Optical Coherence Tomography – Variations on a Theme

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Abstract Optical Coherence Tomography (OCT) has developed extensively over the last 23 years. This paper reviews some of the imaging techniques based on OCT with particular reference to the trade-offs between lateral and axial resolution, working distance, imaging depth, acquisition speed (enabling real time observation and 3D imaging), imaged area/volume, contrast enhancement – including velocity measurement, and system complexity – including detectors, light sources and the optical path.
The majority of applications of OCT are biomedical, especially ophthalmology, endoscopy and intravascular imaging. However, some industrial applications are emerging particularly for non-destructive testing and quality control, such as in the production of MEMS devices, or the non-destructive detection of sub-surface strain fields in injected moulded polymer parts.

Keywords: Optical Coherence Tomography, Optical Imaging, Interferometric Imaging

1. Introduction

Optical Coherence Tomography (OCT) has developed extensively over the last 23 years. This paper reviews some of the imaging techniques based on OCT with particular reference to the trade-offs between lateral and axial resolution, working distance, imaging depth, acquisition speed (enabling real time observation and 3D imaging), imaged area/volume, contrast enhancement – including velocity measurement, and system complexity – including detectors, light sources and the optical path.

Time domain OCT was the original system (Huang, 1991) and required a simple detector, a depth scanning mirror and a short duration pulsed laser light source. Resolution was good but multiple samples were required for each A-scan which made acquisition slow. The development of spectral domain or Fourier domain (SD-OCT), and subsequently swept source (SS-OCT) methods greatly enhanced acquisition speeds. This provided a much better patient experience for retinopathy as well as enabling the possibility of real time 3D imaging. Intra-vascular OCT could also compete with intra vascular ultra-sound (IVUS) by providing both higher resolution and faster draw back times combined with the advantages of a smaller fibre-optic catheter minimizing vessel occlusion.

Various techniques have been introduced to improve image acquisition times, including the use of spatial coherence, alone or in conjunction with temporal coherence, in order to allow simultaneous sampling across multiple sites. Spectral Encoded Endoscopy (SEE) also provides sampling from multiple lateral sites within a single sample sweep, but each location only uses a part of the total bandwidth thus reducing axial resolution. Interleaved OCT on the other hand can sample from several locations simultaneously while employing almost the full bandwidth at each location by using a more complex multi-band demultiplexer (MBDX) (Lee *et al*, 2013).

Ultimate resolution is essentially diffraction limited laterally, and source bandwidth limited axially. In practice it is often necessary to work with low numerical aperture optical systems, such as in retinal

imaging, and typical lateral resolution is around 15µm, axial resolution around 5µm. A number of high resolution OCT scanners are also available which can give an axial resolution down to around 3µm, but it is debatable whether the increased resolution actually enhances the diagnostic ability. Some improvement in lateral resolution may be achieved through the use of sources with low spatial coherence, or through virtually structured detection (VSD) (Wang *et al*, 2013).

OCT may be combined with other detection modalities in order to overcome some of the inherent limitations. Basic contrast en-hancement can be provided through the use of polarization sensitive OCT or Doppler OCT. More advanced processes may use magnetomotive nano-particles in a modulated magnetic field for Magneto-Motive OCT (John *et al*, 2010). Photo-acoustic micro-scopy (PAM) has similar penetration and resolution to OCT, but observes optical absorption rather than scattering. By using a transparent Fabry-Perot interferometer as a detector OCT can be implemented coaxially providing a complementary image. Doppler OCT can be implemented in several different ways – phase resolved Doppler (PR-DOCT), resonant Doppler flow imaging, joint spectral and time domain imaging, optical micro-angiography (OMAG) or single pass volumetric bidirectional blood flow imaging (SPFT).

Choice of light source is crucial to good OCT performance. Time domain OCT was dependent on the use of femto-second pulsed lasers. The introduction of SD-OCT and SS-OCT allowed the widespread use of super-luminescent diodes (SLD) sources with longer lifetimes and far lower cost. SLDs are readily available at wavelengths of 800nm with a bandwidth of 30nm, or at wavelengths of 1300nm providing axial resolutions down to 3µm. For ultra-high resolution systems the use of photonic crystal fibres in conjunction with sub-15fs Ti:sapphire lasers has enabled resolutions down to 0.9µm in air and 0,6µm in biological tissue. It remains to be seen whether recent developments in attosecond pulsed lasers (Villeneuve, 2009) will enable resolution limits to be pushed even further.

The majority of applications of OCT are biomedical, especially ophthalmology, endoscopy and intravascular imaging. However, some industrial applications are emerging particularly for non-destructive testing and quality control, such as in the production of MEMS devices (Merken *et al*, 2011), or the non-destructive detection of sub-surface strain fields in injected moulded polymer parts (Anonymous web reference).

Wojciech *et al* (2005) for example have developed a low resolution interferometric absolute distance gauge for the study of MEMS structures and successfully applied this to measure of *change "of" to "the"* relative distance between two optical interfaces in material transparent at the wavelength of the probing radiation. Also Walecki *et al* (2005) have proposed an interferometric method for measuring the thickness of ultra thin wafers mounted on insulating carriers, which could easily be integrated into production tools to provide accurate measurements of samples as they are being processes. Gauss *et al* (2007) have successfully demonstrated a non-contact OCT technique which was able to precisely measure the 3D spatial characteristics of laser-induced surface damage sites in fused silica, demonstaration *change to "demonstrating"* that OCT can be a practical tool for characterizing damage sites in industrial processes. An advantage of OCT over more conventional techniques is that it can often be used advantageously in hostile environments e.g. within nuclear reactors or at extreme temperatures.

2. Time Domain OCT

The most common configuration of a time domain OCT instrument is that of the Michelson interferometer as shown in Figure 1. As an interferometer the light source is coherent monochromatic light and the intensity at the detector varies as the mirror is moved with peaks when the path lengths are equal or differ by multiples of the wavelength of the light used and is zero when the path

lengths differ by multiples of a half wavelength.

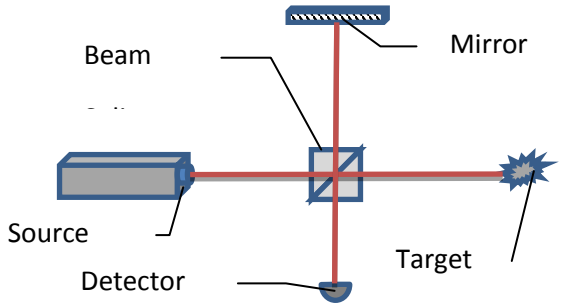

Figure 1 Michelson interferometer configuration for time domain OCT

$$I_D = {}^1\!/_2\, I_{SO} + {}^1\!/_2\, I_{SO} \cos\theta$$
$$= {}^1\!/_2\, I_{SO}(1 + \cos\theta) \qquad (1)$$

Where I_D is the intensity at the detector, I_{SO} is the intensity of the source and cos θ represents a time or distance mismatch.

For OCT the continuous source is replaced with a source that has a very short coherence length – typically a short pulse with a duration of a few femtoseconds. In this case the detector will only produce outputs when the path lengths match within the coherence length of the source and the output for a point target would be the autocorrelation function of the source pulse. For a distributed target, as in the OCT case, at each position of the mirror the output at the detector will represent the reflectivity of the target at the depth corresponding to a zero path length difference. By scanning the mirror samples can be obtained at successive depths and a scan by depth is referred to as an A-scan. The lateral resolution obtained is dependent upon the numerical aperture of the optics used but the depth resolution is defined by the coherence length of the source and is independent of the numerical aperture.

Optical Coherence Microscopy uses the OCT principle in conjunction with high numerical aperture lenses to provide high resolution microscopy images. However, the most common application of OCT is in ophthalmology where the use of low numerical aperture lenses allow long working distances and high resolution sections through the retina can be obtained.

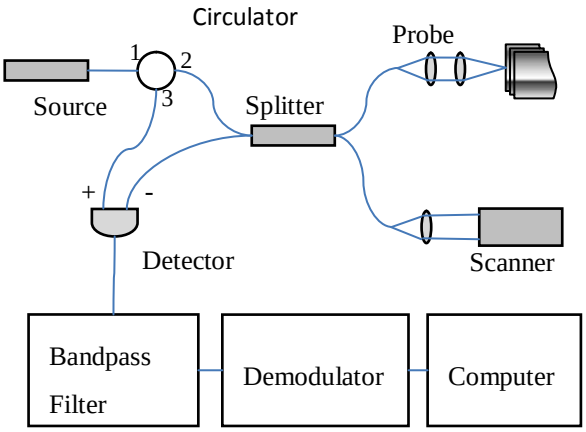

Figure 2 Fibre optic OCT configuration with a circulator and differential detector to reduce source noise and a two dimensional delay

Another common application of OCT is the use for endoscopy and intra-venous imaging. Instead of using a conventional beam-splitter, the light is transmitted through optical fibres and a fibre-optic coupler is used to split the light between two fibres, and to re-combine the returned light into the detector. It is also possible to include a fibre-optic circulator between the beam splitter and the splitter in conjunction with a differential detector in order to reduce noise from the light source (Figure 2).

A fibre optic probe has many advantages over ultrasound intravenous probes, since it has a much smaller diameter and therefore has minimal occlusion of the vessel. Alternatively a single mode optical fibre can be inserted into a 27 gauge or finer needle, with an integral GRIN lens and a microprism. Tissue sections up to 6mm in diameter can be imaged over a wide range of depths with a resolution better then 5μm.

2. Spectral Domain OCT

The main problem with time domain OCT, especially for retinography, is the slow

acquisition times as the mirror is scanned in depth for each of several hundred A-scans required for a complete retinal section. This disadvantage is overcome by using Fourier Domain OCT (FDOCT) or Swept Spectrum OCT (SSOCT). In this case the source is replaced by a broad spectrum light source. In SSOCT this is achieved by rapidly sweeping the source frequency through a wide bandwidth. In the unbalanced interferometer this results in two overlapping frequency sweeps at the detector, one of which is delayed in time and is therefore also offset in frequency. The beat notes between the two sweeps can be detected and the spectrum of all the beat notes from a distributed target represents a simultaneous measurement of the reflectivity at all depths. In this way a complete A-scan can be obtained from a single pulse.

This is the principle used in all current retinal OCT instruments such as the Zeiss Cirrus range, Topcon 3D-OCT-2000 or the Optovue iFusion/iVue. These instruments are typically capable of 30000-70000 a-scans per second with a depth resolution of 5µm, lateral resolution of 8-15µm at a working distance of 20-40mm. The depth of the scan is limited by the wavelength of light used and the absorbance of the tissues and is generally 2-3mm.

3. Coherence Scanning Interferometry

Coherent Scanning Interferometry (CSI) is a technique for measuring surfaces and does not provide a vertical section through the target as OCT does. The technique, however, is very similar to time domain OCT.

In this configuration the upper beam splitter directs the light towards the objective lens to be focused at the target. Within the objective lens complex a beam splitter directs part of the beam towards the sample and the rest onto an internal reference mirror. On reflection the two beams recombine and are focused onto an image sensor. A white light, low coherence source is used so that interference only occurs when the path lengths are equal. The objective complex is scanned vertically and the peak intensity of the interference function is detected.

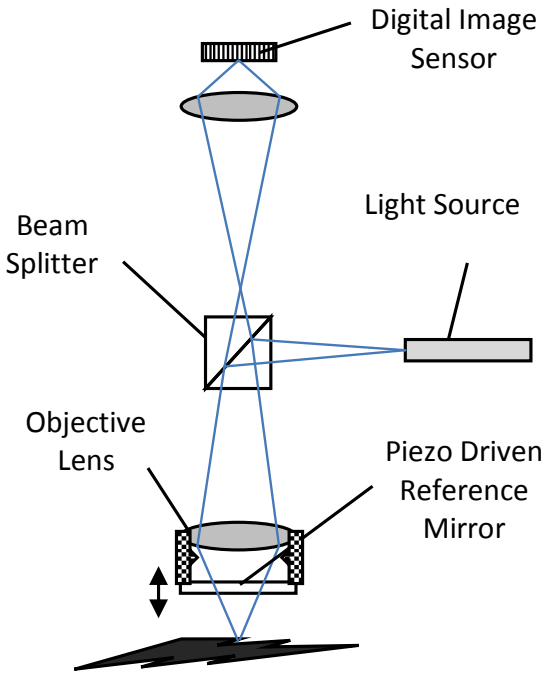

Figure 3 Coherence Scanning Interferometer

Vertically scanned CSI is used in metrology and quality control to determine surface roughness to a resolution of around 3nm. For smoother surfaces the phase information can be used to provide a resolution of around 0.1nm, but only over a limited range of heights.

4. Contrast Enhancement

The system in Figure 2 can be adapted to form a polarization diversity interferometer by replacing the detector with a polarizing beam splitter and two detectors the signals of which are independently filtered and demodulated before being summed. This polarization insensitive technique has the advantage of being independent of stress on the fibre optic catheter or endoscope.

Polarization sensitive OCT can be used in dentistry to image the subsurface structure of teeth. It is possible to measure the thickness of the highly mineralized transparent surface zone of caries lesions in order to distinguish between active and

arrested lesions (Lee *et al*, 2014).

Contrast can be further enhanced by using a high refractive index fluid (ri=1.[illegible] as a coupling agent between the probe and the tooth. This significantly increased the reflectivity of lesion areas in teeth with occluded lesions (Kang *et al*, 2014).

PS-OCT is also of benefit in clinical arthroscopy using a conical scan to supplement variable-incidence-angle PS-OCT. It is possible to locate the "brushing direction" of collagen fibres in articular cartilage, which cannot be done using conventional techniques and which is useful in the design of tissue-engineering scaffolds for cartilage repair (Lu *et al*, 2013).

In conventional microscopy fluorescence labelling is useful for molecular marking. However, with OCT fluorescence cannot be detected as it is not coherent with the source illumination. Spectroscopic OCT can be used to enhance tissue contrast through the use of infra-red absorbing dyes but is limited in resolution (Xu *et al*, 2004; Yang *et al*, 2004).

[illegible]denburg *et al.* (2005) have used superparamagnetic Iron Oxide (SPIO) nanoparticles, which are already approved as contrast agents for MRI and which are taken up by macrophages. The advantage of magnetic nanoparticles is that they can be selectively vibrated by an external magnetic field and the vibrations can be selectively identified by the OCT system. Nano particles can also be coated to allow conjugation with specific antibodies, proteins, nucleotides or peptic ligands (Renu & Boppart, 2011).

Other techniques for contrast enhancement include the use of Coherent Anti-Stokes Raman Scattering (CARS) and Second Harmonic Signal Detection (SHG) (Vinegoni *et al*, 2004).

5. Doppler OCT

As with ultrasound OCT can also be used in Doppler mode to detect fluid velocities, either alone or in conjunction with other OCT modalities.

In a time domain OCT configuration the illumination is typically an ultra-short pulse of monochromatic light. The spectrum of a pulse of this type is a Gaussian distribution about the centre frequency of the laser, with the total bandwidth dependent upon the pulse duration. If the target of the OCT observation is moving with respect to the probe then the entire Gaussian spectrum will be shifted in frequency. The reference mirror is moved continuously and the time varying output of the detector is analysed using short time Fourier transforms (STFT) with a suitable windowing function to determine the velocity as a function of depth (Milner *et al*, 2002). However, regardless of the axial resolution of the OCT system there is a trade off in the STFT between axial (time) resolution and frequency resolution. Good frequency resolution requires a long sample for the Fourier transform and therefore time resolution is poor. Conversely, if a small sample is analysed giving good time/depth resolution then frequency resolution will be poor. For example, at a frame rate of 1 image per second and an image size of 100 x 100 pixels, the maximum data acquisition time for each pixel is 1/10,000 s. Using a wavelength of 1300nm in order to obtain good depth penetration, and at an angle of incidence of 80° the minimum resolvable Doppler shift of 10kHz corresponds to a velocity of 25mm s^{-1} (Zhao *et al*, 2000a).

However, there are a number of other techniques for extracting velocity information from an OCT system which avoid this problem. These include phase resolved Doppler OCT imaging, in which the phase change between adjacent, or sequential depth scans is detected (Zhao *et al*, 2000a); Doppler broadening and shift approaches that allow the velocity to be estimated without knowing the angle of incidence (Proskurin *et al*, 2003); and speckle analysis which allows velocity estimates to be obtained without invoking the Doppler effect (Barton & Stromski, 2005). Velocity estimates can even be obtained from Fourier domain OCT (Leitgeb *et al*, 2003) or from swept source OCT systems (Zhang & Chen, 2005).

Phase resolved OCT was described by Zhao *et al*. in 2000, for the measurement of

blood flow in skin. They used a 1300nm source with a bandwidth of 65nm, split inot sample and reference beams in a 2x2 fibre optic splitter. The reference beam went to a rapid scanning optical delay line with a grating to control group and phase delays separately. This ensures that there is no phase modulation when the group delay is scanned. A separate electro-optic phase modulator was used to produce a stable carrier frequency. In the sample arm a GRIN lens produced a 10µm beam at an angle of 5-10° from the tissue surface normal. Lateral scanning was implemented at the probe by a voice coil translation stage. At each stage in the lateral scan, 8 A-line scans were generated in order to improve the signal to noise ratio. The Doppler frequency shift was then determined by calculation of the average phase shift between sequential A-line scans. With this system it was possible to detect flows as low as 10µm s^{-1} while maintaining a lateral resolution of 10µm.

With this mode of velocity measurement the usual display method is to overlay a velocity coded colour map on top of the structural information. However, it is frequently not possible to estimate the angle of incidence in a complex flow environment and therefore just the Doppler shift information is displayed.

When measuring blood flow in a larger vessel it is often more convenient to display the information in the form of a sonogram, with Doppler shift displayed as a function of time. This is often accompanied by audio output. Power Doppler display is a common approach in ultrasound flow measurement, but is less appropriate with DOCT since it is computationally expensive and the value returned is related to the volume of moving blood and not just the velocity. Also direction information is lost.

The velocity variance (or standard deviation) is however much better suited to DOCT than to ultrasound situations. It is particularly useful when measuring flow near obstructions or bifurcations as increased variance indicates the presence of turbulent rather than laminar flow. Using colour Doppler combined with velocity variance the choroidal capillary vasculature can be mapped without the necessity for correcting for bulk motion (Liu *et al*, 2011).

An alternative approach to velocity measurement which does not rely on the Doppler shift is based on intensity information. Barton and Stromski (2005) used the time varying speckle, manifested as a change in OCT image spatial speckle frequencies, to obtain flow information. This technique has the advantage of being independent of the angle of incidence and can even measure flow normal to the imaging beam and is not affected by the phase stability of the OCT imaging system.

Zhao *et al*. (2000b) used a combination of variance and intensity information to image blood flow in port-wine stain birthmarks before and after laser treatment.

6 Summary

Optical coherence tomography is most frequently encountered in ophthalmology where the advantages of being able to provide detailed sections through the retina at long working distances are not approached by any other technique. It does however have many other applications and is closely related to many other interferometric techniques such as optical coherence microscopy, coherent scanning interferometry and digital holographic microscopy.

In ophthalmology the usefulness of long working distance and high scanning speeds is of more importance than ultimate resolution. In other areas however there have been great developments in ultrahigh resolution OCT with axial resolutions of around 0.5µm in biological tissue (Povazay *et al*, 2002). Lateral resolution is nominally diffraction limited but even here there has been progress in improving resolution through the use of filtering and modified lateral scanning procedures.

OCT is often compared in its performance with ultrasound imaging although its limited penetration depth means that direct

comparisons are only really appropriate in areas such as endoscopy. The two techniques are fully complementary and it is indeed significant that some of the more interesting OCT techniques have been developed by combining OCT with other disciplines.

Velocity measurement is a particularly interesting area within OCT imaging, especially for mapping micro-capillary circulation where speckle techniques allow flow to be measured in all directions without having to provide high angles of incidence of the beam.

Future developments in the field also look very interesting, with the development of attosecond pulse lasers, and quantum techniques which may push the resolution boundaries still further.

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