

Review Article

Advances in Optical Coherence Tomography

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ABSTRACT

Background: The wave-like characteristics of light lie at the heart of Optical Coherence Tomography (OCT), a non-invasive imaging technique widely utilized in ophthalmology. This technique provides detailed, high-resolution images of the intricate internal structure of the eye. This review is dedicated to providing a comprehensive understanding of the foundational principles of OCT, tracing its progression from time-domain to Fourier-domain methodologies, and examining the substantial advancements that have profoundly transformed its role in ophthalmological diagnostics.

Material and Methods: Our methodology involves a comprehensive literature review. The review begins with a meticulous exploration of the fundamental principles of OCT, delving into its profound connection with the wave-like nature of light. We then proceed with an in-depth examination of the progression of OCT methodologies, tracing their journey from time-domain to Fourier-domain. This is followed by an exhaustive discussion of the most recent advancements in OCT technology, including the emergence of vis-OCT, AO-OCT, PS-OCT, High-Res OCT, and FFOCT.

Results: Since its inception, OCT has undergone several evolutions, with each advancement contributing to improved image resolution, increased acquisition speed, and enhanced imaging depth. These technological advancements have allowed for a more precise and early detection of various ocular conditions. Furthermore, innovations such as vis-OCT, AO-OCT, and others, have demonstrated their potential in expanding OCT's diagnostic capabilities.

Conclusions: The continual evolution and refinement of OCT technology underscore its critical role in enhancing our understanding of the eye's microstructure and contribute to more effective diagnostic strategies and targeted interventions for various ocular pathologies. As OCT technology continues to evolve, it promises an exciting future for eye care, with possibilities for even more advanced imaging techniques, better diagnostics, and improved patient care.

Keywords: Optic Coherence Tomography (OCT); AO-OCT; PS-OCT.

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Introduction

The properties of light have long fascinated scientists, displaying dual characteristics that often defy our intuitive understanding. In certain scenarios, light manifests as discrete “particles,” while in others, it exhibits behaviors that can only be explained by its wave nature. This fundamental duality poses a significant ongoing challenge in modern physics. Intriguingly, despite our limited understanding of the underlying reasons for this duality, we have successfully harnessed the wave-particle nature of light to develop invaluable tools. In essence, we utilize light in a pragmatic manner, capitalizing on its instrumental potential while acknowledging our incomplete comprehension of its true essence.

In the modern era, precise measurement tools play a pivotal role in accurately determining distances, sizes, and visualizing otherwise imperceptible structures. Many of these tools leverage the distinctive wave-particle properties of light. One such indispensable tool, widely employed in ophthalmology, is Optical Coherence Tomography (OCT). OCT harnesses the remarkable behavior of light to enable high-resolution imaging and precise measurements in the field of ophthalmology.

In 1993, Swanson et al.¹ achieved a significant milestone by obtaining the first in vivo retinal images, marking a notable advancement in the field. Concurrently, Fercher et al.² from the Medical University of Vienna independently showcased their own demonstrations of retinal imaging, further contributing to the growing body of research in this area. This method is an advancement of a previously established technique known as low-coherence interferometry. It has been effectively deployed to procure in vivo optical cross sections of the anterior segment. Moreover, it

has demonstrated its utility in the diagnosis and analysis of various retinal conditions such as macular detachment, macular hole, epiretinal membrane, macular edema, and idiopathic central serous chorioretinopathy.

Interference in OCT arises when the path length to the reference mirror aligns closely with that of the tissue, falling within the coherence length of the light source. As the reflected beams recombine, they generate an interference profile from which intensity information, represented as a reflectivity profile in depth, can be extracted. The manipulation of the reference mirror's position permits the detection of backscattered tissue intensity levels from various depths within the tissue sample. This particular approach is commonly referred to as time-domain (TD)-OCT, as it directly acquires time-encoded signals.

Subsequently, the preliminary OCT methodology evolved to a more advanced stage, where the intensity profiles, also known as A-scans, are generated via a Fourier transform of the detected frequencies. This advancement significantly enhances the speed at which A-scan data can be collected, further improving the overall efficiency of the OCT process. The acquisition of frequency information can be facilitated through either the utilization of a broad-bandwidth light source in combination with a spectrometer, commonly designated as Spectral-Domain OCT (SD-OCT)^{3, 4}, or by sweeping a narrow-bandwidth source across a wide range of frequencies with a photodetector, a method referred to as Swept-Source OCT (SS-OCT)^{5, 6}.

In this paper, we initially elucidate the fundamental principles of interference, an integral component employed in OCT technology. Subsequently, we provide a detailed description of the various types of

OCT methodologies currently available in the field.

Fundamental Concepts of Optical Coherence Tomography

OCT capitalizes on the intrinsic wave behavior of light, taking advantage of one of the most captivating phenomena in optics: interference. This phenomenon arises when two light beams, characterized by the same frequency and phase, combine, leading to the formation of a composite wave with an amplitude that is the sum of their individual amplitudes. To ensure predictable constructive and destructive interference, incident waves must exhibit a constant phase relationship and possess a narrow bandwidth, giving rise to the property known as coherency. This phenomenon refers to the property of light waves when they exhibit a well-defined relationship between their phases at different points in space or time and it allows for precise interference-based measurements and high-resolution imaging.

OCT capitalizes on the coherency of light using a setup similar to the Michelson-Morley interferometer, which was originally developed in 1887 to determine the speed of light. The Michelson-Morley experiment holds substantial historical significance as its results were later utilized by Einstein in formulating the theory of special relativity. Beyond its initial purpose, the versatile configuration of the Michelson-Morley interferometer has found applications in various fields, encompassing the detection of gravitational waves, spectroscopy, and the study of atmospheric layers.

In light of the significant role played by the Michelson-Morley interferometer in the development of OCT, we present a comprehensive overview of its principal components and their respective functions.

Figure 1 illustrates the primary setup of the Michelson-Morley interferometer. A coherent light source emits a beam that is directed towards a splitter, dividing it into two distinct paths. One path allows half of the beam to pass through, while the other path reflects it, effectively acting as a mirror. The reflected beam then proceeds towards another mirror, where it undergoes another round of reflection. Concurrently, the transmitted beam travels towards a second mirror and is subsequently reflected back towards the splitter. As a result, at the splitter, we observe the presence of two reflected rays, each having completed a round trip to a mirror. It is worth emphasizing that these rays maintain their coherence throughout the entire process.

However, it is important to note that the two reflected rays may accumulate a phase difference due to the different distances they have traveled. Consequently, upon reaching the splitter, they can either interfere constructively or destructively. This interference gives rise to distinct patterns, whose characteristics are directly influenced by the distances between the mirrors and the splitter. The relationship between these interference patterns and the mirror distances, along with the wavelength of light, can be precisely described using mathematical equations based on the wave nature of light. By meticulously analyzing these interference patterns, it becomes possible to accurately determine the distances of each mirror with a high degree of precision.

Now, let's consider replacing one of the mirrors in the Michelson-Morley interferometer with a textured surface. Due to the unique structure and composition of the texture, it naturally reflects a portion of the incident light. As a result, distinctive interference patterns emerge, whose shape and size are contingent upon the properties of the tissue

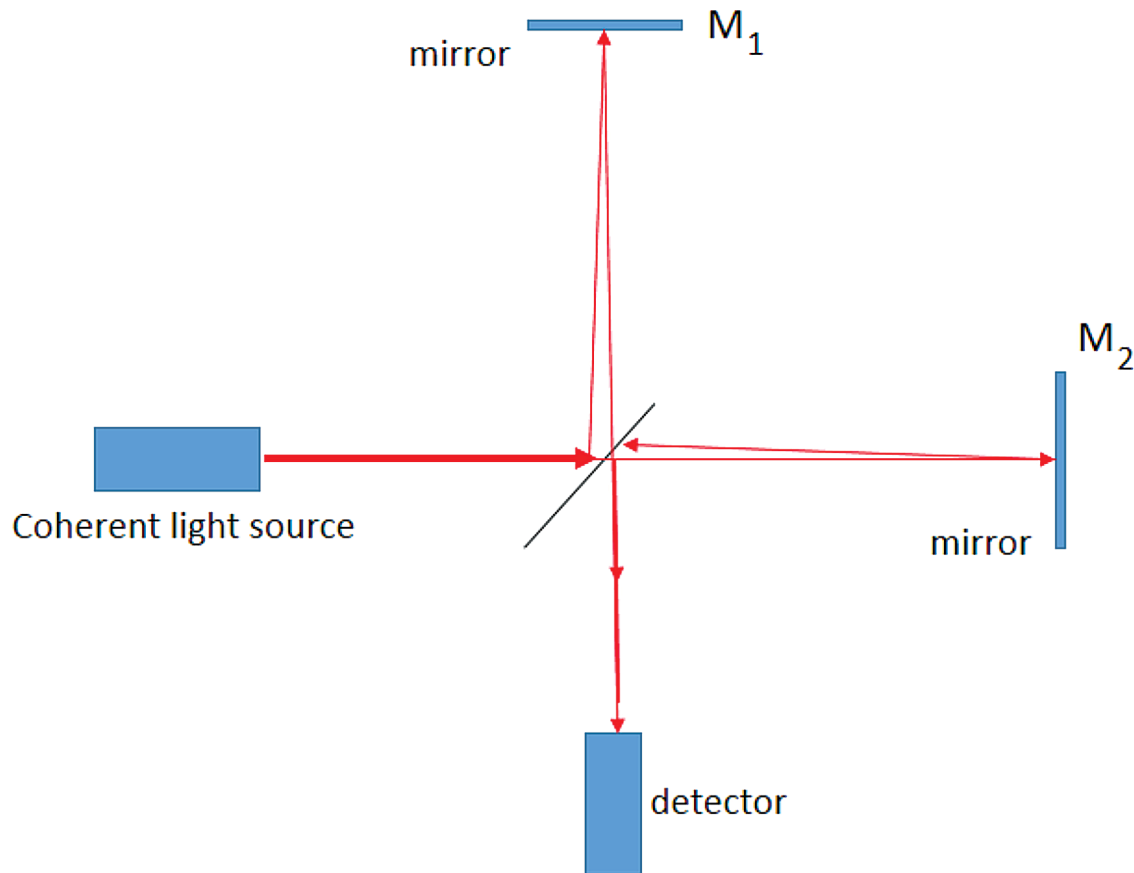


Figure 1: The diagram presents the essential configuration of the Michelson-Morley interferometer

or texture being examined. Remarkably, it becomes possible to reconstruct the shape and characteristics of the reflective texture by analyzing the corresponding interference patterns. This precise principle forms the foundation of an OCT device – a powerful tool that employs coherent light and interprets the interference patterns reflected from the tissue under investigation, enabling comprehensive analysis of the desired tissue condition within the eye. As previously mentioned, in 1993, Swanson et al.¹ achieved a significant milestone by acquiring the first in vivo retinal images, representing a notable advancement in the field. Figure 2 presents the groundbreaking first in vivo OCT image of the normal retina, which has been adapted from Swanson et al.¹ This significant achievement showcases the initial in vivo OCT image of a healthy human

retina, revealing an impressive approximate axial resolution of 15 μm (in tissue) at a wavelength of approximately 840 nm. The image provides a comprehensive depiction of the retinal architectural morphology, encompassing essential features such as the choroid, retinal pigment epithelium, nuclear layers, plexiform layers, and retinal nerve fiber layer.

Varieties of Optical Coherence Tomography Techniques

As previously mentioned, in OCT, low coherence interferometry is employed to obtain 400 axial scans (A-scans) intensity profiles, requiring the division of light into two paths: one directed towards a reference arm housing a mirror and the other directed towards the sample. However, the initial constraint leading

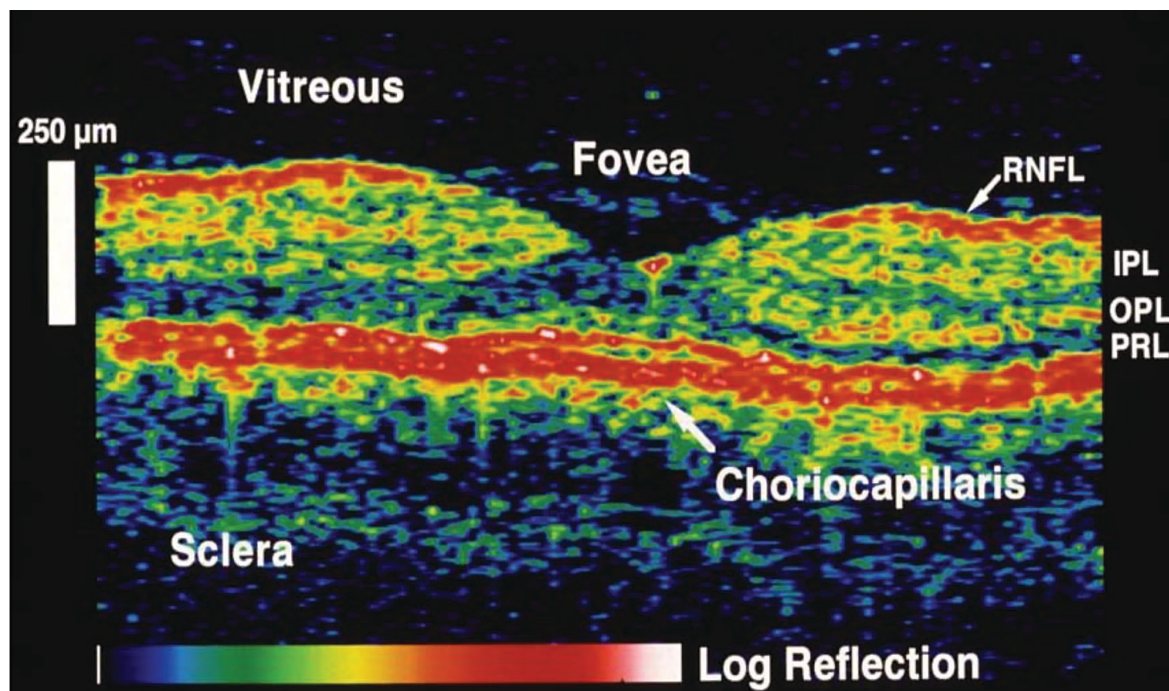


Figure 2: The initial in vivo OCT image of a healthy human retina demonstrates an approximate axial resolution of 15 μm (in tissue) at a wavelength of approximately 840 nm (adopted from Swanson et al.¹).

to a limitation of only A-scans is due to the physical movement of the mirror. Through the manipulation of the reference mirror's position, it becomes possible to detect backscattered tissue intensity levels at different depths within the tissue sample. This innovative technique is commonly referred to as "time-domain (TD)-OCT" owing to its direct acquisition of time-encoded signals. Subsequent to the introduction of the initial commercial TD-OCT system, notable hardware enhancements have been incorporated, encompassing improved axial resolution⁷ and increased scanning speed⁸ within contemporary commercial systems.

Fourier domain OCT (FD-OCT, also known as frequency domain OCT) marks a significant advancement as the second generation of OCT technology, providing a highly efficient implementation of the low-coherence interferometry principle. A fundamental departure from its predecessor,

TD-OCT, FD-OCT capitalizes on spectral information to generate A-scans without the need for mechanical scanning of the optical path length. This technique revolutionizes the imaging process by capturing a comprehensive spectrum of signals simultaneously, enabling faster and more precise data acquisition. The absence of mechanical scanning not only reduces the imaging time but also minimizes potential motion artifacts, resulting in sharper and more detailed images. Moreover, FD-OCT enhances the sensitivity and signal-to-noise ratio, further improving the quality of obtained data. Fourier-domain detection serves as the foundation for additional techniques, including spectral-domain OCT (SD-OCT) and swept-source OCT (SS-OCT), both of which fall under the umbrella of Fourier-domain detection.

At present, the OCT field is predominantly governed by the utilization of SD-OCT

technique. Within SD-OCT, the reference arm remains stationary while the depth information is derived through a Fourier transform of the spectrally resolved interference fringes in the detection arm of a Michelson interferometer^{3, 4}. This methodology has garnered widespread acceptance and application due to its innovative approach⁸. SD-OCT capitalizes on a spatially coherent source characterized by low temporal coherence. This carefully crafted combination allows for enhanced precision and accuracy in imaging, underpinning the immense popularity of SD-OCT. Evidence has established that SD-OCT possesses a substantial sensitivity advantage compared to time-domain detection, primarily due to its ability to essentially measure all light echoes concurrently^{9, 10}. The SD-OCT method demonstrates a notable relationship with Fourier spectroscopy. This relationship is instrumental in the enhancement of its sensitivity, which is dictated by the proportionality between the axial resolution and the imaging depth. Compared to conventional OCT systems, SD-OCT presents an extraordinary enhancement factor, typically ranging between 50 and 100 times. This enhancement leads to a commensurate increase in the speed of image acquisition, thereby revolutionizing OCT research and development^{11, 12}.

The second variation of Fourier-domain detection, known as Swept-Source Optical Coherence Tomography (SS-OCT), employs an interferometer equipped with a narrow-linewidth, frequency-swept laser, along with detectors, to evaluate interference as a function of time. The utilization of a frequency-swept laser within this methodology effectively assigns distinctive time delay labels, which are subsequently detected through the phenomenon of interference. The effectiveness of SS-OCT is intrinsically tied

to the capabilities of the swept laser. As a result, the progress and enhancement of SS-OCT's performance have been significantly influenced by critical developments and improvements in laser technology. SS-OCT exhibits several advantages over its counterpart technologies. Notably, SS-OCT obviates the need for a spectrometer and a line scan camera. Additionally, it can function at extended wavelengths, facilitating faster imaging speeds and a greater imaging range compared to SD-OCT. Furthermore, the utilization of long wavelengths, specifically at 1050 nm, results in reduced attenuation from ocular opacities, thereby enhancing the depth of the imaging output^{5, 6}.

Contemporary Progress in OCT Innovations

The evolution of Optical Coherence Tomography (OCT) technology is not exclusively confined to the types delineated in the preceding section. Indeed, the persistent advancement of more sophisticated and efficient OCT techniques has culminated in remarkable accomplishments. These breakthroughs, which represent significant milestones in the progression of OCT, are discussed in this section.

Visible light OCT (vis-OCT) utilizes visible light as its illumination source for image capture. This distinguishes it from the majority of OCT methodologies, which predominantly rely on near-infrared (NIR) light¹³. The vis-OCT approach, whose initial concept was introduced by Povazay et al.¹⁴, facilitates an enhanced resolution of retinal biological features due to the use of shorter illumination wavelengths. Despite the prevailing preference for NIR light in most OCT devices - a preference driven by its superior tissue penetration and cost-effectiveness - there has been a noticeable shift in recent times. Specifically, the interest in vis-OCT has seen

a marked increase.

Vis-OCT systems primarily operate based on supercontinuum lasers. Inherently, these lasers generate relative intensity noise, which serves as a significant limitation to their clinical application¹⁵. The issue of relative intensity noise can be mitigated to an extent by lengthening the exposure time of the camera. However, this solution is not without its drawbacks. Increasing the camera's exposure time subjects the patients to a higher amount of light. This excess light can induce discomfort and result in increased eye movements by the patient, which in turn, can pose challenges to acquiring high-quality images. Therefore, while the use of supercontinuum lasers in Vis-OCT systems does hold certain advantages, these are somewhat offset by the drawbacks associated with relative intensity noise and its management.

The advancements in vis-OCT have brought forth notable enhancements in image quality, thereby facilitating an improved visualization of neurons across the full depth of the rat retina. This not only broadens the spectrum of research possibilities but also contributes to more accurate and detailed data collection. With the progress in vis-OCT technology, a new frontier has been unlocked in the realm of retinal imaging. It has become capable of capturing high-resolution images of intricate structures within the retina. Specifically, vis-OCT now allows for the imaging of complex structures such as the inner plexiform layer, the retinal pigment epithelium, and Bruch's membrane¹⁶. The ability to clearly visualize these layers enhances our understanding of the microstructural composition of the retina, providing invaluable insights into its physiology and pathology.

The utility of OCT has also been significantly augmented through the integration of a

technique known as Adaptive Optics (AO). Originally conceived to mitigate the effects of atmospheric turbulence on astronomical imaging¹⁷, this methodology has shown to be beneficial in amplifying the competencies of OCT¹⁸. Furthermore, this adoption of AO in the realm of OCT has facilitated the emergence of a novel technology known as Adaptive Optics OCT (AO-OCT).

Figure 3, adopted from the work of Jonnal et al.¹⁹, shows the various constituents of an AO system. These systems typically comprise a wavefront sensor, often a Shack-Hartmann wavefront sensor, tasked with measuring distortions. Concurrently, a wavefront corrector, usually in the form of a deformable mirror, modulates its shape to negate these aberrations. A controller serves as an intermediary, orchestrating the interaction between these elements to optimize system performance²⁰. The most salient advantage of implementing AO in the field of ophthalmology lies in its ability to facilitate the in vivo imaging of individual cells, including photoreceptors^{18, 21}. Moreover, AO-OCT enables the three-dimensional imaging and high-resolution visualization of complex retinal structures, such as photoreceptors and the retinal pigment epithelium. This capability significantly enhances our understanding of these structures and enables the investigation of their roles in various ocular pathologies.

Several methodologies have also been developed to enhance the images procured through AO-OCT. Notably, Computational Adaptive Optics (CAO), which corrects aberrations following data collection, has surfaced as a cost-efficient strategy to augment depth-independent resolution in OCT²². Nevertheless, this technique frequently results in a compromise in image quality. Conversely, Sensorless AO (SAO) employs the inherent

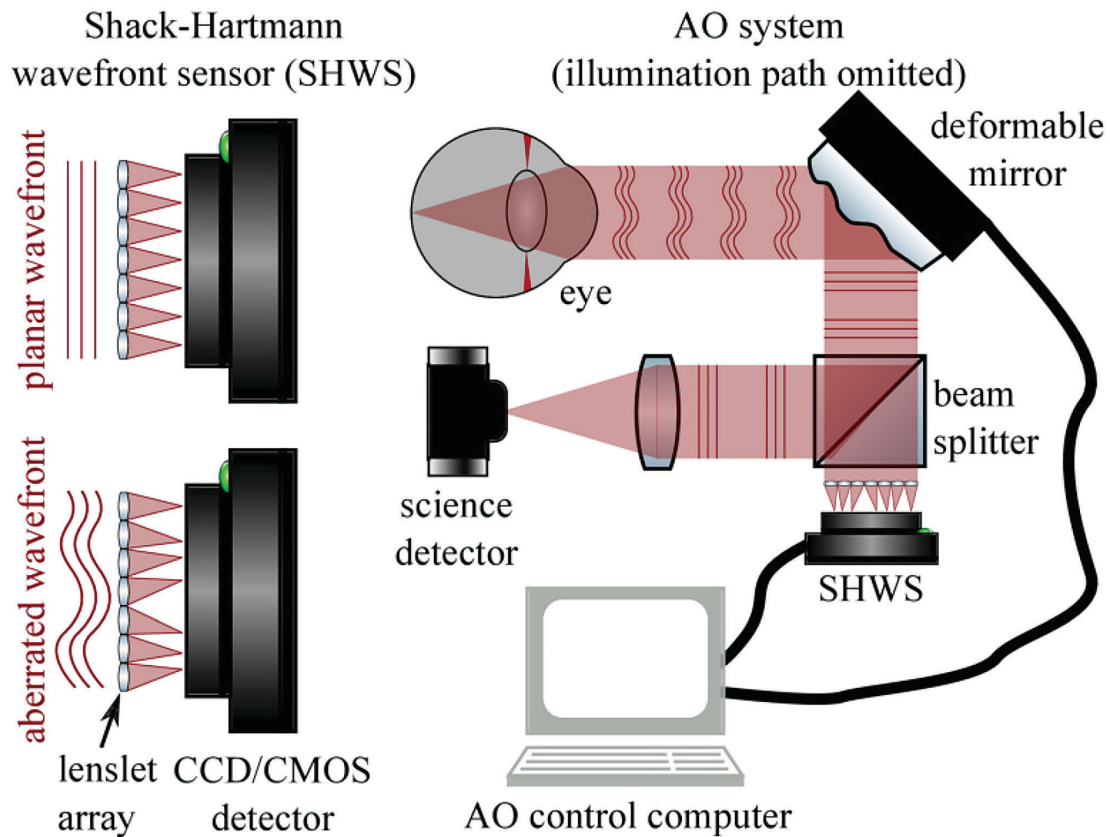


Figure 3: The schematic diagram provided illustrates the various components of an Adaptive Optics (AO) system. This representation is adopted from the work of Jonnal et al.¹⁹

properties of images to measure and rectify aberrations²³. Despite these advancements, the wider implementation of both CAO and SAO within ophthalmology practices remains constrained due to numerous challenges. These include motion artifacts and elevated acquisition expenses.

Several alternative implementations of OCT have been developed, expanding its capabilities in various ways. Polarization-sensitive OCT (PS-OCT), first demonstrated in 1992, works by analyzing the polarization state of backscattered light and measuring the birefringence in the tissue sample, with different tissues known to alter the polarization state of the OCT light source²⁴. In addition, High-resolution OCT (High-Res OCT) broadens the bandwidth of the OCT light source, thereby enhancing optical axial

resolution and enabling the capture of clearer images of small vasculature, including the choriocapillaris²⁵. Full-field OCT (FFOCT) generates two-dimensional enface scans of ocular tissue at various depths, which can be reconstructed into three-dimensional volumetric images with resolutions of up to 1 micron. Other advancements include Wide-Field and Ultrawide-Field OCT (WF-OCT and UWF-OCT), which significantly broaden the field of view in OCT imaging^{26, 27}.

Conclusion

In conclusion, the principle of Optical Coherence Tomography (OCT) is centered around wave-like nature of light, allowing for detailed visualization and accurate measurement of ocular structures. Since its inception, OCT has continually evolved,

introducing new methods and techniques that have significantly advanced ophthalmic diagnostics. The progression from time-domain OCT to Fourier-domain OCT, including the spectral-domain and swept-source methodologies, demonstrates this ongoing development. These technological advancements have not only improved image resolution and speed of acquisition, but they also allowed for greater imaging depth, which has further expanded the potential for accurate and early detection of various ocular conditions.

Moreover, the continuous refinement of OCT technology, as illustrated by developments such as vis-OCT, AO-OCT, PS-OCT, High-Res OCT, and FFOCT, exemplifies the adaptability and potential of OCT in addressing diverse diagnostic needs in ophthalmology. The ever-growing landscape of OCT underscores its pivotal role in enhancing our understanding of the eye's microstructural composition, thereby contributing to more effective diagnostic strategies and targeted interventions for numerous ocular pathologies. As OCT technology continues to evolve, it promises an exciting future for eye care, with possibilities for even more advanced imaging techniques, better diagnostics, and ultimately improved patient care.

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REFERENCE

1. Swanson EA, Izatt JA, Hee MR, Huang D, Lin C, Schuman J, et al. In vivo retinal imaging by optical coherence tomography. *Optics letters*. 1993;18(21):1864-6.
2. AF F. In vivo optical coherence tomography. *Am J Ophthalmol*. 1993;116:113-4.
3. Fercher AF, Hitzenberger CK, Kamp G, El-Zaiat SY. Measurement of intraocular distances by backscattering spectral interferometry. *Optics communications*. 1995;117(1-2):43-8.
4. Häusler G, Lindner MW. “Coherence radar” and “spectral radar”-new tools for dermatological diagnosis. *Journal of biomedical optics*. 1998;3(1):21-31.
5. Považay B, Bizheva K, Hermann B, Unterhuber A, Sattmann H, Fercher AF, et al. Enhanced visualization of choroidal vessels using ultrahigh resolution ophthalmic OCT at 1050 nm. *Optics express*. 2003;11(17):1980-6.
6. Unterhuber A, Považay B, Hermann B, Sattmann H, Chavez-Pirson A, Drexler W. In vivo retinal optical coherence tomography at 1040 nm-enhanced penetration into the choroid. *Optics express*. 2005;13(9):3252-8.
7. Drexler W, Morgner U, Kärtner F, Pitris C, Boppart S, Li X, et al. In vivo ultrahigh-resolution optical coherence tomography. *Optics letters*. 1999;24(17):1221-3.
8. Wojtkowski M, Leitgeb R, Kowalczyk A, Bajraszewski T, Fercher AF. In vivo human retinal imaging by Fourier domain optical coherence tomography. *Journal of biomedical optics*. 2002;7(3):457-63.
9. Leitgeb R, Hitzenberger C, Fercher AF. Performance of fourier domain vs. time domain optical coherence tomography. *Optics express*. 2003;11(8):889-94.
10. De Boer JF, Cense B, Park BH, Pierce MC, Tearney GJ, Bouma BE. Improved signal-to-noise ratio in spectral-domain compared with time-domain optical coherence tomography. *Optics letters*. 2003;28(21):2067-9.
11. Nassif N, Cense B, Park BH, Yun SH, Chen TC, Bouma BE, et al. In vivo human retinal imaging by ultrahigh-speed spectral domain optical coherence tomography. *Optics letters*. 2004;29(5):480-2.

12. Wojtkowski M, Srinivasan VJ, Ko TH, Fujimoto JG, Kowalczyk A, Duker JS. Ultrahigh-resolution, high-speed, Fourier domain optical coherence tomography and methods for dispersion compensation. *Optics express*. 2004;12(11):2404-22.
13. Shu X, Beckmann L, Zhang HF. Visible-light optical coherence tomography: a review. *Journal of biomedical optics*. 2017;22(12):121707-.
14. Povazay B, Bizheva K, Unterhuber A, Hermann B, Sattmann H, Fercher AF, et al. Submicrometer axial resolution optical coherence tomography. *Optics letters*. 2002;27(20):1800-2.
15. Rubinoff I, Miller DA, Kuranov R, Wang Y, Fang R, Volpe NJ, et al. High-speed balanced-detection visible-light optical coherence tomography in the human retina using subpixel spectrometer calibration. *IEEE Transactions on Medical Imaging*. 2022;41(7):1724-34.
16. Zhang T, Kho AM, Yiu G, Srinivasan VJ. Visible light optical coherence tomography (OCT) quantifies subcellular contributions to outer retinal band 4. *Translational vision science & technology*. 2021;10(3):30-.
17. Babcock HW. The possibility of compensating astronomical seeing. *Publications of the Astronomical Society of the Pacific*. 1953;65(386):229-36.
18. Liang J, Williams DR, Miller DT. Supernormal vision and high-resolution retinal imaging through adaptive optics. *JOSA A*. 1997;14(11):2884-92.
19. Jonnal RS, Kocaoglu OP, Zawadzki RJ, Liu Z, Miller DT, Werner JS. A review of adaptive optics optical coherence tomography: technical advances, scientific applications, and the future. *Investigative ophthalmology & visual science*. 2016;57(9):OCT51-OCT68.
20. Akyol E, Hagag AM, Sivaprasad S, Lotery AJ. Adaptive optics: principles and applications in ophthalmology. *Eye*. 2021;35(1):244-64.
21. Kadomoto S, Muraoka Y, Uji A, Ooto S, Kawai K, Ishikura M, et al. Human foveal cone and Müller cells examined by adaptive optics optical coherence tomography. *Translational Vision Science & Technology*. 2021;10(11):17-.
22. Ruiz-Lopera S, Restrepo R, Cuartas-Vélez C, Bouma BE, Uribe-Patarroyo N. Computational adaptive optics in phase-unstable optical coherence tomography. *Optics letters*. 2020;45(21):5982-5.
23. Liu L, Wu Z, Qi M, Li Y, Zhang M, Liao D, et al., editors. *Application of Adaptive Optics in Ophthalmology*. Photonics; 2022: MDPI.
24. Hee MR, Huang D, Swanson EA, Fujimoto JG. Polarization-sensitive low-coherence reflectometer for birefringence characterization and ranging. *JOSA B*. 1992;9(6):903-8.
25. Spaide RF, Lally DR. High Resolution Spectral Domain Optical Coherence Tomography of Multiple Evanescent White Dot Syndrome. *Retinal Cases and Brief Reports*. 2022.
26. Grieve K, Thouvenin O, Sengupta A, Borderie VM, Paques M. Appearance of the retina with full-field optical coherence tomography. *Investigative ophthalmology & visual science*. 2016;57(9):OCT96-OCT104.
27. Scholler J, Mazlin V, Thouvenin O, Groux K, Xiao P, Sahel J-A, et al. Probing dynamic processes in the eye at multiple spatial and temporal scales with multimodal full field OCT. *Biomedical optics express*. 2019;10(2):731-46.

Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.