Strategies to improve phase-stability of ultrafast swept source optical coherence tomography for single shot imaging of transient mechanical waves at 16 kHz frame rate

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(Received 28 December 2015; accepted 25 April 2016; published online 10 May 2016)

We present single-shot phase-sensitive imaging of propagating mechanical waves within tissue, enabled by an ultrafast optical coherence tomography (OCT) system powered by a 1.628 MHz Fourier domain mode-locked (FDML) swept laser source. We propose a practical strategy for phase-sensitive measurement by comparing the phases between adjacent OCT B-scans, where the B-scan contains a number of A-scans equaling an integer number of FDML buffers. With this approach, we show that micro-strain fields can be mapped with ~ 3.0 nm sensitivity at $\sim 16\,000$ fps. The system's capabilities are demonstrated on porcine cornea by imaging mechanical wave propagation launched by a pulsed UV laser beam, promising non-contact, real-time, and high-resolution optical coherence elastography. *Published by AIP Publishing.* [<http://dx.doi.org/10.1063/1.4949469>]

Optical coherence tomography (OCT) is a well-established imaging modality for high resolution 3D imaging of biological tissue.^{1,2} Using phase information available in OCT signals, it has been demonstrated that phase-sensitive (PhS) OCT is capable of measuring tissue microscopic deformation,^{3,4} whose capability indeed promoted the recent development of optical coherence elastography (OCE).⁵ In OCE to measure the mechanical properties, it usually requires a means to perturb the targeted tissue, which is then probed by the PhS-OCT. The perturbation means may include mechanical compressive loading,⁶ air-puff,⁷ or launching a transient mechanical wave within tissue, for example, shear wave,⁸ using acoustic radiation force^{9,10} and photoacoustic effect.¹¹ Shear wave OCE distinguishes itself from other dynamic OCE methods because of its use of the propagating wave velocity to deduce the mechanical properties of the tissue. Since the launched mechanical waves typically propagate within tissue with a kilohertz bandwidth, it requires the OCE system to track them with high temporal resolution (<1 ms). Given the limited imaging speed of typical OCT systems, most prior studies rely on the measurement of changes in phase between adjacent A-scans to achieve high temporal resolution, where multiple M-scans are performed to form an M-B scan to enable 2-D cross sectional imaging of motion amplitude.^{7,8} However, the M-B scan format results in long imaging times that may not be acceptable for many clinical applications. For example, Nguyen *et al.*¹⁰ used the M-B scan format to provide an equivalent 47 kHz frame rate to track propagating mechanical waves launched within tissue; however, the imaging procedure required 2 s to complete. Clearly, there is a need for a PhS-OCE system that can image at near real-time imaging rates to capture propagating mechanical waves launched in a single excitation.

Recently, ultra-fast swept-source OCT (SS-OCT) systems have been demonstrated with multi-MHz A-scan rates, making it possible to perform real time elastography. However, the known timing jitter problem in SS-OCT poses a huge challenge for any technique utilizing OCT phase information, making it difficult to measure tissue displacement at sub-micrometer scales through PhS-OCT. There have been several reports that use post processing to stabilize system phases, where a reference phase obtained either from a mirror placed close to a zero delay line¹² or from a re-calibration interferometer¹³ was employed to correct phases in the OCT signal. However, these approaches require extra hardware and have not been demonstrated with ultrafast SS-OCT operating at MHz A-scan rates. Fourier-domain mode locked (FDML) laser is a type of swept source with enhanced phase-stability, with early reports of 102 pm displacement sensitivity at 370 kHz sweep rate,¹⁴ and 16.8 mrad phase-stability at 1.5 MHz between adjacent sweep cycle,¹⁵ comparable with spectrometer-based OCT. In spite of the outstanding stability of FDML lasers, the best performance of phase stability of 3–5.5 mrad is achieved with *a priori* known phase offset measured in the calibration and post-processing compensation.¹⁵ Inter-B-scan phase stability has not been discussed in previous literature for MHz swept source lasers; hence, a calibration-free MHz swept source phase sensitive approach could benefit dynamic OCE field as an alternative imaging tool.

In this paper, we propose a practical strategy for FDML swept source OCT (SS-OCT) to improve its phase sensitivity and enable measurement of transient mechanical waves launched by pulsed UV laser excitation through photoacoustic thermal expansion. We show the feasibility of the proposed system to capture propagating mechanical waves with a deformation sensitivity of ~ 3.0 nm at a B-scan frame rate of 16 kHz.

A schematic of the system is shown in Fig. 1. To track propagating mechanical waves, we used a commercially available ultra-high-speed FDML swept laser (Optores GmbH,

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FIG. 1. Schematic of FDML swept-source OCT system used in this study.

Germany) as the OCT light source. It was swept at 1.6218 MHz at a center wavelength of 1308 nm with a spectral scanning range of 110 nm, giving an axial resolution of 10 μm in air. The light from the laser is split by a 90/10 fiber coupler with 10% of light supplying a reference arm. The remaining 90% of the power is further split into a recalibration arm and a sample arm. The reference arm and the sample arm form a master interferometer for imaging. The reference arm and the recalibration arm form a slave interferometer whose output is used to resample the master interference signal so that the phase error induced by sweeping jitter can be compensated. Both master and slave interference signals are collected by a balanced photo-detector (PDB480C-AC, Thorlabs, Inc., USA) and digitized by a 12-bit digitizer at 1.8 GS/s (ATS9360, AlazarTech, Canada), giving a depth ranging of ~ 4 mm. For real-time imaging, the probe beam must be scanned. We used a custom-assembled scanning device to provide real-time 3-D data acquisition, in which the slow axis is enabled by a Galvanometer scanner (6215 H, Cambridge Technology) and the fast-axis is fulfilled by a resonant scanner (Electro-Optical Products Corp., USA) working at 7950 Hz. The fast axis is phase-locked through a B-scan synchronization signal available from the FDML laser source. In this study, only 2-D images were formed; both forward and backward scans in the fast axis are utilized for imaging, and hence the B-scan frame rate is 15 900 fps (frames per second). The lateral scan range (B-scan size) is 3.7 mm with a spacing of ~ 37 μm between adjacent A-scans.

Mechanical waves are generated without contacting the sample using a pulsed UV laser (wavelength = 263 nm, pulse duration < 3 ns, TECH-263 Specific, Laser-Export Co. Ltd., Moscow, Russia) to locally induce photoacoustic thermal expansion. The UV pulse is precisely synchronized with the start of each OCT B-scan burst. One burst produces a sequence of 20 repeated OCT B-scans, where phase information is extracted to calculate the displacement between successive B-scans and present propagating mechanical waves within one B-scan cross section. With this setting, the total imaging time for the system to achieve elastic mapping of a cross section is ~ 1.2 ms, representing an OCE frame rate over 800 Hz. Because phase is used to evaluate displacement, the OCT signal must be stable throughout the entire imaging sequence. This means that the scanning strategy and evaluation procedure must be specially designed according

to the working conditions of the FDML swept source, as described below.

In phase-sensitive Fourier domain OCT, $\Delta\Phi$ between two acquisitions is linearly related to the displacement Δd at depth z , given by:³ $\Delta\Phi(z) = 4\pi n \Delta d(z) / \lambda_0 = 4\pi n v \Delta t / \lambda_0$, where λ_0 is the center wavelength of the light source, n is the sample refractive index, and v is the velocity of the moving particle. Because our system runs at an A-scan rate of 1.6218 MHz, we elect to use the phase changes between adjacent B-scans so that Δt is sufficiently large to produce significant phase shifts between measurements. Clearly, the minimal displacement measured between two acquisitions is determined by the phase noise of the system and how stable phases are between the corresponding A-scans in adjacent B-scans used to calculate $\Delta\Phi$.

The FDML laser source is a class of wavelength-swept devices that operates in a quasi-continuous wave regime, having highly stable and low noise performance between sweeps.¹⁴ To boost the imaging speed for OCT implementation, optical buffering is employed in which the FDML cavity runs at a round trip frequency of ~ 405 kHz and its output is coupled into a $4\times$ buffer stage to achieve a continuous laser output with 1.5 MHz sweep rate,¹⁵ each buffer producing a time delayed optical copy of the original sweep of the optical fields. As depicted in Fig. 2, the FDML laser source used in this study generates 4 copies (one cluster) of the original sweep, each separated by a constant time delay. Therefore, the imaging speed is 4 times faster for one sweep of wavelengths, i.e., one sweep produces a cluster of 4 A-scans. The phase correlation between different A-scan clusters is high because of repeatable sweeps. However, there is an unknown amount of phase offset between copies within a cluster, leading to marked degradation in phase stability of the eventual OCT system.

As noted in Fig. 2, a B-scan contains a set of A-Scans where every set of four A-Scans, labeled A, B, C, and D, corresponds to one of the four copies emerging from the FDML source. Because the FDML is repeatable and stable between each sweep, but not between copies, the phase difference between copies must be monitored over each sweep. Namely, “A” in one cluster must be strictly compared with “A” in another cluster (Fig. 2). Therefore, to optimize the phase stability between B-scans, the fast-axis scanner has to be designed to operate at a specific frequency so that each

FIG. 2. Characteristics of interferogram obtained from the buffered FDML laser source. OCT imaging is performed through sequential clusters and each cluster consists of 4 copies of one sweep (i.e., 4 A-scans). The interferograms have phase jitter between different optical copies within a cluster.

B-scan contains an integer number of A-line clusters, as shown in Fig. 3. For the case when the B-scan contains a non-integer number of A-line clusters, the phase difference between B-scans includes errors related to different copies of the optical sweep, producing an unstable phase with periodic offsets as shown in Fig. 3(a). Although phase offsets are periodic, it is difficult to correct in post-processing because the jitter between copied sweeps is not constant, due to the positioning error of the buffering stage in the FDML laser.

Table I provides the measured phase stability of the system for a number of selected configurations, where phase stability was calculated as the standard deviation of the phase difference $\Delta\Phi$ along 400 repeated B-frames using a mirror in the sample arm as the target. It is clear that if an integer number of A-scan clusters is used in the B-scan, then the phase stability of the system reaches about 39 mrad; otherwise the

FIG. 3. Comparison between two configurations for fast axis scanner: (a) each B-scan contains non-integer number of A-line clusters and (b) integer number of clusters. Phase stability between B-scans can be significantly improved in the latter configuration.

system has a phase noise that would not be satisfactory for tissue displacement measurement.

In the experiment presented below, we further improved the phase stability using the slave interference signals to re-calibrate the master interference signal and minimize phase error induced by the FDML laser source. With the B-scan rate at 15 900 Hz, a displacement sensitivity of ~ 3 nm was measured for the system between adjacent frames. Although this sensitivity is worse than the sub-nm performance of previous slow M-B scan systems developed in our laboratory,¹⁶ it is still several orders of magnitude more sensitive than high-frequency ultrasound displacement measurements¹⁷ and should be sufficient for transient mechanical wave tracking at high spatial resolution.

To demonstrate high-speed imaging of propagating mechanical waves, the setup in Fig. 1 was first used to image mechanical waves launched by a pulsed UV laser through photoacoustic thermal expansion and propagating in a tissue mimicking phantom. The phantom was made of 5% (W/V) gelatin solution, augmented with 0.02% TiO_2 micro powder as optical scatterers for OCT contrast and ink for optical absorption. The mixed solution was then solidified and cased in a petri-dish; transient mechanical waves were then launched by UV excitation and simultaneously imaged by the PhS-OCT system at a frame rate of 15 900 fps. The temporal resolution was $1/15.9 \text{ kHz} \approx 63 \mu\text{s}$.

The results for single-shot excitation of a mechanical wave are shown in Figs. 4(a1)–4(a5) for the first five instants in the imaging sequence, where the measured displacement field is overlaid onto the structural image. The phase map was derived from phase difference between adjacent B-scans, and 2-D median filter with 5×3 window was applied to further suppress phase noise. This clearly demonstrates that our designed PhS-OCT system can track propagating mechanical waves launched by a single UV excitation. Due to the intrinsic limitation of phase sensitive OCT motion detection, however, the detected mechanical wave is contaminated with surface ripple artifact. This artifact was removed by an automated software routine described in a previous study.¹⁶ Corrected wave propagation images are given in Figs. 4(b1)–4(b5), where the stripe artifacts indicated by arrows in Figs. 4(a1) and 4(a2) are removed. Since the images must be analyzed quantitatively to extract elasticity information from patterns of wave propagation, it is critical to correct the distortion induced by the resonant scan's sinusoidal movement. In addition, A-lines at different positions within a single B-mode image are not exactly acquired at the same time, so the sampling time, which is the line interval of the system, must be taken into account to realign the sample in time. 2-D interpolation was performed accordingly, resulting in the final images shown in Figs. 4(c1)–4(c5), demonstrating that propagating transient waves can be captured with high spatial ($10 \mu\text{m}$) and temporal ($\sim 63 \mu\text{s}$) resolution. These results are comparable with those previously demonstrated for M-B scan mechanical wave imaging, but at a frame rate over a thousand times faster.

Next, we tested whether the proposed system can capture transient mechanical waves (bounded wave related to Lamb wave propagation in a plate) launched within an *ex vivo* porcine cornea by a single UV excitation. In this

TABLE I. Configurations of B-scan rate and resulting phase stability performance.

B-scan frequency (Hz)	A-scan frequency (MHz)	Number of A-lines ^a	Phase stability (rad) ^b
6800	1.621684 ^c	476.97	1.3
6813.8	1.6217	476	0.039
16 000	1.621684	202.71	1.3
15900.0	1.6218	204	0.039

^aA-line number in a round-trip B-scan.^bMeasured OCT sensitivity = 90 dB.^cSweep frequency determined by automatic FDML locking.

FIG. 4. Propagating transient mechanical waves launched in a tissue-mimicking phantom by a pulsed UV laser are captured by the ultrafast PhS-OCT system. (a1)–(a5) Original frame sequence of phase-differences between adjacent B-scans at 5 time instants. (b1)–(b5) Corresponding frames after compensating surface ripple artifacts. (c1)–(c5) Corresponding frames after scan linearization, eliminating resonant scan distortions in both space and time. (d) OCT structural image.

experiment, a whole eyeball was used within 4 h of animal death. It was immobilized on a custom made holder, and immersed in balanced salt solution to avoid dehydration. A needle was inserted into the anterior chamber of the eyeball to supply 16 mm Hg intraocular pressure, comparable with normal levels in the eye. The first 9 images in the wave propagation sequence are shown in Figs. 5(a)–5(i), demonstrating that the proposed system has sufficient sensitivity to detect tiny mechanical wave amplitudes below $1\ \mu\text{m}$ within biological tissue at a frame rate of 16 kHz. We note, however, that in Figs. 5(a) and 5(c) some phase-wrapping can be observed in the vicinity of the mechanical wave source origin, where the displacement field presents false sudden changes of motion direction due to the push of the UV laser pulse onto

tissue. However, in the region away from the source, tissue displacements due to propagating mechanical waves are within a range of $[-\pi, +\pi]$ phase difference, which can be used to deduce elasticity maps of the tissue using a time-of-flight algorithm.¹⁸ The proposed system took only $\sim 1.2\ \text{ms}$ to capture 20 B-scans to represent the propagating mechanical wave launched by a single push of the pulsed UV laser. Post-processing to reconstruct quantitative elastography images can be performed within a similar time scale, leading to real-time mapping of the elastic properties of the targeted tissue.

With the proposed strategy, phase drifts caused by synchronization jitter between buffered sweep copies in the FDML system can be minimized. However, phase instabilities arising from other factors in the swept laser source still must

FIG. 5. High-speed imaging of transient mechanical wave propagation in a porcine cornea, where waves are induced by a single UV laser pulse. (a)–(i) Sequential images of displacement field of first 9 frames, after surface ripple correction and scan linearization. (j) OCT structural image.

be corrected by conventional approaches, e.g., using the reference phase signal from the slave interferometer. While this approach is feasible and cost-effective, future development may include the use of the k-clock to precisely trigger A-scan data acquisition, which would stabilize OCT signal phases between each sweep copy.

In summary, we have proposed a single-shot, high speed, cross-sectional vibrometry method based on a FDML SS-OCT system with 1.62 MHz A-line rate and ~ 16 kHz B-scan rate. All data required for OCE measurements over the region covered by the B-Scan can be acquired in just over 1 ms, making 3-D OCE data acquisition at real time volume rates of 50–100 Hz possible for ultimate clinical applications. We have shown that by carefully designing the scan protocol, a displacement sensitivity of ~ 3 nm can be achieved, sufficient for tracking propagating mechanical waves within tissue at high spatial resolution. The combination of ultrafast OCT and depth-resolved vibrometry would open up opportunities to efficiently track mechanical wave propagation in biological tissue, thus promising high-resolution, real-time, quantitative elastography.

This research was supported in part by grant from the National Eye Institute (R01EY026532). The content is solely the responsibility of the authors and does not necessarily represent the official views of grant giving body.

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