortem (Research 87 Inc., Boylston, MA). The tissues were wrapped in a wet towel to keep them well-hydrated until use. Three measurements were performed on the cortical surface of the bone. Four measurements were performed on the femoral condyle region covered by articular cartilage. To measure the thickness of calcified cartilage layer, we made a cross-sectional cut after the OCE experiments.

**Human subject**

We measured the skin of the left index finger on a 31-year-old male subject. The study was conducted at the Massachusetts General Hospital following approval from the Institutional Review Board of Massachusetts General Hospital and the Mass General Brigham Human Research Office. Written informed consent was obtained from both subjects prior to the measurement. All methods were performed in accordance with the relevant guidelines and regulations. The clinical trial is registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (National Clinical Trial Identifier: NCT03230981). The measurement site was marked by a surgical grade skin marker. For the hydration test, the whole index finger was immersed in warm water for 20 min, wiped with a clean towel, and then measured immediately.

**Statistics and reproducibility**

All the statistical analysis was performed using Microsoft Excel (Microsoft Inc.), and MATLAB R2019a (MathWorks, Inc.) software. All quantitative results were presented as mean ± standard deviation. All the wave speed measurements in the main text and supplementary information have been repeated three times or more independently with similar results.

**Reporting summary**

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

**Data availability**

The authors declare that all data supporting the findings of this study are available within the article, and the Supplementary Information/Source Data file. Source Data file has been deposited in Figshare under accession code DOI link. Additional data are available from the corresponding authors.

**Code availability**

Code for analysis is provided on GitHub under accession code DOI link. Additional codes related to this study are available from the corresponding authors.

**References**

1. Nia, H. T., Munn, L. L. & Jain, R. K. Physical traits of cancer. Science 370, eaaz0868 (2020).
2. Guimarães, C. F., Gasperini, L., Marques, A. P. & Reis, R. L. The stiffness of living tissues and its implications for tissue engineering. Nat. Rev. Mater. 5, 351–370 (2020).
3. Cross, S. E., Jin, Y.-S., Rao, J. & Ginzwecki, J. K. Nanomechanical analysis of cells from cancer patients. In Nano-Enabled Medical Applications 547–566 (Jenny Stanford Publishing, 2020).
4. Pelleg, J. Mechanical Properties of Materials. (Springer Science & Business Media, 2012).
5. Sharpe, W., Yuan, B. & Edwards, R. A new technique for measuring the mechanical properties of thin films. J. Microelectromech. Syst. 6, 193–199 (1997).
6. Menard, K. P. & Menard, N. R. Dynamic Mechanical Analysis, (CRC press, 2020).
7. Krieg, M. et al. Atomic force microscopy-based mechanobiology. Nat. Rev. Phys. 1, 41–57 (2019).
8. Ando, T. et al. A high-speed atomic force microscope for studying biological macromolecules. Proc. Natl. Acad. Sci. 98, 12468–12472 (2001).
9. Rigato, A., Miyagi, A., Scheuring, S. & Rico, F. High-frequency microrheology reveals cytoskeleton dynamics in living cells. Nat. phys. 13, 771–775 (2017).
10. Yamada, S., Wirtz, D. & Kuo, S. C. Mechanics of living cells measured by laser tracking microrheology. Biophys. J. 78, 1736–1747 (2000).
11. Kennedy, B. F., Wijesinghe, P. & Sampson, D. D. The emergence of optical elastography in biomedicine. Nat. Photonics 11, 215 (2017).
12. Itoh, A. et al. Breast disease: clinical application of US elastography for diagnosis. Radiology 239, 341–350 (2006).
13. Chang, J. M. et al. Clinical application of shear wave elastography (SWE) in the diagnosis of benign and malignant breast diseases. Breast Cancer Res. Treat. 125, 89–97 (2011).
14. Murphy, M. C. et al. Measuring the characteristic topography of brain stiffness with magnetic resonance elastography. PloS One 8, e81668 (2013).
15. Li, G.-Y. & Cao, Y. Mechanics of ultrasound elastography. Proc. R. Soc. A Math. Phys. Eng. Sci. 473, 20160841 (2017).
16. Sigrist, R. M., Liu, J., El Kaffas, A., Chammas, M. C. & Willmann, J. K. Ultrasound elastography: review of techniques and clinical applications. Theranostics 7, 1303 (2017).
17. Cartagena-Rivera, A. X., Wang, W.-H., Geahlen, R. L. & Raman, A. Fast, multi-frequency and quantitative nanomechanical mapping of live cells using the atomic force microscope. Sci. Rep. 5, 1–11 (2015).
18. Ramier, A. et al. In vivo measurement of shear modulus of the human cornea using optical coherence elastography. Sci. Rep. 10, 1–10 (2020).
19. Larin, K. V. & Sampson, D. D. Optical coherence elastography–OCT at work in tissue biomechanics. Biomed. Opt. Express 8, 1172–1202 (2017).
20. Li, R. Time-temperature superposition method for glass transition temperature of plastic materials. Mater. Sci. Eng. A 278, 36–45 (2000).
21. Su, Z., Ye, L. & Lu, Y. Guided Lamb waves for identification of damage in composite structures: a review. J. Sound Vibration 295, 753–780 (2006).
22. Blitz, J. & Simpson, G. Ultrasonic Methods of Non-Destructive Testing, (Springer Science & Business Media, 1995).
23. Kirby, M. A. et al. Spatial resolution in dynamic optical coherence elastography. J. Biomed. Opt. 24, 096006 (2019).
24. Xu, H. & Luo, Z.-P. Assessment of viscoelasticity of ex vivo bovine cartilage using Rayleigh wave method in the near-source and far-field region. J. Biomech. 116, 110252 (2021).
25. Whittimore, K. R. Jr, Merchant, S. N., Poon, B. B. & Rosowski, J. J. A normative study of tympanic membrane motion in humans using a laser doppler vibrometer (LDV). Hear. Res. 187, 85–104 (2004).
26. Moeendarry, B. et al. The soft mechanical signature of glial scars in the central nervous system. Nat. Commun. 8, 1–11 (2017).
27. Zvietcovich, F. & Larin, K. V. Wave-based optical coherence elastography: the 10-year perspective. Prog. Biomed. Eng. 4, 012007 (2022).
28. Schmitt, J. M. OCT elastography: imaging microscopic deformation and strain of tissue. Opt. Express 3, 199–211 (1998).
29. Ramier, A., Tavakol, B. & Yun, S.-H. Measuring mechanical wave speed, dispersion, and viscoelastic modulus of the cornea using
optical coherence elastography. Opt. Express 27, 16635–16649 (2019).
30. Vinas-Pena, M., Feng, X., Li, G.-Y. & Yun, S.-H. In situ measurement of the stiffness increase in the posterior sclera after UV-riboflavin crosslinking by optical coherence elastography. Biomed. Opt. Express 13, 5434–5446 (2022).
31. Foo, K. Y. et al. Optical palpation for tumor margin assessment in breast-conserving surgery. Biomed. Opt. Express 12, 1666–1682 (2021).
32. Zvietcovitch, F. et al. Longitudinal shear waves for elastic characterization of tissues in optical coherence elastography. Biomed. Opt. Express 10, 3699–3718 (2019).
33. Feng, X., Li, G.-Y., Ramier, A., Eltony, A. M. & Yun, S.-H. In vivo stiffness measurement of epidermis, dermis, and hypodermis using broadband Rayleigh-wave optical coherence elastography. Acta Biomater. 146, 295–305 (2022).
34. Yun, S., Tearney, G., De Boer, J. & Bouma, B. Motion artifacts in optical coherence tomography with frequency-domain ranging. Opt. Express 12, 2977–2998 (2004).
35. Huber, R., Wojtkowski, M. & Fujimoto, J. Fourier Domain Mode Locking (FDML): a new laser operating regime and applications for optical coherence tomography. Opt. Express 14, 3225–3237 (2006).
36. Wieser, W., Biedermann, B. R., Klein, T., Eigenwillig, C. M. & Huber, R. Multi-megahertz OCT: high quality 3D imaging at 20 million A-scans and 4.5 GVoels per second. Opt. Express 18, 14685–14704 (2010).
37. Kim, T. S. et al. 9.4 MHz A-line rate optical coherence tomography at 1300 nm using a wavelength-swept laser based on stretched-pulse active mode-locking. Sci. Rep. 10, 1–9 (2020).
38. Zhao, Y. et al. Phase-resolved optical coherence tomography and optical doppler tomography for imaging blood flow in human skin with fast scanning speed and high velocity sensitivity. Opt. Lett. 25, 114–116 (2000).
39. Wang, R. K. & Nuttall, A. L. Phase-sensitive optical coherence tomography imaging of the tissue motion within the organ of Corti at a submicrometer scale: the tissue motion within the organ of Corti at a submicrometer scale. J. Biomed. Opt. 15, 056005 (2010).
40. Chorna, M. A., Ellerbee, A. K., Yang, C., Creazzo, T. L. & Izatt, J. A. Spectral-domain phase microscopy. Opt. Lett. 30, 1162–1164 (2005).
41. MatWeb, L. Material property data. MatWeb [Online]. Available: http://www.matweb.com (2022).
42. Achenbach, J. Wave Propagation In Elastic Solids (Elsevier, 2012).
43. Miyake, K., Satomi, N. & Sasaki, S. Elastic modulus of polystyrene film from near surface to bulk measured by nanoindentation using atomic force microscopy. Appl. Phys. Lett. 89, 031925 (2006).
44. Basavalingappa, A., Shen, M. Y. & Lloyd, J. R. Modeling the copper microstructure and elastic anisotropy and studying its impact on reliability in nanoscale interconnects. Mech.Adv. Mater. Mod. Process. 3, 1–10 (2017).
45. Bouras, N., Madjoubi, M., Kolli, M., Benterki, S. & Hamidouche, M. Thermal and mechanical characterization of borosilicate glass. Phys. Procedia 2, 1135–1140 (2009).
46. Kim, J., Zhang, G., Shi, M. & Suo, Z. Fracture, fatigue, and friction of polymers in which entanglements greatly outnumber cross-links. Science 374, 212–216 (2021).
47. Pitre, J. J. Jr et al. Super-shear evanescent waves for non-contact elastography of soft tissues. Appl. Phys. Lett. 115, 083701 (2019).
48. Li, G.-Y., Feng, X., Ramier, A. & Yun, S.-H. Supershear surface waves reveal prestress and anisotropy of soft materials. J. Mech. Phys. Solids 169, 105085 (2022).
49. Yasar, T. K., Royston, T. J. & Magin, R. L. Wideband MR elastography for viscoelasticity model identification. Magn. Reson. Med. 70, 479–489 (2013).
50. Rubino, E. & loppolo, T. Young’s modulus and loss tangent measurement of polydimethylsiloxane using an optical lever. J. Polym. Sci. Part B: Polym. Phys. 54, 747–751 (2016).
51. Mata, A., Fleischman, A. J. & Roy, S. Characterization of polydimethylsiloxane (PDMS) properties for biomedical micro/nano-systems. Biomed. Microdevices 7, 281–293 (2005).
52. Huang, L., Hum, J., Fox, W. & Weiss, R. G. Neat linear polysiloxane-based ionic polymers: Insights into structure-based property modifications and applications. Macromolecules 1, 2–17 (2020).
53. Hassan, S. & Kim, J. Polyacrylamide hydrogels. IV Near-perfect elasticity and rate-dependent toughness. J. Mech. Phys. Solids 158, 104675 (2022).
54. Astaneh, A. V. & Guddati, M. N. Dispersion analysis of composite acousto-elastic waveguides. Compos. Part B Eng. 130, 200–216 (2017).
55. Lopez, O., Arram, K. K., Manduca, A. & Ehman, R. L. Characterization of the dynamic shear properties of hyaline cartilage using high-frequency dynamic MR elastography. Magn. Reson. Med. 59, 356–364 (2008).
56. Espinosa, M. G., Otarola, G. A., Hu, J. C. & Athanasiou, K. A. Vibrometry as a noncontact alternative to dynamic and viscoelastic mechanical testing in cartilage. J. R. Soc. Interface 18, 20210765 (2021).
57. Park, A. Rheology of stratum corneum-II: A physico-chemical investigation of factors influencing the water content of the corneum. J. Soc. Cosmet. 23, 13–21 (1972).
58. Darvin, M. E., Schlesener, J., Lademann, J. & Choe, C.-S. Current views on noninvasive in vivo determination of physiological parameters of the stratum corneum using confocal raman microspectroscopy. Skin Pharmacol. Physiol. 35, 125–136 (2022).
59. Bilston, L. E. Soft tissue rheology and its implications for elastography: challenges and opportunities. NMR Biomed. 31, e3832 (2018).
60. Parker, K., Szabo, T. & Holm, S. Towards a consensus on rheological models for elastography in soft tissues. Phys. Med. Biol. 64, 215012 (2019).
61. Rossetti, L. et al. The microstructure and micromechanics of the tendon–bone insertion. Nat. Mater. 16, 664–670 (2017).
62. Zhao, H. et al. Multiscale engineered artificial tooth enamel. Science 375, 351–356 (2022).
63. Moutos, F. T., Freed, L. E. & Guink, F. A biomimetic threedimensional woven composite scaffold for functional tissue engineering of cartilage. Nat. Mater. 6, 162–167 (2007).
64. Kirby, M. A. et al. Optical coherence elastography in ophthalmology. J. Biomed. Opt. 22, 121720 (2017).
65. Sun, Q. et al. Elastin imaging enables noninvasive staging and treatment monitoring of kidney fibrosis. Sci. Transl. Med. 11, eaat4865 (2019).
66. Fuhs, T. et al. Rigid tumours contain soft cancer cells. Nat. Phys. 18, 1510–1519 (2022).
67. Patz, S. et al. Imaging localized neuronal activity at fast time scales through biomechanics. Sci. Adv. eaav3816 (2019).
68. Li, G.-Y., Gower, A. L., Destrade, M. & Yun, S.-H. Non-destructive mapping of stress, strain and stiffness of thin elastically deformed materials. Commun. Phys. 5, 1–7 (2022).
69. Raisi, M., Perdikaris, P. & Karmiadakis, G. E. Physics-informed neural networks: a deep learning framework for solving forward and inverse problems involving nonlinear partial differential equations. J. Comput. Phys. 378, 686–707 (2019).
70. Ramier, A., Cheng, J. T., Ravicz, M. E., Rosowski, J. J. & Yun, S.-H. Mapping the phase and amplitude of ossicular chain motion using sound-synchronous optical coherence vibrography. Biomed. Opt. Express 9, 5489–5502 (2018).
71. Yun, S.-H., Tearney, G. J., De Boer, J. F., Ifitima, N. & Bouma, B. E. High-speed optical frequency-domain imaging. Opt. Express 11, 2953–2963 (2003).
72. Song, S., Huang, Z. & Wang, R. K. Tracking mechanical wave propagation within tissue using phase-sensitive optical coherence tomography: motion artifact and its compensation. J. Biomed. Opt. 18, 121505 (2013).
73. Feng, X., Li, G.-Y. & Yun, S.-H. Ultra-wideband optical coherence elastography from acoustic to ultrasonic frequencies. Figshare https://doi.org/10.6084/m9.figshare.23162636 (2023).
74. Feng, X., Li, G.-Y. & Yun, S.-H. Ultra-wideband optical coherence elastography from acoustic to ultrasonic frequencies, GitHub, https://zenodo.org/record/8148674 (2023).

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Author contributions
S.H.Y. conceived the idea. G.Y.L. and S.H.Y. developed the theory and signal processing. X.F. and G.Y.L. carried out the experiments and analyzed the results. All authors wrote and reviewed the manuscript.

Competing interests
The authors declare no competing interests.

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Correspondence and requests for materials should be addressed to Seok-Hyun Yun.

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