Bahrain Medical Bulletin, Vol. 27, No. 3, September 2005

Optical Coherence Tomography of the Retina. New Technology - New Insights

Mohinder Singh, FRCS,FRCOphth*

Optical imaging is an emerging new technology, which can produce cross-sectional images of very high resolutions. Micro architecture of biological tissues is tomographically imaged by measuring the echo time delay and intensity of backreflected or backscattered light[1]. This technology is now able to generate real-time in situ images of normal and abnormal tissue architecture with resolution of 1.5 to 15 microns, which are not possible with other conventional imaging tools such as ultrasound, MRI or CT [2].

Bahrain Med Bull 2005; 27(3):

High-resolution images obtained with the new revolutionary optical coherence tomography (OCT) have wide clinical applications in many disciplines[3]. Since images can be quantitatively analysed, objective assessment of a variety of features can be performed. In ophthalmology OCT was introduced in 1991 and it is fast becoming a powerful tool complimentary to fluorescein angiography in the investigation of posterior segment pathology of the eye[4]. Its potentials as an imaging aid in the study of anterior segment of the eye are also being actively pursued[5]. Since OCT utilizes the light beam in the infrared region, without any contact to the eye, it is well tolerated by the patient. Clear optical media of the eye made it possible to rapidly develop OCT technology as a noninvasive, noncontact imaging tool in Ophthalmology.

Optical coherence tomography has been largely used to study the retinal and optic disc disorders of the eye. However, it can be applied to investigate pathology in a wide range of tissues other than the eye[6]. It is possible to obtain "optical biopsy" of 10 um resolution

*Consultant Eye Surgeon
Specialized Eye Centre
Ibn Al-Nafees Hospital
Kingdom of Bahrain.

in vivo by placing the endoscopic probe close to the hollow viscus and it offers obvious potential in the early diagnosis of internal tumours. Contrary to conventional histopathology, OCT is able to visualize tissue architecture in situ and in rear time

without the need to excise and process the tissue specimen. Because of this unique advantage of obtaining optical tissue biopsy, OCT can be clinically very helpful in:

1. Where conventional biopsy is dangerous as in the eye, coronary artery and brain.
2. Sampling errors and false- negative results.
3. To guide the interventional approach to therapy.

Optical Principle

Optical coherence tomography is analogous to ultrasound B mode imaging except that it uses light instead of sound[4]. Standard ultrasound detects reflections of high frequency sound waves and is limited to a resolution of 150 um. OCT depends on reflection of short coherence length light and produces resolution in the order of 10 um. High-resolution ultrasound systems allow up to 20 um resolution but because of the sound attenuation in biological tissues their penetration is limited to 4-5 mm only[7].

When a beam of light is directed onto the eye it is reflected back from boundaries between different tissues and backscattered differently from tissues that have different optical properties. By measuring the echo time delay of reflected or scattered light from different structures at different axial distances, dimensions of different tissues can be determined[8,9]. The technology of optical imaging is totally different from ultrasound. It is challenging because the speed of light is one million times faster than the speed of sound. Because direct detection of high-speed light echoes is impossible, only indirect methods using co-relational techniques make it possible to perform high-resolution measurements. OCT employs interferometry to measure the echo time delay of light and correlate echoes of light from the retina with light, which have traveled a known reference path delay[10]. Superluminiscent diode is used as the source of light which is projected onto the retina via a slit lamp incorporated with +78 diopter biomicroscopy lens. A beam of 200 microwatts is reflected at each interface between ocular structures and the time taken for its reflection is compared with a reference beam by using an Interferometer, which calculates the distance and relative position of structures by measuring the time delay of optical reflections from intraocular structures.

Interferometry

Figure 1

Interferometer is an optical device, which compares one optical beam or light wave with another reference optical beam or light wave. Optical coherence tomography makes use of low coherence interferometry to perform high-resolution time and distance measurements for imaging. Low coherence interferometry is a well-established technique for performing high-resolution optical measurements in fibreoptic and optoelectronic components[11,12]. A fibreoptic Michaelson interferometer uses a reflecting mirror, which divides the low-coherence light into two beams. The reference beam is reflected by the reference mirror towards the detector. The second beam enters the eye and is reflected back from the different ocular structures towards the beam splitter

as a measurement beam. A complex measurement echo and a single reference echo combine at the reflecting mirror and produce optical interference pattern, which is detected by a photoelectric cell. This interference pattern from the measurement beam can be varied by moving the position of the reference mirror and electronically analysed by the detector[13]. The reflected signal is an A-scan of a small crossection of the eye and the intensities of the various signal returns are converted into a false- colour rainbow scale. If the axis of the scan is moved horizontally, sequential sections can be aligned to create a composite cross-sectional colour image similar to B-scan ultrasound image. Modern OCT 3 images are generated by 512 A- scans, hence gain high resolution. It must be however understood that each interface in the optical image does not represent anatomical differences of structures but differences in their optical properties, although greater anatomical details can be shown with new ultrahigh resolution tomography[7].

Scan patterns

Various scan patterns can be used to produce the optical image like single line of differing length and orientation, radially aligned lines, annular scans of various diameters and sequential parallel lines. Each scan takes about one second to acquire. OCT 3 can acquire 6 scans simultaneously in one second. Image can be obtained in moderate cataract and vitreous blood and the view is limited to 30 degrees only.

Normal appearances

OCT is proving extremely useful in ophthalmology because it provides real time, noncontact cross-sectional images of the ocular structures with imaging resolution. It helps to view the retina and optic nerve as a whole as well as the internal architecture of different retinal layers. High-resolution images of the cornea, iris, lens and anterior chamber including its angle can be generated. Morphometeric measurements of the optic nerve head, retinal layers and anterior segment can be easily carried out because captured optical images can be quantitatively analysed using a variety of algorithms. Such an objective data can play a significant role in the study of disease progression and effect of treatment modalities. The normal OCT 3 image of the central retina is shown in Figure 2. The RPE/choriocapillaris complex is the central reference point in the mid-thickness of the trace and is represented as hyper-reflective red line. Anteriorly the retina is represented as yellow/green layer of lower reflectivity above the RPE. It is practically a homogeneous layer with a well-defined foveal depression. Its nerve fibre layer can sometimes be seen separately as hyper reflective redline especially nasal to the fovea. The normal foveal thickness is about 160 um. The posterior vitreous face may be visible as thin red white line against the black hypo reflective vitreous cavity only if this layer is separated from the retina. Deep to the RPE/choriocapillaris the signal is weak due to attenuation and the anterior choroid is partially visible as hyporeflective (green) layer.

Figure 2.

Applications

OCT is conveniently applicable to ophthalmology because of clear optical media of the eye. Diagnosis of many ocular diseases has become easy and their monitoring has also become possible since the settings of imaging parameters can be memorized and used to scan the same area during the periodic follow up[14]. Morphometric measurements of retinal thickness are feasible which allows quantitative follow-up of diseases like macular oedema, central serous retinopathy (CSR). Abnormalities of the vitreoretinal interface and intraretinal pathologies may change the optical properties of retinal tissue. Haemorrhages, hard exudates, inflammatory exudates and scar tissue may cause hyper reflectivity in the retina and choroid. If these lesions are dense then they can mask the signal from the underlying tissues. Fluid accumulation causes hypo reflectivity such as in macular oedema or sub retinal fluid, the location of which is easily determined thus helping to differentiate between CSR, RPE detachment and retinoschiasis. Serous fluid is optically dark, blood is hyper reflective and cloudy exudates are intermediate in relectivity. As OCT imaging gains wide spread applications in ophthalmology its usefulness has become apparent in the study of:

1. Normal retinal anatomy.
2. Macular holes, epiretinal membranes and posterior vitreous detachment.
3. Fluid accumulation within the retina such as central serous retinopathy, RPE. detachment, cystoid macular oedema, diabetic retinopathy, retinoschiasis.
4. Disorders of the optic nerve head like congenital pit, inflammatory optic neuropathy.
5. Glaucoma.
6. Age-related macular disease.

Figure 3.

Optical imaging technology can become low-cost and portable. Since it can be easily interfaced with optical fibres to catheters, endoscopes, laparoscopes and surgical probes, it is drawing increased attractions from many surgical and medical disciplines. This technology offers distinct advantages like:

a. In situ real time images of tissue structure at micron scale
b. Unlike conventional histopathology, it provides instant optical biopsy.
c. Reduces sampling error in excisional biopsy
d. Guide surgical interventions
e. Imaging of organs inside the body
f. Images of ultrahigh resolutions one to two order above the conventional ultrasound.

Further advances

Ultrahigh resolution OCT

Research in optical imaging technology is producing many exciting new developments. Improving the image resolution has attracted considerable effort. The axial image in OCT is determined by the light bandwidth. Superluminiscent diode light currently employed can support only 10um axial resolution. Ultrahigh resolution (UHR) imaging of 3um axial resolution has been recently reported by using femtosecond laser light source[15]. This has allowed more detailed visualization of the individual layers of the retina especially detailed morphology of the photoreceptors. Even the boundaries between the inner and outer segments of the photoreceptors as well as the external limiting membrane can be seen. Even high performance low-cost superluminiscent light sources are under development [16].

High speed UHR imaging

High-speed imaging techniques have allowed high pixel density and high definition imaging and it also reduces eye movement artifacts. A large number of images can be acquired to cover more retinal area. Tenfold to one hundredfold increase in image speed has now become possible to capture and measure by employing Spectral/fourier detection method which uses interferometer, spectrometer and high speed CCD camera simultaneously to detect all of the light echoes from all time delays and process it digitally into fourier transform[17]. Acquisition speed of up to 30,000 axial scans per second is possible as compared to 400 axial scan per second imaging speed of standard OCT [18-20]. The high pixel density gives high definition image with improved clarity similar to high definition television, which can be zoomed to enlarge to examine the fine details.

Three-dimensional imaging

High speed ultrahigh resolution imaging using fourier domain promises new exciting possibilities of 3D mapping of all the major retinal layers and retinal morphology can be assessed using virtual perspectives as in MRI[21]. In addition, measurement algorithms may be applied to individual layers. However 3D imaging of the retina is still in early stage of development and at present too slow to become clinically relevant.

CONCLUSION

Advances in electronic imaging and photonics have continuously improved the performance of OCT over the last ten years. Further research into optical technology is providing the emergence of ultrahigh resolution 3D viewing of the retinal architecture. It will be possible in the near future to visualize the morphology of the intact retina at a level of resolution previously not possible. Advances in detailed in vivo imaging of the ocular tissues promises to enhance our understanding of the natural history of disease processes, more accurate earlier diagnosis, monitoring of disease progression and response to various therapeutic modalities.

REFERENCES:

1 Fujimoto JG, Pitris C, Boppart SA, Brezinski ME. Optical coherence tomography: an emerging technology for biomedical imaging and optical biopsy. Neoplasia. 2000;2:9-25.
2 Fujimoto JG, Brezinski ME,Tearney GJ et al. Optical biopsy and imaging using optical coherence tomography. Nat Med 1995;1:970-2.
3 Fujimoto JG. Optical coherence tomography for ultrahigh resolution in vivo imaging. Nature Biotechnology 2003;21:1361-7.
4 Huang D, Swanson EA, Lin CP et al. Optical coherence tomography. Science 1991;254:1178-81.
5 Radhakrishnan S, Rollins AM, Roth JE et al. Real-time optical coherence tomography of the anterior segment at 1310 nm. Arch Ophthalmol 2001;119:1179-85.
6 Brezinski ME, Tearney GJ, Bouma BE et al. Optical coherence tomography for optical biopsy. Properties and demonstration of vascular pathology. Circulation 1996;93:1206-13.
7. Thomas D, Duguid G. Optical coherence tomography- a review of the principles and contemporary uses in retinal investigation. Eye 2004;18:561-70.
8 Stern D, Lin WZ,Puliafito CA et al. Femtosecond optical ranging of corneal incision depth. Invest Ophthalmol Vis Sci 1989;30:99-104.
9. Fujimoto JG, De Silvestri S, Ippen EP et al. Femtosecond optical ranging in biological systems. Optics Letters. 1986;11:150-3.
10. Chauhan DS, Marshall J. The interpretation of optical coherence tomography images of the retina. Invest Ophthalmol Vis Sci 1999;40:2332-42.
11. Takada K, Yokohama I, Chida K et al. New measurment system for fault location in optical waveguide devices based on interferometric technique. Appl Opt; 1987;26: 603-8
12. Gilgen HH, Novak RP, Salathe RP et al. Submillimeter optical reflectmetry. IEEE Journal of Lightwave Technology 1989; 7: 1225-33.
13. Hee MR, Izatt JA, Swanson EA et al. Optical coherence tomography of the human retina. Arch Ophthalmol 1995;113:325-32.
14. Schuman JS, Puliafito CA, Fujimoto JG. Optical coherence tomography of ocular diseases , 2nd edition. Thorfare, NJ: Slack Inc.2004.
15. Drexler W, Morgner U, Ghanta RK et al. Ultrahigh-resolution ophthalmic optical coherence tomography. Nature medicine 2001; 7: 502-7.
16. Ko TH, Adler DC, Fujimoto JG et al. Ultrahigh resolution optical coherence tomography imaging with a broadband superluminiscent diode light source. Optics Express 2004;12:2112-9
17. Wojtkowski M, Leitgeb R, Kowalczyk A et al. In vivo human retinal imaging by Fourier domain optical coherence tomography. Journal of Biomedical Optics. 2002;7:457-63.
18. Cense B, Nassif NA, Chen TC et al Ultrahighigh-resolution high speed retinal imaging using spectral-domain optical coherence tomography. Optics Express 2004; 12:2435-47
19 .Leitgeb RA, Drexler W, Unterhuber A et al. Ultrahigh resolution Fourier domain optical coherence tomography. Optics Express 2004;12:2156-65.

20. Wojtkowski M, Srinivasan VJ, Ko TH et al. Ultrahigh resolution, high speed Fourier domain optical coherence tomography and methods for dispersion compensation. Optics Express 2004; 12: 2404-22.
21. Wojtkowski M, Bajraszewski T, Gorczynska I et al. Ophthalmic imaging by spectral optical coherence tomography. Am J Ophthalmol 2004; 138:412-9.

Legends to illustrations

1. Figure No 1. Ray diagram illustrating the interferometry principle as used in OCT.
2. Figure No 2. OCT image of the normal posterior pole retina.
3. Figure No 3. OCT images of posterior retinal pathology.
   (a) Cystoid macular oedema. Multiple hyporeflective spaces and increased thickeness of the central retina with loss of foveal depression.
   (b1) Vitreomacular traction syndrome. Posterior hyaloid traction on the fovea resulting in loss of foveal depression .
   (b2) Follow-up image showing spontaneous release of traction and restoration of normal foveal contour.
   (c1) Central serous retinopathy. Full thickness neurosensory retinal layer elevation separated from RPE with an empty space.
   (c2) Follow-up image showing partial resolution with decrease in elevation.
   (d) OCT image showing CNV as thickening of the RPE layer with new vessel complex breaking through the RPE.