High-performance multi-megahertz optical coherence tomography based on amplified optical time-stretch

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Abstract: As the key prerequisite of high-speed volumetric structural and functional tissue imaging in real-time, scaling the A-scan rate beyond MHz has been one of the major pursuits in the development of optical coherence tomography (OCT). Along with a handful of techniques enabling multi-MHz, amplified optical time-stretch OCT (AOT-OCT) has recently been demonstrated as a viable alternative for ultrafast swept-source OCT well above MHz without the need for the mechanical wavelength-tuning mechanism. In this paper, we report a new generation of AOT-OCT demonstrating superior performance to its older generation and all other time-stretch-based OCT modalities in terms of shot-to-shot stability, sensitivity (~90dB), roll-off performance (>4 mm/dB) and A-scan rate (11.5 MHz). Such performance is mainly attributed to the combined contribution from the stable operation of the broadband and compact mode-locked fiber laser as well as the optical amplification in-line with the time-stretch process. The system allows us, for the first time, to deliver volumetric time-stretch-based OCT of biological tissues with the single-shot A-scan rate beyond 10 MHz. Comparing with the existing high-speed OCT systems, the inertia-free AOT-OCT shows promises to realize high-performance 3D OCT imaging at video rate.

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1. Introduction

Well-recognized for its capability of label-free in-vivo deep-tissue (>1mm) imaging in three-dimensional (3D) with micrometer-resolution (~10 μm or less), optical coherence tomography (OCT) is continuously gaining popularity in clinical diagnostics. Moving from its most successful utility in ophthalmology [1], OCT is now proven to be effective in intravascular assessment in cardiology [2]. It also finds niches in intravital cancer detection in oncology [3–5]. One key momentum in OCT technological development is the scaling of imaging speed. More specifically, the A-scan rate of OCT has been progressively increased in the past twenty years from kHz (by time-domain OCT, e.g [6]) to sub-MHz or even multi-MHz (in spectral-domain and swept-source OCT (SS-OCT) e.g [7]). The rationale of scaling the A-scan rate up to 1 MHz with a competitive sensitivity [21]. SD-OCT based on wavelength division multiplexing together with parallel photodiode arrays has also been demonstrated to achieve more than 10 MHz A-scan rate [9, 22]. The system is however considerably bulky and complex. Swept–source OCT (SS-OCT) is another viable approach to achieve the high A-scan rate of hundreds kHz. Such rate is limited by the mechanical

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scanning speed of the spectral filters based on e.g. rotating polygonal mirrors [23], piezoelectric-driven bulk Fabry-Pérot cavity [7] or micro-electromechanical system (MEMS) [24]. Notably, multi-MHz A-scan rate can be realized using these modalities by implementing buffering (time interleave) technique to multiply the fundamental scan rate [7]. Nevertheless, long-term system reliability in these SS-OCT modalities hinges on robust continuous mechanical scanning or actuation against the motion artifact and instability.

To mitigate such problem, an inertia-free and passive wavelength-swept mechanism is the key. Based upon group velocity dispersion (GVD), optical time-stretch represents an attractive all-optical ultrahigh-speed wavelength-swept mechanism for multi-MHz SS-OCT [25–30]. Prior demonstrations of time-stretch-based OCT are mostly unable to prove its utility in practical in-vivo bioimaging. The main reasons stem from (1) the limited source bandwidth (~10 nm) which yields insufficient axial resolution of OCT [26, 27], and (2) the absence of broadband optical gain process which results in low sensitivity (< 40 dB) [25]. We have recently demonstrated broadband amplified optical time stretch OCT (AOT-OCT) which achieved 7.14 MHz fundamental A-scan rate over 80 nm bandwidth with a sensitivity of >80 dB [28]. While this was the first demonstration of applying time-stretch-based OCT for in-vivo biological specimen imaging, the sensitivity and thus the image quality is yet to be satisfactory for practical research and clinical applications. One key challenge is to maintain stable as well as broadband shot-to-shot wavelength-swept waveforms at a rate of multi-MHz. This feature is critical to minimize the intensity noise and thus the sensitivity of AOT-OCT. To achieve broadband AOT-OCT (few tens to even hundred nm), one can traditionally opt for ultrashort femtosecond (fs) mode-locked laser source (<100 fs) or supercontinuum (SC) source which can be pumped by either fs-lasers or longer-pulse lasers (ps-ns) [31]. From a practical point of view, any source relying on fs-laser is susceptible to ambient perturbation and thus requires dedicated pulse shape management, which usually comes at the expense of the large form-factor of the system. On the other hand, broadband source by SC generation has been a common choice for time-stretch-based OCT. However, SC generation is well-known to be highly sensitive to input noise [31]. This feature makes the SC pulse train exhibits a large shot-to-shot fluctuation and poor temporal coherence. This is particularly true for picosecond SC generation [32, 33]. Such temporal instability mainly rendered the sensitivity of our prior demonstration on AOT-OCT to be ~15 dB lower than the shot-noise limit [28, 34]. In this paper, we present a new generation of AOT-OCT system which shows a significant improvement in sensitivity (~90dB) at an even higher A-scan rate of >10MHz. It is made possible by a highly compact mode-locked fiber laser (MLFL) based on a polarization additive pulse mode-locking (APM) mechanism. It facilitates broadband time-stretched pulse generation (~60 nm) with a superior shot-to-shot stability [35, 36]. It has been proven to be effective for other ultrafast time-stretch imaging modality [37]. We here specifically exploit its utility in achieving multi-MHz AOT-OCT and characterize of the system performance in detail. Owing to the simple and compact broadband fiber laser configuration as well as the all-optical passive ultrafast wavelength-swept mechanism, the AOT-OCT system presented here is an attractive alternative for practical multi-MHz OCT and thus video-rate 3D OCT if high-throughput data acquisition is available.
2. Experimental implementation

Figure 1 shows the experimental setup of our AOT-OCT system. The underlying mechanism of MLFL is based on the technique of polarization APM which delivers broadband pulse with superior stability and coherence. Detailed laser configuration can be referred to ref [35, 36]. In brief, the laser cavity consists of both positive- (erbium-doped fiber as the gain medium) and negative-dispersive fibers (standard single-mode fiber), together with a compact optical integrated module (incorporating with multiple functions such as wavelength-division multiplexing (WDM), beam splitting and polarization-sensitive isolation), a 980 nm fiber-pigtailed laser diode pump (FPL4916TW-U2, Agilent) and an in-line polarization controller (PLC-900, Thorlabs). With a total fiber length of ~17 m in the MLFL cavity, the laser source generates an ultrashort pulse train at a repetition rate of 11.5 MHz with a full-width-half-maximum (FWHM) intensity bandwidth of 56 nm, centered at 1558 nm. The output mode-locked pulses, with an average power of ~2 mW, are launched into a 9.5 km dispersion compensation fiber (DCF) (DCS-080/SSMF, ADVA Optical Networking) which has a total GVD as high as ~1.5 ns/nm. This is the optical time-stretch process in which the broadband spectra of the pulses are mapped into time. To compensate the optical loss in the dispersive fiber, fiber Raman amplification (FRA) of a backward pump (PYL-3-1455, IPG Group) with ~200 mW at 1455 nm is implemented simultaneously with the time-stretch process, which provides ~8 dB on/off gain for the swept source. A broadband booster optical amplifier (BOA) (BOA 1004, Covega) is employed as the second-stage amplification to further boost the optical power of the ultrafast wavelength-swept waveform, and thus to enhance the OCT sensitivity. Then the amplified wavelength-swept light is launched into a fiber-based Michelson interferometer. We split the light into the reference arm and the sample arm by a 50/50 fiber coupler, which leads to an incident power of ~7 mW on the sample. Such illumination power is within the safety standard, such as ANSI [38], assuming continuous illumination. With a pair of galvanometric mirrors, we can generate 2D or 3D images in our AOT-OCT system. We employ a balanced amplified photodetectors (PDB480C-AC, Thorlabs) with a bandwidth of 1.6 GHz to capture the interferogram signals, which are subsequently digitized by a high-speed real-time oscilloscope (bandwidth: 16 GHz; sampling rate: 80GS/s; analog-to-digital conversion resolution: 8-bit). Note that for the sake of revealing the intrinsically high-speed operation of the MLFL source and verifying the long-range imaging capability of the present system, the laser and the roll-off performances...
presented in the paper are measured by a high-bandwidth (15-GHz) photodetector (Fig. 2 and 3). For a fair comparison of the AOT-OCT system between the use of SC source and the MLFL source, the images are all captured by the 15-GHz photodetector (Fig. 4). The AOT-OCT images show in Fig. 5 are otherwise captured by the 1.6GHz balanced-detector. As it will be shown later that the spectral shape of the time-stretch waveform is non-Gaussian and thus leads to image artifact, we apply a hamming window to digitally reshape the swept waveform during AOT-OCT image reconstruction in order to minimize the side-lobe artifact of the axial point spread function (PSF) and hence to improve the AOT-OCT image quality [39].

3. System performance

3.1 Laser source performance

Shot-to-shot temporal stability of the swept-source critically governs the ultrafast imaging performance of AOT-OCT. We first evaluate the temporal stability of the all-optical swept source, enabled by the MLFL together with optical time-stretch, by investigating its real-time optical power statistics, as shown in Fig. 2(a). 2048 single-shot wavelength-swept waveforms are captured by a 15-GHz photodetector in real-time and are overlapped to visualize the spectrally-resolved power histograms. Similar approach has been employed for real-time characterization of supercontinuum generation (SC) [40]. Here, each waveform has a wavelength span from 1531 nm to 1587 nm bandwidth, corresponding to a total GVD of ~1.5 ns/nm. Note that the nonlinear wavelength-time mapping is calibrated by retrieving the wavelength-dependent dispersion curve of the DCF by a phase-retrieval algorithm based on Hilbert transform of the raw wavelength-swept waveform [28]. It is clear that the high temporal stability across the entire spectrum is maintained and is superior to the all-optical swept-source based on SC generation, as shown in Fig. 2(b). The configuration of the SC source is detailed in ref [28], which is generated from a 50-m-long highly-nonlinear fiber (HNLF) pumped by a high power ps laser. We quantify the fluctuation by defining an average ratio of standard deviation to the mean of the time-stretched waveforms, i.e. the noise-to-signal ratio (N/S) [41]. The all-optical swept-source based on our MLFL is measured to be N/S = 7.9%, which is significantly lower than that based on SC generation, N/S = 25.2%. Figure 2(c) shows three single-shot time-stretch interferograms generated by this OCT system, with a mirror placed in the sample arm. With the total GVD of ~1.5 ns/nm in the DCF, each stable interferograms are time stretched with a duty cycle of ~95%.

We note that the conventional rationale of employing SC source for OCT is its ultrabroadband spectrum that results in high axial resolution [25]. However, SC generation, as a highly nonlinear optical process which involves assorted and inter-related mechanisms, is very sensitive to input noise, and thus is typically a noisy source in the single-shot time scale. For instance, an effective approach to-date to generate ultrabroadband SC, which is also generally adopted in the commercial SC sources, is to pump a highly nonlinear fiber at the anomalous dispersion regime by a high-power ps or fs laser [31]. While it offers an ultrawide bandwidth beyond 100 nm, the SC generated in this way is initiated by a stochastic process called modulation instability (MI), and the noise is nonlinearly amplified along with the spectral broadening dynamics. Dedicated dispersion engineering (e.g. [42]) or active seeding (e.g. [33, 43, 44]) is needed to suppress the noise. Another more straightforward approach is to perform averaging in time in order to reduce the intensity noise. This explains why practical OCT (more precisely SD-OCT) based on SC source demonstrated so far can only achieve the A-scan rate typically well below 100kHz, which is limited by the necessity of averaging in order to minimize the signal noise and enhance the sensitivity [45]. In contrast, the all-optical swept-source presented here provides ultrafast, stable and broadband operations. It should be noted that this MLFL demonstrates continuous operation with superior long-term stability (<0.1 dB power variation for more than 24 hours at room temperature) [36]. Together with the simple and compact all-fiber configuration, it is a
practical alternative enabling high-quality imaging in the AOT-OCT system without compromising the imaging speed by line-scan averaging.

Fig. 2. Real-time spectrally-resolved histograms of (a) the time-stretch MLFL pulses and (b) the time-stretch SC pulses. 2048 pulses are overlapped to construct the histograms. (c) The real-time single-shot interferograms generated by the AOT-OCT system at a repetition rate of 11.5 MHz.

3.2 Roll-off performance

By changing the axial position of the reference mirror, we evaluate the roll-off performance of the AOT-OCT system (Fig. 3(a)). Sharp axial PSF with a full-width at half-maximum (FWHM) is measured to be 19 μm, which is consistent with the estimation based on the spectral bandwidth of 56 nm, centered at 1558 nm. We note that engineering the broadband gain spectrum of the MLFL gain medium as well as incorporating carefully with different deterministic nonlinear processes in the fiber (such as spectral broadening by self-phase modulation) can be the promising ways to broaden the lasing spectrum of MLFL which thus improves the resolution for AOT-OCT [46]. The sensitivity is measured to be as high as ~90 dB, which shows a ~10 dB improvement compared with the previous work [28]. The roll-off performance is determined by the instantaneous linewidth (or coherence length) of the swept-source. Unlike the conventional swept-sources, such as based on FDML, in which the linewidth is limited by the spectral filter in the laser cavity, the linewidth in our system is intrinsically governed by the ambiguity in the wavelength-to-time mapping during time-stretch. Our recent theoretical analysis showed that AOT-OCT can achieve a coherence length as long as centimeters at an A-scan rate at ~10 MHz [34]. We here employ a high-speed photodetector with a wider electrical bandwidth of 15 GHz for experimental verifying the long-range imaging capability. We plot the axial PSFs in a step size of 1 mm over a depth range of 40 mm. It shows that our current AOT-OCT system can achieve 4.1 mm/dB roll-off number within 30 mm, which is ~40 times better than the FDML-OCT system with a single-spot effective A-scan rate of 5.2 MHz [7]. The sensitivity drop beyond 30 mm is due to the bandwidth limitation of the photodetector and digitizer [28]. Figure 3(b)–3(c) show the AOT-OCT of a stack of multiple glass slides at 2 different depth positions which are ~30 mm apart. Figure 3(d) and 3(e) are the zoom-in OCT images of the glass slides at these different positions. We can clearly identify the surface of the sample supporting stage at a depth of ~16 mm, as shown in Fig. 3(b). The interfaces of the glass slide stack can still be clearly
distinguished even at the depth position of $\sim 30$ mm. The back surface of the glass slide stack at 33.6 mm is still visible, albeit lower quality. It is again because that this depth position corresponds to the bandwidth exceeding that of the photodetector (see Fig. 3(a)). Figure 3(f) and 3(g) demonstrate a similar experiment of AOT-OCT of a cucumber at 2 different depth positions, which are again $\sim 30$ mm apart. The seed beneath the surface of the cucumber at $\sim 31$ mm is still clearly visible with relatively lower signal-to-noise ratio (SNR). It should be noted that the superior roll-off performance of AOT-OCT here originates from both the highly coherent property of the mode-locked fiber laser and the large amount of GVD in time-stretch [34]. This unique feature of AOT-OCT is particularly beneficial for applications which require long range imaging applications such as full eye imaging, or endoscopic imaging of large lumen in-vivo.

3.3 AOT-OCT performance

To better illustrate the critical role of high shot-to-shot stability in the MHz regime for ultrafast AOT-OCT, we compare the image quality taken by two different AOT-OCT systems: the new generation based on our home-built MLFL source while an earlier generation with the SC source described in the earlier section (c.f. Fig. 2). Figure 4(a) and 4(b) are the 2D cross-sectional AOT-OCT images of the human finger print and finger nail regions, respectively, using the SC source. Clearly, the image quality is not satisfactory for practical in-vivo imaging because of the unstable A-scans as well as the inability of revealing deeper tissue structure beneath the surface, even though the system operates as an ultrafast A-scan rate of $\sim 7$ MHz. As discussed earlier, the poor image quality and sensitivity are mainly attributed to the severe shot-to-shot fluctuation of the SC source (as shown in Fig. 2). In contrast, when the MLFL is employed in the AOT-OCT system operated at 11.5MHz, the dermis tissue and sweat duct under the epidermis and the nail bed beneath the surface of the nail plate in human finger can be clearly visualized as shown in the OCT images of Fig. 4(c) and 4(d). The significant improvement in imaging quality is attributed to the robust temporal stability of the MLFL as well as the optical amplification scheme in our AOT-OCT system [28, 34].
Fig. 4. Images of human finger print (a) and finger nail (b) captured by an earlier generation of AOT-OCT (a 7-MHz AOT-OCT system with a SC source). (c) and (d) are the human finger print and finger nail captured by the new generation of AOT-OCT (a 11.5MHz AOT-OCT system with MLFL). E: epidermis, D: dermis, SD: sweat duct, NP: nail plate, NB: nail bed.

Using the MLFL source, we further demonstrate the performance of this 11.5-MHz AOT-OCT system for in-vivo imaging by imaging an anterior segment of the mudfish eye (Fig. 5). The iris is clearly visualized under the cornea (Fig. 5(a)), while the anterior surface of the lens can be also observed (Fig. 5(b)). Figure 5(c) and 5(d) show the 3D AOT-OCT images which display the anterior segment of the mudfish eye from different perspectives. The volumetric data set contains 500 × 100 axial scans which covers an area of 5mm × 2mm. The 3D images provide good contrast which allows us to clearly visualize the tissue structure such as cornea, iris, pupil, eye contour and the limbal skin of the anterior segment. We note that this is the first demonstration of 3D biological image using ultrafast time-stretch-based OCT. It should be noted that current demonstration of the 3D imaging is not performed at the video-rate, which is mainly limited by the data transfer and processing time as these steps are currently done off-line. It can be easily remedied by the implementation of high-speed data processing, e.g. graphics processing unit (GPU) or field-programmable gate array (FPGA) [8, 47]. Together with the compact fiber-based configuration, inertia-free wavelength-swept mechanism, as well as the superior roll-off performance, AOT-OCT shows its promise as a practical alternative to achieve video-rate 3D OCT in real-time.

Fig. 5. Cross-sectional 11.5-MHz AOT-OCT images of an anterior segment of a mudfish eye near the edge area (a) and center area (b), which are indicated by the red and yellow arrows in (c). The corresponding 3D AOT-OCT images are shown (Media 1) from top view (c) and bottom view (d). C: cornea, I: iris, L: lens, S: skin, EC: eye contour, P: pupil.
4. Discussion

To illustrate further how the performance of AOT-OCT is compared with the existing state-of-the-art high-speed OCT systems based on different techniques (A-scan rate of >100kHz), we construct an “OCT performance scatter plot” to evaluate three main metrics of the representative high-speed OCT systems (Fig. 6): sensitivity, A-scan rate, and axial spatial resolution [7, 17, 20–30, 48–50]. Each circle represents each OCT system whereas the size of the circle represents the resolution, i.e. the smaller circle, the higher the resolution (see the reference circle, which corresponds a resolution of 10 μm (Fig. 6)). The shot-noise-limited sensitivity scenarios defined by $S_{\text{shot}} = 10 \log \left( \rho P_s / \rho e A f \right)$ (dB) [34] are shown in the same plot.

$\rho = IA / W$ is the detector responsivity, $P_s$ is the optical power incident on the sample, $e$ is elementary electric charge, and $f_A$ is the A-scan rate. As $S_{\text{shot}}$ is a function of $P_s$, we color-code the curves $S_{\text{shot}}$ for a range of $P_s$ values from −4 dBm to 16 dBm which covers the power range in all the chosen cases, i.e. ref [7, 17, 20–30, 48–50]. Note that individual circles are filled with the same color code to represent the adopted optical power $P_s$ such that their performance can be compared to the corresponding shot-noise limits in the same plot.

Current SD-OCT systems with the use of high-speed line scan cameras can typically achieve up to ~200 kHz A-scan rate [20, 50], which is not sufficient for enabling video-rate 3D OCT imaging, as discussed in the introduction section. Utilizing a high-speed area-scan camera together with a streak scanner, the imaging speed of the SD-OCT can be boosted up to ~1 MHz, but in streak-mode [49]. Another SD-OCT system based on optical demultiplexers has demonstrated an A-scan rate as fast as 60 MHz with a good sensitivity of 88 dB [22]. However, the system employed as many as 256 photoreceivers and 32 data-acquisition (DAQ) boards, which incur significant cost and system complexity.

SS-OCT is to-date another modality which promises high A-scan rate well beyond 100 kHz. For an example, using a spectral-filter based on a rotating polygonal mirror can provide an A-scan rate of 402 kHz [23]. Incorporating MEMS system with a vertical cavity surface emitting laser (VCSEL) showed a superior coherence length and can operate at an A-scan rate ranging from ~100 kHz to 1 MHz [24, 48]. FDML-OCT typically employs piezoelectric-tunable Fabry-Pérot (FP) filter for rapid wavelength sweep. The swept-rate is intrinsically limited by the resonance frequency of the FP cavity, which can now achieve a fundamental frequency up to few hundred kHz. Further swept-rate scaling can be achieved by operating the FP cavity at its higher harmonics and the fiber buffering technique. Together with multi-
spot illumination, an A-scan rate of ~1-10MHz was achieved [17]. With strong illumination power of ~15 – 30 mW incident on the sample, the sensitivity of such multi-MHz FDML-OCT can achieve as high as ~100 dB, close to the shot-noise-limited operation [7]. Recently, video-rate 3D OCT has been demonstrated by this modality [8]. Note that we adopt the single-spot A-scan rate in the work by Wieser et. al. [7], i.e. 5.2MHz, in Fig. 6 due to that the sensitivity values compared in the same plot are measured by the single-spot illumination scheme.

These SS-OCT systems show high sensitivity and resolution. Nevertheless, long-term robust operation inevitably hinges on the stability as well as the fatigue of the mechanical moving part used in the swept source. Inertia-free and passive wavelength-swept at ultrahigh-speed is thus an attractive alternative. So far, time-stretch-based OCT via GVD in a long dispersive fiber or a fiber Bragg grating (FBG) can easily achieve an A-scan rate well above multi-MHz. Previous time-stretch OCT systems suffered from either narrow-band operation and/or weak optical signal accompanied with strong nonlinear noise, leading to poor resolution and low sensitivity [25–27, 29]. Recent work used chirped FBG, to further improve the sensitivity to 82 dB at 5 MHz A-scan rate [30]. Broadband optical amplification plays an important role in maintaining high sensitivity for any time-stretch modalities [25–30]. It thus made the first generation of AOT-OCT system possible for in-vivo bioimaging [28]. However, the shot-to-shot fluctuation in SC source hindered further improvement in sensitivity and thus practical clinical imaging applications. In this work, we employed the home-built MLFL in the AOT-OCT system, which delivers highly stable and coherent broadband wavelength-swept waveforms at an ultrafast A-scan rate of 11.5 MHz, without additional buffing technique. This gives the record sensitivity (~90dB) in time-stretch-based OCT, 6 dB lower than the shot-noise limit. The difference is mainly attributed to the amplifier noise as well as the intensity noise of the source [34]. It should be noted that the rationale of scaling the A-scan rate further beyond 10 MHz, or even 100MHz diminishes, in view of the required high-sensitivity (> 90dB) for practical clinical imaging. It can be clearly justified by the fact that the shot-noise limit easily falls below 90dB at the A-scan rate beyond few tens of MHz, unless resorting to stronger illumination, which is on the other hand limited by the safety standard. As a result, AOT-OCT should be designed to operate at no more few tens of MHz if it is to be applied for video-rate 3D OCT in clinical applications. Hence, the key future development of AOT-OCT is recommended to be further optimization of the broadband amplifiers with lower noise figure, broadband stable MLFL.

5. Conclusion

In summary, we have demonstrated a new generation of AOT-OCT system with a compact MLFL source for stable and ultrahigh-speed wavelength-swept operation at an A-scan rate of 11.5MHz. The system also demonstrated a superior roll-off performance (>4mm/dB) with a high sensitivity of ~90 dB. This feature is particularly beneficial for long-range imaging applications such as full eye imaging, or endoscopic imaging of large lumen in-vivo. The current all-optical and inertia-free AOT-OCT system enabled high-quality biological imaging in-vivo in both 2D and 3D. While speed scaling is important for high-speed OCT development, one should also be aware of the fundamental degradation of sensitivity (governed by shot-noise limit) with progressively higher A-scan rates. We note that an A-scan of tens of MHz (of a single scanned-beam) should be considered as the practical limit if the sensitivity has to be maintained at ~90dB for clinical applications. Compared to the existing high-speed OCT systems, AOT-OCT is expected to be a robust alternative to realize multi-MHz OCT and thus real-time video rate 3D OCT with high-speed data processing.

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