En face optical coherence tomography: a technology review [Invited]

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Abstract: A review on the technological development of en face optical coherence tomography (OCT) and optical coherence microscopy (OCM) is provided. The terminology originally referred to time domain OCT, where the preferential scanning was performed in the en face plane. Potentially the fastest realization of en face image recording is full-field OCT, where the full en face plane is illuminated and recorded simultaneously. The term has nowadays been adopted for high-speed Fourier domain approaches, where the en face image is reconstructed from full 3D volumes either by direct slicing or through axial projection in post processing. The success of modern en face OCT lies in its immediate and easy image interpretation, which is in particular of advantage for OCM or OCT angiography. Applications of en face OCT with a focus on ophthalmology are presented. The review concludes by outlining exciting technological prospects of en face OCT based both on time as well as on Fourier domain OCT.

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1. Introduction

Optical coherence tomography (OCT) [1] provides image slices of tissue with high optical resolution in a non- or minimally invasive manner. There are numerous excellent reviews and book sections highlighting the many applications of OCT in medical imaging today [2], although its most successful application is still retinal imaging, in ophthalmology [3]. Conventional OCT scans an illumination spot across a tissue surface and records at each spot the depth structure. A depth scan is called amplitude scan (A-scan), analogous to ultrasound imaging. Arranging successively recorded A-scans along one scanning direction in a 2D array forms a tomogram or brightness scan (B-scan). The retina with its preferentially layered structure has been the ideal target for OCT, since this structure is well appreciated in recorded tomograms. Abnormal morphological changes can immediately be spotted as disruption of the layered structure even by non-specialists. Together with the easy operation of OCT systems this formed the basis for the huge success of this relatively young medical imaging technology. Also, the technology development coincided with perfect timing with the market release of antiVEGF drugs for treatment of wet AMD. OCT has already become the golden standard for the treatment planning and monitoring of AMD as well as of many other retinal diseases, such as diabetic retinopathy.

In the early days of OCT, the recording speed of tomograms was still slow, due to the in effect low detection efficiency of by that time established time domain OCT. Faster depth scanning critically reduced the detection sensitivity. However, for disease evaluation and treatment monitoring, it was often important to evaluate lesion extensions such as in geographic atrophy, or lesion volumes of edema or drusen. For this task it was necessary to record full tissue volumes. To keep the measurement times low, only a few tomograms were recorded for covering a volume, with increased risk of missing important pathological details. This gap was for the first time closed by en face transverse scanning (TS) time domain (TD)
OCT. In en face TS OCT the preferential scanning direction is not in depth, but laterally. Equipped with resonant scanners, en face OCT was thereby capable to record already densely sampled en face images with rates of several tens of Hz. However, in this case, it is necessary to distinguish the actual coherently gated interference or OCT signal at a defined sample depth from the axially non-localized backscattered sample light intensity. This is accomplished by introducing a defined temporal modulation to the OCT signal and using a lock-in detection scheme (see section 6.2). This allows recording of a temporally gated OCT signal from a given sample depth as defined by the reference arm length. In order to produce a depth scan, the reference arm delay is changed slowly or in a stepwise manner. The resulting en face images are similar to fundus photographs, that ophthalmologists are used to, but with the additional benefit of exhibiting also information about the layered retinal structure. Figure 1 demonstrates the scanning preferences for conventional OCT to produce fast tomograms versus the TS OCT configuration for fast en face or C-scan imaging.

Fig. 1. Scanning preference for conventional TD OCT in the axial direction (lhs). En face TDOCT uses the transversal direction for fast scanning (rhs) and is comparably slow in axial direction. This figure sets also the axis notations for the following discussions in the text.

The en face view is the standard view in most microscopy techniques. Full field (FF) OCT enhances the capabilities of standard bright field microscopy with additional coherence gating, helping to efficiently reject multiply scattered-light with gain in imaging depth and contrast [4] (see section 5). In TD FFOCT the focal plane can be kept centered with the coherence gate during reference arm scanning, thereby maintaining both gating mechanisms. In swept source (SS) FFOCT the signal is collected from all depths in parallel, causing less efficient suppression of scattering cross talk, which results in reduced image contrast as compared to TD FFOCT. The critical loss of contrast is less pronounced with line field OCT (LF OCT) that still keeps half of the confocal gate.

Nowadays, with ultrafast Fourier domain OCT systems, en face images slices are selected retrospectively from full recorded volumes, or are calculated by depth projection along selected depth ranges. Fourier domain system can be distinguished into the earlier spectral domain OCT and swept source OCT. In ophthalmology, en face OCT has become of particular interest for evaluating OCT angiographies or for retinal imaging with high lateral resolution. The combination of FFOCT with SS OCT is in fact the most compact OCT realization with the benefit of higher detection sensitivity. Figure 2 depicts the different OCT modalities and sets the common terms. Note that line field (LF) SS OCT, that is not shown, is similar to FF SS OCT, but with the need of a single scan axis.
In the following we will shortly review the historical development of en face OCT. We will further highlight some details about modulation techniques, address challenges related to axial motion artifacts, and review multimodal functional extensions of en face OCT.

Fig. 2. Overview on OCT technology with TDOCT on the left and FDOCT on the right hand side: (a) TS en face OCT with SLO channel and balanced detection (b) FFOCT and SS FFOCT (c) SS OCT with balanced detection (d) spectral domain OCT using a spectrometer with a diffraction grating and a line array sensor.

2. Historical overview

As already mentioned, first en face systems were based on time-domain OCT. The advantage of en face OCT is its similarity to confocal microscopy or scanning laser ophthalmoscopy, with the additional benefit of providing coherent depth gating. The first en face OCT system was reported by Izatt et al. for optical coherence microscopy [5]. Later, Podoleanu et al. were able to image the human retina in-vivo with en face TS OCT introducing carrier modulation through lateral scanning [6,7]. The latter system was multimodal by combining OCT with scanning laser ophthalmoscopy (SLO) [8] (see section 6.1). Further improvements regarded the data visualization [1] and the extension to perform quantitative 3D tissue evaluation [2].

At the same time full field OCT emerged, exhibiting excellent resolution and image quality as first shown by Beaurepaire et al. [3] and further improved by Dubois et al. [4] and Grieve et al [5]. The highest OCT imaging speed at that time was reported by Hitzenberger et al. in 2003 [6]. They recorded a full volume in only about 1 sec.

This came just before the advent of FDOCT, that had by that time already been demonstrated for high speed in-vivo retinal imaging by Wojtkowski, Leitgeb et al. in 2002 [7]. The concept of recording the interference signal as a function of optical frequency instead of time delay was introduced to biomedical imaging by Fercher et al. [8]. As already mentioned above, such FD OCT system might also employ a tunable light source such that the spectral interference signal is recorded over time. The latter modality termed swept source OCT (SSOCT) was introduced in the same year by Lexer et al. and Chinn et al. [9,10].
The intrinsic higher sensitivity of FDOCT, that was derived for the shot noise limit by Leitgeb et al [11] and was later on generalized to include other noise sources [12,13] as well as to SSOCT [14]. The recognition of the sensitivity advantage marked a paradigm change in OCT since high speed imaging came at no cost regarding sensitivity.

Volumetric imaging and the generation of arbitrary en face planes through depth projection had a strong impact on retinal diagnostics. Ophthalmologists could now use densely sampled en face maps of total retinal thickness, as well as thickness of specific layers, and could evaluate lesion size, and monitor treatment more precisely [15–17]. SS OCT pushed the speed even further into the multi MHz range through the development of novel fast light sources [18]. Especially the functional extension of OCT angiography owes much of its success to the high-speed capability and sensitivity of FDOCT. It is however difficult to name the key paper for OCTA, since the visualization of vascular structure and the quantification of flow had been a continuous effort from the early days of OCT on [19–21].

Figure 3 below plots the number of publications concerning en face OCT until 2017. There are three peaks visible that might be used to discern three eras of en face OCT. It starts with TS OCT, that was commercialized, followed by a second rise in publications after the commercialization of FDOCT, and finally the currently strongest increase to today triggered by OCT angiography.

3. En face time domain OCT

3.1 Carrier frequency generation

As previously mentioned an important technical challenge of en face TDOCT is to distinguish the collected incoherent backscattered intensity from sample and reference from the actual cross correlation or interference terms, that carry the information about the axial sample structure.

Time domain FFOCT implementations use phase shifting techniques introduced by displacing the reference arm by defined fractions of the wavelength (see section 4) [3]. Those phase shifts are in general dependent on the wavelength, and are therefore intrinsically chromatic which becomes critical for large optical bandwidths. Reconstruction of the complex OCT signal would need three recordings of the interference pattern with different phase shifts. By using more than three phase shifts it is possible to reduce the chromatic error, leading however to longer measurement times [22]. The latter is critical especially for in-vivo imaging due to motion induced signal distortions.
Parallel recording of different phase shifted signal copies or employing modern sensors with fast frame rates has helped to obtain impressive results with FFOCT, even for in-vivo retinal imaging [23,24].

Recent FFOCT and in general parallel OCT approaches adapt techniques from holography by introducing spatial signal modulation for complex OCT signal reconstruction (Fig. 4(b)) [25–28]. Using an off-axis reference arm configuration, a spatial modulation across the parallel sensor is introduced. The spatial modulation frequency $v_x$ is proportional to the angle $\xi$ between reference and sample beam at the sensor and inverse proportional to the center wavelength of the source. The angle is chosen such that the modulation shifts the cross-correlation signal approximately to the center of the spatial frequency axis, given that the unmodulated intensity background can be subtracted. This holographic configuration has successfully been implemented for both FFOCT and LFOCT.

For en face raster scanning OCT a faster modulation technique is needed. Resonant scanners allow already several kHz of line rates, leading to single spot transit times in the μs range. First implementations of en face TDOCT took advantage of the path length modulation during scanning, that results from off-setting the sample beam from the pivot point or rotational center of the galvo scanner mirrors. This method has been introduced by Podoleanu et al. for TS en face OCT [29–31]. The situation is plotted in Fig. 4(a). Off-setting the beam laterally by say $\Delta x$ leads to an axial delay $\delta z$ during scanning through an angle $\delta \alpha$. Knowing the time $\delta t$ needed for scanning through $\delta \alpha$ leads to the modulation frequency $f_{\text{mod}} = 2k \frac{\delta z}{(2\pi \delta t)} = 2 \frac{\delta z}{(\lambda \delta t)}$, where $\lambda$ is the center wavelength, and $k$ is the center wavenumber. As a side note, a similar technique has been adapted for FD OCT to suppress complex conjugate mirror artefacts [32].

![Fig. 4. Carrie frequency generation for en face TDOCT (a) setting the sample beam off the pivot position on the fast scanning galvo mirror; (b) using an off-axis reference arm configuration in parallel OCT variants for holographic signal reconstruction. The red edge shows the Fourier filter function to filter out the spatially modulated OCT signal.](image)

The elegance of this approach is that no additional and in general expensive fast phase shifting device such as electro-optic or acousto-optic modulators (AOM) are needed. There are however some disadvantages related to the technique. The generated carrier frequency depends on the scanning range and the acquisition or sampling rate. Changing the scanning amplitude requires a change of the sampling rate, and/or readjustment of the lock-in detection frequency band. Furthermore, the local path length shift depends on the actual position of the scanners and changes slightly across the laterally scanned range. As a result, the carrier frequency itself is not fully constant across the field of view, leading to reduced sensitivity when using a rigid lock-in technique. Another drawback is the chromaticity of the phase shift, that might become more relevant for high resolution en face OCT systems [33,34].
those short-comings, such en face system was successfully commercialized (OTI OCT/SLO) and extensively used in clinical studies [35,36]. Figure 5 shows an example for results with such a clinical en face imaging system that combines SLO and TS OCT [37].

Despite the higher costs, acousto-optic modulation is advantageous because of the well-defined heterodyne carrier frequency. The acousto-optic effect is based on phonon-photon interaction. The phonon is produced as a travelling acoustic wave within a crystal. The travelling acoustic wave leads to periodic changes in the refractive index of the crystal medium that act as a dynamic grating structure and cause the incoming light to be diffracted and modulated. The phonon-photon interaction shifts the frequency of the diffracted light wave by the frequency of the acoustic wave as \( f_\text{s} = f_\text{L} \pm f_\text{AOM} = f_\text{L} \pm \Omega t \), where \( \Omega \) is the modulation frequency of the AOM. The sign depends on the relative orientation between the incident light and the travelling acoustic wave. It is important to notice, that the induced modulation is independent of the wavelength avoiding therefore chromatic phase shifting errors [38]. Hitzenberger et al. reported in 2003 the fastest retinal 3D OCT system by that time using a single AOM in the reference arm [6]. The system could record a retinal volume with \( 256(x) \times 128(y) \times 64(z) \) pixels at a rate of 1.75 MVoxels/s. This speed has only been matched and exceeded by FDOCT systems. Lower modulation frequencies can be achieved using two modulators in the reference arm, and orienting them with respect to the incident light such that the first AOM induces an upshift \( f_\text{AOM1} \), whereas the second AOM induces a downshift \(-f_\text{AOM2}\). The resulting effective modulation frequency is then \( f_\text{AOM1}+f_\text{AOM2} \) [39].

| Disease                  | Pattern                                                                 | C-scan OCT/SLO Image | B-scan OCT image |
|--------------------------|-------------------------------------------------------------------------|----------------------|-----------------|
| RPE detachment           | Rings of light (isolated bright circles surrounding dark spaces)        | ![C-scan OCT/SLO Image](image1) | ![B-scan OCT image](image2) |
| Central Serous Retinopathy | Bullseye target (concentric rings of alternating bright and dark lines) | ![C-scan OCT/SLO Image](image3) | ![B-scan OCT image](image4) |
| Macular hole             | Petaloid wreath (ring of cysts around a central axis)                   | ![C-scan OCT/SLO Image](image5) | ![B-scan OCT image](image6) |
| Cystoid macular edema    | Swiss Cheese Wheel (cluster of circular holes)                          | ![C-scan OCT/SLO Image](image7) | ![B-scan OCT image](image8) |
| Epiretinal membrane      | Shining star (radiating lines)                                          | ![C-scan OCT/SLO Image](image9) | ![B-scan OCT image](image10) |

Fig. 5. Clinical examples of combined en face TS OCT and SLO. Reproduced from [37] with permission from The Optical Society (OSA).

3.2 Focus control

As has been already outlined by Izatt in 1994 [40], OCT enhances the imaging depth range of confocal microscopy in strongly scattering media through the axial coherence gating that efficiently reduces scattered light from outside the coherence plane, in addition to the
confocal effect. The optimum effect is obviously achieved when the coherence gate is axially centered with the confocal gate.

Schmitt et al. introduced the method of dynamic focusing, by observing that the confocal gate shifts axially in proportion to the square of the refractive index \( n \), whereas the coherence gate scales axially linear with the group velocity \( n_g \). For dynamic focusing, a linear stage tunes the reference arm length by a factor of two with regard to the axial displacement of the confocal gate [41]. This approximately compensates for the different scaling factors of coherence and confocal gate over the in general small depth penetration range of OCT. Various sophisticated configurations have been developed for high speed dynamic focusing through the galvo-scanners [42] or by employing tunable lenses [43]. The possibility of dynamic focusing is in part responsible for the in general much better depth performance of time domain OCT as compared to Fourier domain OCT. Dynamic focusing has in particular been successfully applied in time domain FFOCT for high-contrast digital pathology [44,45].

In FDOCT the axial structure is recorded in parallel, with an axially fixed confocal gate. C-mode scanning enables to record several sub-volumes, where the confocal range is axially shifted between recordings [43,46]. In post-processing the in-focus sections can be extracted from each recording and synthetically reassembled using a Gabor fusion method [47] to enhance the focus depth. This comes however at the expense of time. Alternative approaches to enhance the focal depth in FDOCT used several light beams focused at different depths [48], Bessel beams [49–54] at the expense of sensitivity, or exploited the intrinsic phase stability and speed of FDOCT, and especially of LFOCT and FFOCT, to perform digital refocusing [25,55–58].

### 3.3 Axial tracking

Despite the high en face image rate of time domain en face OCT, the axial tuning for recording tomograms and volumes is relatively slow. The biggest challenge in time domain en face OCT is therefore the presence of axial motion artifacts. For retinal imaging axial motion speed is of the order of 1mm/s [59]. With a typical en face rate of 10Hz, and a minimum of 200 sampling points axially, the recording of a volume would take already 20 seconds. Even, when taking single tomograms at 4kHz lateral scanning, with 200 lateral sampling points, results in a tomogram rate of 20Hz with 50ms recording time per tomogram. During this time, the retina has already moved in average by an amplitude of 50µm, which is about 5 times the axial resolution of the system. Hence, for recording depth sections in-vivo it becomes evident that means for axial stabilization are necessary.

Miller et al. used axial tracking realized with an auxiliary TD interferometer to keep the coherence gate together with the confocal image plane [60]. This system was however too slow to work in-vivo. Pircher et al. demonstrated high resolution retinal en face time domain OCT in 3D using a second high-speed Fourier domain reference interferometer by axially tracking the cornea apex signal. The axial position of the reference interferometer is used for real time adjustment of the coherence gate with a rapid scanning delay line to keep it at fixed axial position in time [61] (see Fig. 6).
Axial tracking is less critical for SD OCT, since the axial information is recorded synchronously for all depths, avoiding axial motion distortions. The same holds in principle true for SS OCT, however motion during recording of the spectral interference pattern in time leads to a chirp, which in turn broadens the OCT signal peaks and causes loss of resolution and signal to noise ratio (SNR) [62]. Motion occurring along the slow scanning direction can be corrected by cross-registration of the tomograms in postprocessing. More sophisticated algorithms use fast reference B-scans [63] or orthogonal scanning patterns [64]. En face sections can therefore be easily extracted from 3D volumes in postprocessing and even be averaged over several registered volumes. Thereby impressive contrast has been achieved even for highly transparent neural tissue in the living human retina [65].

3.4 Phase stability

OCT is an intrinsically complex imaging technique which gives access to the full sample field information. This includes both signal amplitude as well as signal phase. Motion artifacts during in-vivo imaging in general distort the phase. Keeping the phase distortions within the unambiguous range of $2\pi$ leaves the option to correct for those motion distortions in postprocessing. This has been successfully employed for Doppler OCT to correct for bulk motion phase artifacts and to distinguish them from actual blood flow induced phase changes. The only efficient way to avoid phase decorrelation due to motion is to increase the recording speed. Pircher et al. demonstrated phase contrast images of cell samples with high-speed en face OCT [66] (Fig. 7).
As already mentioned before, en face OCT is capable to run at kHz line rate. At that speed the phase shift due to typical motion artifacts (assuming 1mm/s axial motion speed) is still within the $2\pi$ range, and thus can be corrected for in post-processing. En face phase corrected images are the basis for recently successful digital refocusing and furthermore for full aberration correction based on digital wavefront sensing (see section 6.2). Intrinsically phase stable systems in the en face plane are LFOCT and FFOCT systems. Figure 7(c) shows a quantitative phase of a blood smear obtained with FF SS OCT. The particular advantages will be reviewed in section 5.

4. En face Fourier domain OCT

The recognition of the sensitivity advantage of Fourier domain OCT as compared to time domain OCT led to a paradigm shift and set the basis for the many exciting developments in OCT [13,14,68,69]. Functional extensions such as OCT angiography or Doppler OCT, OCT elastography, but also high-speed real time volumetric OCT would have been impossible or at least impractical without the higher sensitivity and speed. Since volumetric imaging was now possible within a second and less, en face OCT became an easily accessible and versatile tool. Arbitrary en face cross sections of tissue and lesion sites could be analyzed off-line and carefully evaluated [15,16]. Lesion extension development could be followed up during treatment, and in general treatment planned more precisely. Especially the development of rapidly tuning swept sources up to the multi MHz range opens new avenues for real time volumetric imaging and thus also for en face OCT and OCT angiography [18–20,70–74] (see section 6.4). It is however outside the scope of this review article to cover all aspects of FDOCT with software extraction of en face sections, instead, the interested reader is referred to recent review papers on the development of FDOCT and its functional extensions [75,76].

Apart from software based en face FDOCT, Biedermann et al. [77] introduced a method for hardware based SS OCT signal demodulation in order to extract and visualize a single particular depth layer. In the case where the sweep is linear in wavenumber $k$ and the interferometer dispersion balanced, a single depth layer corresponds to a narrow spectral modulation frequency band. Using lock-in detection, this frequency can be filtered out, and single en face planes be recorded. The authors state that single plane FDOCT has no sensitivity gain over en face TDOCT, however, as soon as several planes are used for averaging and speckle reduction the sensitivity will be enhanced.

The strong limitation of the method however is the importance of a constant modulation frequency across the spectrum, which might be only fulfilled by linearly sweeping swept sources without presence of strong dispersion effects [78,79]. This restriction does not apply to another hardware based FDOCT signal analysis approach coined master/slave OCT introduced by Podoleanu and Bradu [80–82]. The method employs first a training step with a
mirror as a sample, that produces master copies of the spectral interference signal for all depth positions. For the actual measurement, the slave mode, the mirror is replaced by the sample and the spectral interference signal measured. However, instead of performing the mapping to k-space and taking the Fourier transform in wavenumber k, the original signal is correlated with the master signals for each depth of interest. Thereby, the method is intrinsically correcting also for system related dispersion [83]. Implementing the correlation on a CPU allows for calculating and displaying en face images in real time [84]. The system was successfully employed for various in-vivo imaging applications such as the human eye fundus, or basal cell carcinoma of the eyelid [85,86].

5. Full field OCT

Already in 1998 Beaurepaire et al. demonstrated the concept of full field time domain OCT by illuminating the full en face field of view with a low coherent light source [3]. The backscattered light is detected through a high NA microscope objective superposed with the reference light on a 2D CCD sensor. A 3D stack was recorded by moving the sample axially. The heterodyne signal in order to distinguish OCT signal from unmodulated background intensity terms is produced through photo-elastic birefringence modulator and square modulation of the linearly polarized light source [3,87]. The use of phase shifting techniques for FFOCT has been discussed in section 3.1. Images of plant cells such as onion cells were demonstrated over a field of view of 500x500µm up to a depth of 200-350µm.

Further resolution improvement was achieved by Dubois et al. using a Linnik interferometer design employing exactly matched microscope objectives in sample and reference arm [4]. Despite the by that time unrivaled lateral resolution with OCT of 0.7µm and resulting en face image quality, the low speed however limited application of the method in-vivo. Also, the depth ranging was limited to 150µm although still better than for confocal microscopy given the high numerical aperture of 0.5.

Impressive optical coherence microscopy (OCM) images of ocular tissue ex-vivo were demonstrated by Grieve et al. using a broad bandwidth tungsten halogen lamp centered at 770nm with an axial resolution of 0.7µm [5] (Fig. 8(c-f)). Better depth penetration has been shown by Oh et al. [89] by shifting to the longer wavelength range from 0.9 - 1.4 µm and employing an InGaAs array sensor. Due to reduced scattering at longer wavelengths, structures down to a depth of 800µm within human thyroid tissue ex-vivo have been successfully imaged with high isotropic resolution of about 2µm.

The main drawbacks of TD FF OCT for in-vivo application are on the one hand the critical sensitivity to motion and on the other hand the low detection sensitivity. The speed limitation was relaxed by using a parallel recording of phase-shifted signal copies on two synchronized sensors as shown by Akiba et al. [23]. An interesting variant of parallel en face OCT was based on a smart pixel sensor, that allowed to perform the analog signal demodulation for each pixel on the sensor, thereby efficiently digitizing the OCT signal [90]. A sample volume of 210x210x80 µm³ (corresponding to 58x58x58 voxels) was imaged at a volume rate of 25 Hz [91]. A main challenge for TD FF OCT is the fact that incoherent background signal consumes much of the dynamic range of the CCD sensor. This results in lower detection sensitivity which challenges the application in-vivo, where speed and thus lower integration times are needed to avoid signal distortion due to involuntary patient motion.

Actual in-vivo FF TDOCT images of corneal cellular structures down to the endothelium have been demonstrated using a high-power LED together with an high speed high full-well capacity CMOS sensor running at 550Hz. The high full well capacity enabled enhanced dynamic range and therefore higher sample illuminance leading to improved sensitivity. The OCT signal was recorded through reference arm modulation with a piezo actuated mirror [92].
An attractive feature of employing a spatially incoherent source for FF OCT is the fact that the system becomes in theory insensitive to wavefront aberrations [24]. Instead of degradation of the lateral point spread function only a reduction in detected signal is observed.

Combining FFOCT with Fourier domain signal recording promised to overcome the limitation in detection sensitivity of TD OCT. However, other limitations had to be tackled before first convincing in-vivo images had been shown. Combining FF OCT with swept source OCT is probably the most compact OCT realization. It does not require any complex hardware signal modulation and demodulation, nor mechanical movement of the reference arm. A full 3D volume is recorded with a single sweep of the source as the 2D sensor records the light backscattered from the sample volume across the en face plane in parallel for each optical frequency sequentially. Hence, the spectral interference pattern is recorded in time.

The spectral interference signal can also be recorded for each wavelength in the Fresnel region or the Fourier plane instead of the image plane which is usually done in digital holography. Either in-line holography by phase stepping of the reference arm or using an off-axis configuration can be used to distinguish the cross-correlation terms from the unmodulated intensity background. Digital holographic reconstruction is then performed for each wavelength, followed by standard FDOCT signal reconstruction using the Fourier transform along the time or wavenumber coordinate.

Using such wavelength scanning wide field digital interference holography, Kim [93] demonstrated 3-D imaging of a biological sample across a millimeter with an axial resolution of only 100µm. In 2006 Povazay et al. [94] presented an improved SS FFOCT system employing a Ti:Sapphire laser and an acousto-optic tunable frequency filter. The achieved lateral and axial resolution were 3µm and 4µm, respectively. In order to reduce speckle, an acoustic mode-mixer was used with a multi-mode fiber in the illumination path. The speed, however, was too slow for in-vivo imaging, therefore only ex-vivo images of drosophila were shown.

In order to keep distortions of the spectral fringe signal during in-vivo application small, the recording time between sequential frames should ideally be below 1ms. Such high-speed sensors are existing, but expensive and complex to operate. Usually, the camera would first stream the data onto on-board memory, and then via slow connection to the computer, where the signal can be processed and displayed. Important signal preview for adjustment is therefore limited or even missing.

Employing such sensor, Bonin et al. [95] demonstrated in-vivo retinal imaging in 2010 with an equivalent A-scan rate of 1.5 MHz for a small sample volume of 640(x) x 24(y) x 512(z) pixels. The authors stated, that for keeping significant signal blurring due to involuntary motion artifacts small, a sweep rate of higher than 100Hz was needed. They developed correction algorithms in post-processing to compensate for axial motion distortions, which introduce a non-linear chirp to the spectral interference signal [96].
Hillmann et al. proposed a configuration termed [25,97] holoscopy, which combines coherent depth gating with the digital lensless holography. The lensless approach has the advantage of collecting light from the full tissue volume limited only by the apparent numerical aperture given by the size of the sensor and the distance to the sample. Post-processing applying an angular spectrum propagation on the data multiplied with the conjugate of the reference wave allows then to propagate the signal to arbitrary sample depth planes for each wavelength. For 3D imaging without defocus blur across the depth, the algorithm needs to be applied for all depth planes. The achieved axial and lateral resolution were 14.7µm and up to 7µm, respectively. With a phantom sample consisting of iron-oxide particles suspended in resin an improvement in focus depth of over 30 Rayleigh ranges was demonstrated. Later on, Hillmann et al. [97] presented an improved holoscopy reconstruction similar to the reconstruction used in inverse synthetic aperture microscopy (ISAM) as proposed for SS FFOCT [55] operating in spatial frequency space. After proper linearization of the 3D k-space following the ISAM technique, the 3D Fourier transform is taken to get an OCT volume of the sample. The proposed algorithm is different in the sense, that the recorded sample field is numerically propagated back to the sample space, instead of calculating the pseudo inverse of the forward propagating kernel. Kumar et al introduced a digital aberration correction method, which is in fact a digital scene based equivalent of a Shack-Hartmann sensor. The method senses local wavefront slopes through synthetic split of the aperture and calculating image shifts between the subapertures after 2D Fourier transform.
It is a non-iterative method that has equally been applied to correct also for non-isotropic aberrations across the image field.

Master/slave OCT was also realized in a SS FFOCT setting using a high speed 2D sensor. In-vivo images at a frame rate of 10kHz of drosophila larvae and human fingertip skin have been shown.

A more severe drawback for imaging in scattering tissue is the missing confocal gating in FF OCT. It causes critical loss of contrast within tissue especially in SS FF OCT, since the individual spectral channels collect ballistic and multiply scattered light from the full depth region. This is in particular visible for imaging choroidal structures below the retinal pigment epithelium (Fig. 8(b)) or within skin tissue. The situation is slightly relaxed when scanning the axially confined coherence gate in TD FFOCT and by employing spatially incoherent illumination (Fig. 8(c-f)). LF OCT has been shown to perform better in scattering tissue since it maintains still half of the confocal gate. Other more sophisticated solutions to overcome even this physical limitation are structured illumination as recently demonstrated experimentally for FFOCT by Grebenyuk et al. or the use of the scattering matrix approach.

6. Multimodal en face OCT

Combining OCT with other modalities in general has the purpose to mitigate intrinsic shortcomings of OCT alone. One of the limitations of OCT is the contrast mechanism that is based on backscattering differences without being highly tissue specific. Another challenge are motion distortions during recording of volumes, that could for example be corrected by correlation with a faster en face imaging modality. Confocal scanning systems also help for proper adjustment of focus positions, for example for retinal OCT. In the following a few selected examples of multimodal extensions of en face OCT are discussed.

6.1 En face OCT/scanning laser ophthalmoscopy (SLO)

Traditional en face TDOCT can be viewed as laser scanning confocal microscopy with low coherent light and a reference arm. It is of advantage to keep the confocal gate of scanning OCT axially co-centered with the coherence gate as selected by the reference arm position. Proper adjustment is particularly critical for high numerical aperture and thus high-resolution systems since slight misalignment causes strong signal loss and defocus blur.

First combined scanning laser ophthalmoscopy (SLO) and OCT systems were based on TD OCT. As an example from Pircher et al., the setup depicted in Fig. 1 (a) accommodates both en face OCT for retinal imaging with balanced detection as well as SLO. Since SLO can potentially run faster than OCT, it may be efficiently used for correction of motion distortions of the OCT channel, when recorded synchronously. Such correction has been presented by Pircher et al. in combination with axial tracking for reconstruction of retinal volumes in 3D with negligible motion artifacts to the level of individual photoreceptors. The latter included as well the correction of in-frame distortions, which is crucial for high resolution imaging.

6.2 Adaptive optics en face OCT

High resolution retinal imaging requires medium to large beam diameters at the cornea. The maximum numeric aperture that determines the lateral spot size at the retina is ultimately
limited by the maximum pupil diameter. Large beam diameters however pick up critical amount of wavefront aberrations due to the cornea, lens and ocular media [114]. In healthy eyes with clear media it is possible to visualize cone photoreceptors at large eccentricities from the fovea using OCT alone [111,115]. Cone photoreceptors are responsible for photopic day and color vision, whereas rod photoreceptors enable scotopic monochrome night vision. The density of cone photoreceptors decreases with larger eccentricities and their size increases. On the other hand, the density of rod photoreceptors is lowest for the fovea and increases towards the retinal periphery.

Being able to resolve foveal cones is an indication for a diffraction limited imaging system supporting a large beam diameter. Diffraction limited imaging requires however correction of wavefront aberrations. This has been achieved by recruiting technology used in astronomy for correcting for atmospheric aberration influences. Roorda et al. demonstrated adaptive optics for scanning ophthalmoscopy on the cellular level [116]. Miller et al. and Hermann et al. were the first to demonstrate the advantage of adaptive optics correction also for OCT using a first flood illumination version of AO OCT and ultrahigh resolution TD OCT respectively [60,117].

The first of those systems included already an auxiliary axial tracking device. However, fundamental technical limits in speed precluded the clinical use. AO OCT potentially allows for a much stronger axial gating due to the short coherence of the light source than possible with SLO and allows therefore to image photoreceptors and other cellular details in 3D [118,119]. In order to appreciate the photoreceptor pattern as well as cellular details similar to microscopy fast en face recording is required keeping motion distortions small. En face OCT seems therefore to be a natural candidate for this task.

Cellular resolution imaging combining en face OCT and adaptive optics have been demonstrated by Merino et al. and Pircher et al. [120,121]. Further improvements of the latter system included fast axial tracking [61], which according to the discussion in section 3.3 is crucial for en face OCT to properly work in-vivo, as well as dynamic focusing [122] and has been realized in a compact lens-based design [123,124] (Fig. 9).

![Figure 9](image)

Fig. 9. en-face SLO image (a) and averaged OCT image (b) (over 40 frames) (recorded at an imaging depth corresponding to the layer between RPE and end tips of cones at 8 degrees temporally from the fovea). (c) Composite false color image of end tips of cones (red), and layer displayed in (b) (green) (scale bars: 30μm). (reproduced from [124] with permission from The Optical Society (OSA))

Based on this system temporal photoreceptor dynamics have been studied with high resolution and image quality [125]. When combining AO correction with FDOCT the axial stabilization is no longer required, since the full depth range is recorded synchronously [126–128].

The limited tomogram rate of first AO FDOCT systems however led to strong motion distortions in the en face plane. Parallel recording using a line-field configuration helped to improve the volume rate to 6.7Hz [129]. This minimized motion artifacts and enabled en face visualization of cone photoreceptors. By interlacing four fast spectrometers [65], Kocaoglu et al. demonstrated 1MHz adaptive optics OCT [130]. The speed allowed them together with
sub-pixel registration algorithms to average several volumes to enhance the sensitivity and to reduce speckle noise. With such system they were successfully visualizing mostly transparent neural cells in the human retina in-vivo [65] (Fig. 10). Apart from improving the recording speed, combining adaptive optics assisted FDOCT with simultaneous high-speed SLO allows for efficient motion-correction by image co-registration. For further details on the development of hardware-based AO OCT the reader is referred to excellent review articles [119,131,132].

An interesting development is to perform the wavefront correction digitally by exploiting the complex valued OCT signal that gives access to the backscattered sample field. Since the reconstruction of the wavefront requires highly phase stable systems, first demonstrations of the concepts were based on high speed en face TDOCT [133], FF OCT [134] and later on LF OCT [59]. High speed OCT might however be equally apt to produce phase stable images, that can further be corrected for aberration in pure post-processing.

6.3 Polarization sensitive en face OCT

Tissue might exhibit microstructural properties that change the polarization properties of incident light. Those properties are however invisible to conventional intensity-based OCT. Fibrous tissue such as muscle or nerve fibers or collagen rich tissue exhibit form birefringence, pigmented tissue on the other hand is strongly depolarizing. Exploiting therefore also the polarization contrast potentially yields important additional information on the tissue organization and composition.

First polarization sensitive (PS) OCT devices were based on TD OCT [135] and used by de Boer et al. for skin imaging [136]. Retardation [137] and axis orientation [138] of birefringent skin and muscle were the first quantities, that were measured.

First application in the human eye was the measurement of retardation of the retinal nerve fiber layer (NFL) [139] which is the most important birefringent structure in the eye. Alteration of its thickness due to ganglion cell loss is an important indicator of neurodegenerative diseases such as glaucoma. Already with TD OCT en face maps of NFL thickness have been produced using radial scanning patterns. PSOCT added retardation contrast that correlated well with the thickness maps. Studies even indicated earlier signs of birefringence loss before NFL thinning was observed [140].

Retardation and optical axis en face maps have been produced also for the cornea [141] which can for example be used keratoconus diagnostics. PS OCT was soon adapted for a transverse scanning configuration by Pircher et al demonstrating PS OCT images of skin and the retina with high resolution [39,142–144].

PS OCT images of skin and the retina with high resolution have been demonstrated [39,142–144]. Shifting to the faster FDOCT modality with enhanced phase stability allowed for multimodal tissue imaging including polarization contrast in 3D. It enabled much denser
sampling leading to better layer segmentation and more precise en face maps of retinal thickness as well as birefringence properties [141,145–147]. An important observation was the depolarizing effect of the retinal pigment epithelium [138]. The effect of depolarization has been described by introducing the notion of degree of polarization uniformity (DOPU) that efficiently helped for detailed segmentation of the RPE and evaluation of its integrity in various retinal pathologies [148–151] (Fig. 11). High quality en face maps enabled precise tracking of nerve fiber bundles giving insight into interconnectivity of retinal areas as well as their function [153].

A thorough recent review on PS-OCT including the various technologies as well as theory of can be found in de Boer et al. [152]. Finally, also FFOCT as an important proponent of en face OCT with its high phase stability has been enhanced to assess polarization properties of tissue [154–156]. En face images at a frame rate of 3.5 Hz of ex vivo muscle tissues have been demonstrated with an isotropic spatial resolution of ~1.0 μm.

6.4 OCT angiography

Fluorescence fundus angiography has long been the gold standard in ophthalmology for investigation of the blood circulation and perfusion dynamics in the eye fundus. For contrasting retinal vessels fluorescein is applied, whereas for the deeper choroid indocyanine green dye (ICG) is used, as it emits at longer wavelengths and suffers therefore less scattering loss. The combination of such functional imaging techniques with OCT in a co-registered manner, promised therefore enhanced diagnostic capabilities.

First combined OCT and ICG fundus imaging systems based on TS OCT were reported by Dobre et al. [157]. Later on, also commercial OCT devices included both FD OCT and fundus fluorescence imaging (SPECTRALIS HRA + OCT). The drawback of fluorescence angiography is however its invasive character, as the dyes need to be administered intravenously. This comes with potential adverse side effects for the patients, and the method can only be applied in clinical routine in case of indications of disease.

The situation changed dramatically with the introduction OCT Angiography (OCTA), which has been by far the most successful functional extension of OCT [19–21]. In
Ophthalmic clinical practice, the notion of en face OCT is already synonymously used for OCT angiography. OCTA provides depth resolved angiographic maps of the tissue vascular structure down to the level of smallest capillaries. The vascular contrast is fully non-invasive as it does not require any administration of dyes, with an enormous benefit for the patients by avoiding adverse side effects and the possibility of treatment monitoring and screening. The method is based on sensing OCT signal fluctuations due to moving blood constituents. The fluctuations can be equally sensed by observing intensity changes, phase decorrelation, or complex signal changes over time by taking for example the variance or simply pairwise signal differences. This suppresses static bulk tissue, but enhances structures at motion. If the difference is calculated for example between sequentially recorded tomograms at the same or close to the same position, the time period is much larger than for recorded A-scans, and thus signal decorrelation occurs already for small structural changes such as capillary flow. Angiographic en face maps are typically generated by calculating motion signal projections along a selected depth region in tissue. The en face direction is in fact the most intuitive view on the vascular structure, although the method itself would in theory allow full 3D angiographic maps (Fig. 12). However, axial OCT angiography patterns are strongly affected by shadowing artifacts, and considerable efforts are currently spent on reducing those artifacts [159].

![Fig. 12. Scheme of OCT angiography (OCTA) processing steps.](image)

Current technology development aims at enhancing the field of view by employing rapidly tuning swept sources [18,20,71,74,160,161] (Fig. 13). The speed opens additional flexibility in optimizing the tomogram rate for best vascular visibility [72,73] as well as for producing quasi-quantitative en face flow maps [162].

Recent combination of OCT angiography with adaptive optics by Salas et al. [163,164] showed improved axial performance due to the additional strong confocal gating together with a high-resolution representation of all capillary beds within the retina. In general, the impressive vascular en face maps revived again the interest in en face OCT [165].
Fig. 13. OCTA of geographic atrophy; (a) B-scan (grey) with overlaid OCTA tomogram (red); (b) en face OCTA with depth color coding according to the color bars to the right of (a) (with permission from [160] by The Optical Society (OSA)).

7. Outlook

We reviewed different technologies for structural as well as functional en face OCT. The most compact en face OCT technology is FFOCT. Advances in sensor technology and the availability of cheaper high-speed cameras will be an important driving force for translating and commercializing FF OCT for in-vivo applications. As pointed out in section 3.4 an important advantage of en face TS OCT, LFOCT and FFOCT is the intrinsically high phase correlation across the en face plane. This opens new and exciting applications for highly sensitive probing of structural and possibly even chemical changes that lead to variations in optical path length. The group of Boccara et al. used this sensitivity for label-free metabolic contrast of cells and their substructure based on their motility [166,167]. A time series of en face images was analyzed via taking the standard deviation for each pixel over time identifying various frequency ranges. Faster changes were due to moving blood cells similar to OCT angiography. At lower frequencies a different motility or correlation contrast between normal and pathological tissue has been found which could potentially help to discriminate tumor tissue during surgery without the need of exogenous contrast agents.

Recent work by Hillmann et al. demonstrated with SS FFOCT sensing of subtle changes in the retinal structure during excitation of photoreceptors with defined excitation patterns [168]. They were not only able to confirm earlier results by intrinsic signal imaging in-vivo [169,170], but could even find replicas of the illumination pattern in the response signals from the ganglion cell layer [171]. The well-defined phase across the image plane allows also for manipulation of the wavefront in the pupil plane or Fourier plane. Synthetic splitting of the pupil in postprocessing also allowed for fully directional sensing of dynamic structural changes. The ability for 3D motion vector field reconstruction in tissue during laser photocoagulation in ex-vivo porcine retina was shown recently [172].

Realizing an en face LF TDOCT with holographic reconstruction (Fig. 4(b)), Liu et al. [28] were able to record high frequency oscillations after air-pulse excitation of porcine cornea with a line rate of 200kHz. With a similar setup, Ginner et al. showed retinal imaging as well as en face Doppler OCT of retinal capillaries [27]. En face retinal images of 2048 x 1000 pixels were recorded with up to 100Hz allowing to identify flowing red blood cells.
Although the rapid development of fast light sources might allow similar en face image rates even with point scanning devices [18], parallelization of detection will play an important role. The spectrum ranges from few channels to LF or FFOCT. The latter might be problematic concerning laser safety for the anterior chamber, as the illumination field might easily be focused at strongly absorbing iris tissue. LF OCT is more relaxed in that regard, but the combination with a swept source is still limited by the availability of fast line sensors. However, such technological limitations of today might be less of an issue in the next few years.

We can certainly expect, that en face OCT will continue to play an important role in OCT. With improved performance of graphics processor units and algorithms we will however gradually see a shift from tomographic OCT and en face OCTA to full resolution volumetric real time display. The latter has the advantage to exhibit important details on axial interconnections that are less visible in en face views alone. The volumetric real time performance is certainly most critical for intra-surgical OCT [173]. Other developments aim at quantitative imaging of tissue perfusion, motility and biomechanics. Also, displaying functional en face information on top of the tissue surface in an augmented reality setting will further enhance the diagnostic capabilities in the future.

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