Retinal blood flow measurement

Douglas Clarkson looks at how new OCT technology is changing the way retinal vasculature may be investigated

At first sight optical coherence tomography (OCT) would appear to be a technology with a single technique of implementation. The original technique of detection of signal by coincidence detection of a reference delayed signal and a returning signal from a tissue interface is also known as time domain OCT (TDOCT). This technology was first applied to imaging applications during the early 1990s. The typical value of resolution associated with this technique is in the region of 20 to 30 microns. Where specialist high resolution techniques are applied, the resulting method of ultra-high resolution OCT (UHROCT) can achieve values of axial resolution as low as 3 microns.

Spectral domain OCT

The technique of spectral domain optical coherence tomography (SDOCT) was first described by Fercher[1] and is illustrated in Figure 1. Light from a source is split to a reference arm and a sample arm. Recombined light from both optical paths is reflected from a diffraction grating which spits the light into its spectral components which are subsequently detected in a linear detector array. Information of depth contained in the spectra is derived from a Fourier transform of the detected array signal – with the frequency of the original light source having been modulated by a time varying signal. The technique of SDOCT provides for an increase in signal detection of around two orders of magnitude compared with conventional TDOCT. Also, the reference arm in the basic interferometer does not require a scanning mechanism such as a moving mirror or ultrasonic compression of optical elements. This in turn significantly increases the speed at which scanning takes place.

Initially, developed systems using SDOCT were able to increase scanning rates by a factor of around 40 with typically a line sampling rate of 30 KHz being achieved. In the literature, rates of several 100 KHz are now reported. The achievement of increased sensitivity and typical axial resolution values of around 3 microns, coupled with increased speed, have essentially created a new generation of OCT imaging systems for the retina and which would appear to eclipse conventional TDOCT systems. One of the basic advantages of SDOCT is that as the time of imaging a specific tissue volume decreases – artefacts due to motion of the imaged volume are correspondingly reduced. One of the drawbacks of SDOCT, however, remains the degree of depth-dependent sensitivity.

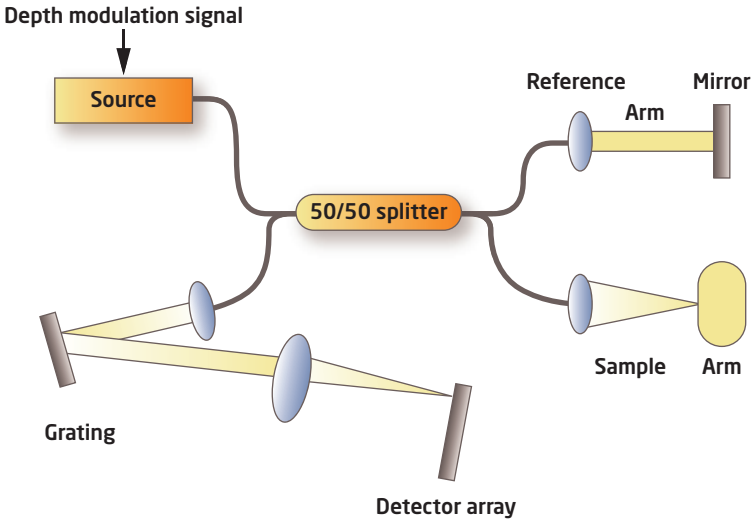

Figure 1 Detail of basic SDOCT system indicating spectral source with depth modulation signal, beam splitter, reference and sample arm and detection circuit incorporating diffraction grating and spectral detector array. Data from the detector array is processed using Fourier transform to decode signal depth information

Measuring retinal blood flow

Measurement of retinal blood flow using the laser Doppler technique has previously been reported by Gilbert.[2] Such a technique makes possible estimation of total retinal blood flow through measurement of directly observable vessels. The specific technique also requires Doppler shift spectra for a single selected site to be measured simultaneously in two separate directions.

While Doppler flow measurements have also been undertaken using the TDOCT technology, more significant recent developments relate to the use of SDOCT for measurements of blood flow down to vessels as small as 10 microns. The increased depth penetration of SDOCT also allows sampling within deeper structures in the choroid. Cense[3] describes an experimental system using SDODT where the pulsatile characteristics of vessels fed by arteries can be distinguished from that within veins. In the example of artery-connected vessels, the detected flow signal is more closely identified with the cardiac cycle while the venous circulation demonstrates a less pulsatile waveform which lags slightly behind that of the arterial circulation. Also, it is anticipated that this technique could ultimately allow rapid identification of sites of origination of feeder vessels within the retinal circulation.

Leading work in SDOCT has been undertaken by researchers at Ecole Polytechnique Federale de Lausanne in Switzerland. Their specific technique is described as Fourier domain optical coherence tomography (FDOCT) emphasising the feature that the light signal frequency is modulated as a function of depth – so that the Fourier analysis of detected signal returns information of the depth of origin of the detected light.

While it is one thing to demonstrate technology in the laboratory, it is always a challenge to translate such processes into effective systems that can be used in the exacting clinical environment. A system with simplified implementation for FDOCT has been described ▶

by Leitgeb[4] which in the first instance has been demonstrated for use in skin imaging at 1,300nm.

The effect of moving structures causes phase shifting in the returned signal. Without compensation this would degrade the image information from non-static structures such as regions of blood flow within vessels. However, by detecting this phase shift and introducing a balancing contribution of phase in the reference arm of the interferometer, the image detail of moving structures can be enhanced and with the phase correction providing information of the nature of movement within the sample volume. In the context of flow mapping within a selected volume, this allows separate identification of areas associated with blood flow and also static areas in which no flow is taking place. The technique also identifies the direction and magnitude of such flow. In the hardware setup used in one configuration in Lausanne, use was made of two super luminescent laser diodes of wavelength 827nm and 853nm, with corresponding bandwidths of 25nm and 34nm.

In the measurement of blood flow, the detected signal is typically originating from vessels at an angle to that of the incident scanning direction. The group at Lausanne has also implemented an algorithm which determines the angle of orientation of specific vessels in order to compute the flow along the axis of the specific vessel.[5]

Similar work is also reported by Makita[6] and Wang.[7] In particular the work undertaken by Wang describes specific values of venous velocity for a specific patient in the range 16.26mm/s to 29.7mm/s and with corresponding variation in arterial flow in the range 38.35mm/s to 51.13mm/s. The sum of both venous and arterial flow was estimated to be 54 microl/min.

While most centres developing Doppler flow techniques in retinal imaging are using SPOCT technology due to its higher scan rates and better signal penetration, some centres are still investigating Doppler techniques using TDOCT technology. Work undertaken by Xu *et al*[8] describe how a zero-crossing detection method used with TDOCT can give more precise results – especially for measurement of higher velocities. Comparisons between Doppler processing techniques were undertaken using a test flow system of a 1.4mm glass capillary tube filled with 1 per cent intralipid solution.

Summary

The technology of OCT has undergone significant technological advance from the earliest systems developed in the early 1990s. Techniques based on SPOCT which utilise depth encoding within the frequency modulation of light sources have increased the performance of the imaging technique significantly on many counts and introduced the capability of quantitative blood flow determination down to the level of small vessels. Such techniques provide yet another refinement of investigative methods for analysis of retinal function which are potentially of significant benefit for diagnosis of eye disease and as a means of determination of the effectiveness of emerging and existing treatment processes.

References

1 Fercher AF, Hitzenberger CK, Kamp G, El-Zaist SY. Measurement of intraocular distances by backscattering spectral interferometry. *Opt Commun*, 1995; 117, 43-48.
2 Gilbert TF, Togawa H, Deupree DM, Goger DG, Setbag J, Weiter JJ. Blood flow in the normal human retina. *Invest Ophthal Vis Sci*, 1989; 30(1); 58-65.
3 Cense B, Chen TC, Nassif N, Pierce MC, Yun SH, Park BH, Bouma BE, Tearney GJ and de Boer JF. Ultra-high speed and ultra-high resolution spectral domain optical coherence tomography and optical Doppler tomography in ophthalmology. *Bull Soc Belge Ophthalmol*, 2006; 302,123-132.
4 Leitgeb RA, Michaely R, Lasser T, Sekhar SC. Complex ambiguity-free Fourier domain optical coherence tomography through transverse scanning. *Opt Lett*, 2007; 32(23):3453-5.
5 Michaely R, Bachman AH, Villiger ML, Blatter C, Lasser T, Leitgeb RA. Vectorial reconstruction of retinal blood flow in three dimensions measured with high resolution resonant Doppler Fourier domain optical coherence tomography. *J Biomed Opt*, 2007; 12(4):041213.
6 Matika S, Fabritius T, Yasuno Y. Quantitative retinal blood flow measurement with three dimensional vessel geometry determination using ultra high resolution Doppler optical coherence angiography. *Opt Lett*, 2008; 33(8), 836-8.
7 Wang Y, Bower BA, Izatt JA, Tan O, Huang D. *In vivo* total retinal blood flow measurement by Fourier domain optical coherence tomography. *J Biomed Opt*, 2007; 12(4):041215.
8 Xu Z, Carrion L, Maciejko R. A zero-crossing detection method applied to Doppler OCT, *Optics Express*, 2008; 16(7);4394.

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Book review

Bill Harvey is impressed by a book on a rather specialist area

As seen on page 31 of this issue, there are many potential applications for anterior OCT assessment of the eye. A new book (*Anterior Segment Optical Coherence Tomography*, edited by Roger Steinert and David Huang) offers a comprehensive and clear review of this.

The book begins with an easy to understand explanation of optical coherence tomography with schematic diagrams adding to the clarity. The following chapters then each address a specific clinical use. These include the monitoring of keratoconics, evaluation of Lasik flaps, assessment of pre- and postoperative lamellar keratoplasty, assessment of intacs and assessment of the anterior chamber angle. Other sections show that corneal and lenticular opacities may be detected and, more importantly, monitored.

A last chapter tantalisingly looks to the future and the development of yet faster and higher resolution scans. This is a well illustrated guide to a technique which is likely to become more and more familiar and important in the coming years.