Anterior Segment Optical Coherence Tomography in Glaucoma

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Imaging technology such as X-ray, ultrasound, computed tomography and magnetic resonance imaging have found widespread applications in medicine. Many situations in clinical ophthalmology require precise understanding of the spatial relationships and dimensions of the various structures in the anterior segment. A technique capable of anterior segment imaging with micrometer resolution would be extremely valuable in obtaining such information.

Several techniques have been employed for high-resolution noninvasive or marginally invasive examination of the anterior eye. Ultrasound biomicroscopy (UBM) provides resolution ranging from 20-60 µm with a depth of resolution of about 4 mm and can obtain images of structures concealed by opaque media. Imaging time is 8 frames per second, allowing in vivo observation of movement of ocular structures in real time. This technique however requires immersion of the eye in a water bath solution and it is difficult to determine the exact location of the examined area.

Confocal microscopy has been used for high resolution imaging in transparent tissue of anterior segment and provides en face images of corneal layer. Video rate imaging have been achieved with scanning slit confocal microscopy, which has a lateral resolution of 0.8 µm and scans optical section that are 10 µm in thickness. The technique requires the use of an index matching gel to optically couple the tip of the microscope objective to the cornea. It requires short focal distances and can image only a small area of the eye at a time.

Slit illumination imaging techniques such as Scheimpflug photography or the Orbscan system can also provide cross-sectional images but accurate biometry is difficult. Pentacam, Scheimpflug Camera (Oculus) and Galilei, dual Scheimpflug Camera (Ziemer) are the two available Scheimpflug Camera. The Scheimpflug technique gives a complete image of the AC, but the complex and inaccurate mathematical reconstructions make it difficult to evaluate the anterior segment with precision. The disparities in the obliquity of the cross-sectional and projection plane of photographic images can lead to measurements being obtained through extrapolation.

Magnetic resonance imaging using special receiver coils has achieved an in vivo intraocular imaging resolution of 230 µm in human eye with an acquisition time of 6.5 minutes per sequence. To obtain MRI images of good quality, patients have to maintain eye and head positions for the duration of imaging and chemical shift artifacts have to be considered before interpretation of the images. This technique may be useful for elucidation of physiologic or pathologic disease mechanisms; however it is impractical in many clinical situations.

Optical coherence tomography (OCT) is a cross-sectional, three-dimensional, high-resolution imaging modality that uses low coherence interferometry to achieve axial resolution in the range of 3-20 µm. It can overcome many of the limitations of the current techniques used to image the anterior segment of the eye. OCT is similar to ultrasound except that light is used instead of sound. It is a completely noninvasive technique. As it uses interferometry for depth resolution it can have a long working distance and a wide field of transverse scanning compared to confocal microscopy. OCT has predominantly been used so far for posterior segment imaging of the eye because of various reasons.

Anterior segment imaging using OCT was first demonstrated in 1994 by Izatt et al using light with a wavelength of 830 µm. Not much attention was paid to anterior segment applications until Lubech group described OCT imaging of Laser thermokeratoplasty lesion in 1997 and Maldonado et al reported imaging of LASIK flap in 1998.

The primary limitation of OCT imaging of the anterior segment is speed and penetration. The OCT systems used in commercial retinal scanner thus far have used 830 nm wavelength, with image acquisition time of 1 to 5 seconds. The wavelength higher than 830 nm in posterior segment had more dissipation in vitreous hence was discarded from posterior segment use, but it found its lace in anterior segment. Wavelength of 1310 nm allowed deeper penetration and cross-
sectional imaging of the anterior chamber, including visualization of the angle.

Very recently, ophthalmic OCT in 1310 nm wavelength has been described, with an acquisition time of 3.3 seconds. All of these systems require image-processing technique to remove artifacts caused by patient motion during data acquisition.

A system capable of faster data acquisition would not be affected by involuntary eye movement and would allow real time display. This anterior segment OCT is described as an attractive technique for optical biopsy because it can permit the imaging of tissue microstructure in situ yielding micron-scale image resolution without the need for excision of a specimen and tissue processing. Ocular imaging with 1.3 µm wavelength ASOCT was first reported by Radhakrishnan et al.6

**PRINCIPLE OF OPTICAL COHERENCE TOMOGRAPHY**

In a typical optical coherence tomography system (Fig. 1), light from a broadband, near-infrared source and a visible aiming beam is combined and coupled into one branch of a fiber-optic Michelson interferometer. Broadband sources include super luminescent diodes, fiber amplifiers, and femtosecond pulse lasers in the wavelength range of 800-1550 nanometers. The light is split into two fibers using a 2 × 2 coupler, one leading to a reference mirror and the second focused into the tissue. Light reflects off the reference mirror and is recoupled into the fiber leading to the mirror. Concurrently, light is reflected from index-of-refraction mismatches in the tissue and recoupled into the fiber leading to the tissue. Reflections result from changes in the index of refraction within the structure of the tissue, for instance between intercellular fluid and collagen fibers. Light that has been back-reflected from the tissue and light from the reference arm recombine within the 2 × 2 coupler.

Because the broadband source has a short coherence length, only light which has traveled very close to the same time (or optical path length) in the reference and tissue arms will interfere constructively and destructively. By changing the length of the reference arm, reflection sites at various depths in the tissue can be sampled. The depth resolution of the optical coherence tomography system is determined by the effectiveness of this time gating and hence is inversely proportional to the bandwidth of the source. An optical detector in the final arm of the Michelson interferometer detects the interference between the reference and tissue signals. During optical coherence tomography imaging, the reference-arm mirror is scanned at a constant velocity, allowing depth scans (analogous to

![Fig. 1: High-speed corneal and anterior segment optical coherence tomography at 1.3 µm wavelength](image-url)
ultrasound A-scans) to be made. Either the tissue or the interferometer optics is mounted on a stage so that the beam can be scanned laterally across the tissue to build up two- and three-dimensional images, pixel by pixel.

OCT at 1.3 µm wavelength of light is better suited for anterior segment imaging due to two significant properties. First, the amount of scattering in tissue is lower at this wavelength. This enables increased penetration through scattering ocular structures such as the sclera and the iris so that more detailed anterior segment morphology is visualized. Second, 1.3 µm wavelength is strongly absorbed by water in ocular media and therefore, only 10 % of the light incident on the cornea reaches the retina. The absorption and scattering in most tissue constituents decreases with wavelength in the near infrared spectrum whereas absorption in water (the primary constituent of vitreous humor) increases sharply. The improved retinal protection allows for the use of high power illumination that, in turn, enables high-speed imaging. The permissible exposure level at 1.3 µm wavelength is 15 mW according to the current standard set by the American Laser Institute and the American National Standard institute (ANSI 2000). This level is 20 times higher than the 0.7 mW limit at the 0.8 µm wavelength. The high-speed imaging eliminates motion artifacts, reduces examination time, allows for rapid survey of relatively large areas and enables imaging of dynamic ocular events. The ASOCT image represents the differential backscattering contrast between different tissue types on a micron scale. It is a gray scale or false color two-dimensional representation of backscattered light intensity in a cross-sectional plane. Highly detailed image of the cornea and angle region including the iris root, the angle recess, the anterior ciliary body, the scleral spur, and, in some eyes, the canal of Schlemm is possible.\(^7\)

Recently two anterior segment OCT systems Visante ASOCT (Carl Zeiss Meditec, Inc, Dublin, CA, USA) and SLOCT (Heidelberg Engineering GmbH, Germany) (Figs 2A and B) have been launched.

**SPECIFICATIONS AND RESOLUTIONS**

The scanning speed is 4000 axial scans per image, giving an image acquisition rate of 8 frames per second. With standard software, the lateral resolution of ASOCT is 60 µm and the axial resolution is 18 µm compared to 50 µm and 25 µm respectively by UBM. With high-resolution corneal software, axial resolution of ASOCT can reach 8 µm. The scan geometry is telecentric (rectangular) allowing wide field capability, which is essential for corneal and anterior chamber studies. SLOCT has in addition a slit lamp attached to it and use a charge couple device (CCD) camera to visualize the scan area in real time. Scan area is 15 mm × 7 mm. It can image to a depth of 7 mm, which is up to posterior lens capsule in case of transparent lens.

**OCULAR STRUCTURES AND IMAGING MODES OF AS OCT**

**Angle Region**

Due to lower scattering loss at 1.3 µm, highly detailed AC angle imaging is possible, and angle structures including the iris root, the angle recess, the anterior ciliary body, the scleral spur, and in some eyes, the canal of Schlemm can be visualized. Scleral spur particularly is highly reflective and can be easily identified on OCT. Digital gonioscopy allows objective anterior chamber angle assessment which is noncontact and fast angle assessment. As same landmark (scleral spur) used every time for objective angle assessments, digital angle measurement is highly accurate and reproducible.

Currently, Gonioscopy is the gold standard for evaluating the anterior chamber angle; however it is subjective, contact method, likely to cause some distortion of cornea and angle, semi quantitative with poor reproducibility and requires specialized training. Also there are no uniform criteria for identifying angles that require treatment. Cross-sectional imaging of the anterior chamber can provide quantitative data and may prove to be less subjective than gonioscopy.

ASOCT can be used to assess angle width. The images obtained are processed using computer to correct image distortion arising from 2 sources. First, the fan shaped scanning geometry of the OCT beam and second, the effect of refraction at the cornea air interface.

Angle can be measured manually (only ACA feature) or automatically. Various parameters available from the image are ACA (Anterior chamber angle at 500 µm and 750 µm) with Spaeth grading (SG), AOD (Angle opening distance at 500 µm and 750 µm) TISA (Trabecular-iris space area) (Figs 3A and B).

Ultrasound biomicroscopy and Schiempflug photography have been used for quantitative angle evaluation. OCT can provide with the added advantage of being noncontact, devoid of artificial opening of angle and easy to perform.

Since the posterior layer of the iris (pigment epithelium) is not transparent for infrared light the area of the sulcus is in most of the cases not presentable. As the infrared light is absorbed on its way through the sclera, the area of the ciliary body is not visible entirely.

**SIMULTANEOUS IMAGING OF ANTERIOR SEGMENT AND OCT**

Simultaneous anterior segment digital image and OCT image can be obtained with the SLOCT system. Hoerauf et al\(^8\) evaluated the diagnostic potential of a SLOCT system as an in vivo imaging device for routine clinical examination of the anterior segment of the eye and found it to be a useful diagnostic tool which allows in vivo microscopic cross-sectional imaging of
Figs 2A and B: The Visante ASOCT (Carl Zeiss) and SLOCT (Heidelberg engineering)
the anterior segment and precise measurement of ocular structures (Figs 4 A to F).

CLINICAL APPLICATIONS IN GLAUCOMA

Screening of Angle Closure Glaucoma

Glaucoma is the second cause, after cataract, of world blindness (WHO). Approximately 50% is thought to be primary angle-closure glaucoma (PACG). In China and South-East Asia, the mechanism of angle closure appears to be more varied and complex and its detection may require more elaborate imaging.

According to 3rd Consensus Meeting of the Association of International Glaucoma Societies (AIGS) held 3rd May 2006, PACG is a leading cause of blindness throughout Asia and is maybe more common in European populations than previously recognized. Even though POAG is more common than PACG, it has been estimated that nearly half of all glaucoma blindness is due to PACG because it tends to be more severe than POAG. Every person over 40 should be screened for PACG by assessing the anterior chamber angles. Treating anatomically narrow angles with a laser peripheral iridotomy may prevent development of angle closure. Therefore, early detection of anatomically narrow angle is important.
The ASOCT provides a useful tool for assessment of corneal thickness. Digital goniometry with ASOCT was compared with current gonioscopic clinical parameters in the evaluation of the anterior chamber angle by Wirbelauer et al. They found a significant correlation with the clinical parameters of gonioscopic grading and ASOCT findings. Nolan et al evaluated ability of ASOCT to detect primary angle closure when compared with gonioscopy in Asian subjects. It was found to be highly sensitive in detecting angle closure when compared with gonioscopy. More persons are found to have closed angles with ASOCT than with gonioscopy (Figs 5 to 6B).

OTHER APPLICATIONS OF ASOCT IN DIAGNOSIS OF GLAUCOMA

Evaluation of the structural causes of angle closure glaucoma such as plateau iris syndrome, malignant glaucoma, and pupillary block glaucoma can be performed. Wirbelauer et al showed markedly decreased anterior chamber angle with extreme shallowing of the anterior chamber depth during the acute malignant glaucoma phase by SLOCT which resolved after PPV and deepening of the anterior chamber with viscoelastic.

Mechanism of glaucoma in secondary glaucomas can be studied. It can be done easily with great details in cases of corneoiridic scar and opaque graft with secondary glaucoma.

STUDY OF DYNAMIC PHYSIOLOGICAL CHANGES OF ANTERIOR SEGMENT

Study of alterations in anatomical configuration of angle structures in response to light and accommodation can be performed. This may help detection of conditions such as plateau iris syndrome, pigmentary glaucoma, malignant glaucoma (Fig. 7) and primary angle closure glaucoma. See et al in their study to study the mechanism of glaucoma and help in deciding the placement of Trabeculectomy or valve in synechiae free region.
by ASOCT have shown that increased illumination resulted in significant widening of the anterior chamber angle (Figs 8A and B).

Baikoff et al\textsuperscript{17} studied biometric modifications of the anterior segment with accommodation and age and determine possible applications in areas of anterior segment surgery, particularly implantation of refractive lenses using ASOCT. The equipment has a fixation target that can be focused and defocused with negative lenses to stimulate natural accommodation. The horizontal diameter of the AC, the anterior chamber depth (ACD), the horizontal pupil diameter, and the horizontal radius of curvature of the crystalline lens’ anterior pole were measured in the unaccommodated state and after stimulating accommodation. They found with 1.0 D of accommodation, the anterior pole moved forward by a mean of 30 µm, the radius of curvature decreased 0.3 mm, and the pupil diameter decreased 0.15 mm.

Real time imaging is possible during performance of provocative tests for assessment of angle occludability, such as the dark room and the prone provocative tests.

**Evaluation of Therapy of Glaucoma**

Other applications of the ASOCT includes its use in the evaluation of the efficacy of various treatments, such as laser peripheral iridotomy (Figs 9A and B), laser iridoplasty or cataract extraction, where the angles may be shown objectively to open after such treatment. Chalita et al\textsuperscript{18} have shown by OCT, the reduction of iris concavity and patent iridotomies after iridotomy. Quantitative measurements of TISA on the OCT images showed widening of the angles to nonoccludable values in their study.

The ASOCT may also be helpful in the assessment of tube patency or position in cases of corneal opacity. It has also been shown to be helpful to outline the Ex-PRESS miniature glaucoma implant in the anterior segment.\textsuperscript{19} ASOCT is expected to aid in providing answers to the question regarding which parameters will determine the success or failure of such a device.

**APPLICATION IN IMAGING TRABECULECTOMY BLEBS**

Bleb morphology is an important clinical parameter in filtering surgery. It indicates function of the filtration shunt created by the trabeculectomy procedure and guides the ophthalmologist in performing interventions such as needling and suture lysis in order to optimize shunt function. ASOCT has been used to image trabeculectomy blebs to provide information about internal structure that is not available at the slit lamp. It is able to provide clear images of the bleb wall, cavity, flap and ostium as displayed below (Figs 10A to 11B).

Successful blebs display conjunctival thickening as a hallmark of success, regardless of degree of bleb elevation. This reflects facility of transconjunctival aqueous flow. Highly elevated blebs sometimes display marked conjunctival thickening and only a small cavity. In failed blebs, ASOCT is particularly useful in imaging failed blebs to demonstrate the level of failure. Ostial closure, flap fibrosis and presumed episcleral fibrosis in the absence of the former two situations are all clearly demonstrated. In the early postoperative period, a failing bleb with a closely apposed scleral flap may be resuscitated by suture lysis, resulting in a more expanded bleb.

Singh et al\textsuperscript{20} imaged trabeculectomy blebs using ASOCT. They identified the following bleb characteristics: total bleb height, bleb cavity, bleb wall thickness, tangential and radial dimensions, scleral flap thickness, and patency of the internal ostium. The majority of successful blebs displayed thickening of the bleb wall. Failed blebs were mostly low and were characterized by ostial occlusion, apposition of conjunctiva-episclera to sclera or apposition of the scleral flap to its bed.
Thickening of the bleb wall was typically absent. ASOCT was able to demonstrate features of bleb morphology not visible with the slit lamp.

Dada et al.\textsuperscript{21} have described another use of the SLOCT by performing SLOCT guided needling for restoration of bleb function (Figs 12A and B). This technique allowed visualization of the internal bleb architecture, which is often not visible on routine slit lamp evaluation in eyes with a vascularized fibrotic bleb or under a thick Tenon’s capsule. SLOCT guided bleb intervention is a useful technique for restoration of bleb function allowing precise anatomical localization of bleb pathology and in vivo imaging of the effect of needling on bleb function. The depth of the needle can be precisely located and adjusted while doing the revision. Fibrous septae within the bleb can be
localized and incised and the aqueous track visualized from the trabeculectomy ostium to the subconjunctival space. It helps to achieve good accuracy, as the targeted area can be selectively imaged and intervention performed with minimal damage to the adjacent functional areas. In addition, the internal scleral ostium can also be visualized without the use of a gonioscope and this may have future implications for intervening under the scleral flap.

**Advantages of the ASOCT**

- It is a noncontact method therefore do not cause indentation of the angle by placement of the scleral cup on the eye (which is required to maintain the water bath in UBM).
- Do not cause corneal abrasion or punctuate epithelial erosions (possible with UBM).
- It is a more physiological examination as patient is imaged sitting upright. (Lying supine may artificially widen the anterior chamber angle as the iris-lens diaphragm moves posteriorly due to gravity).
- Shorter imaging time. (Patient setup in UBM takes longer. Also, only one angle is imaged at a time with the UBM).
- Rapid image acquisition. Eight frames can be captured per second, allowing operator to choose best image.
- Requires less expertise to perform. Small learning curve for the operator.
- Target may be used to induce accommodation in the eye being imaged. (This is useful in the evaluation of accommodative intraocular lenses).
- More comfortable for the patient, due to noncontact technique, upright position and rapid imaging acquisition.
- Less interoperator variability, due to noncontact technique.

**Disadvantages of the ASOCT**

- Since the posterior layer of the iris (pigment epithelium) is not transparent for infrared light the area of the sulcus is in most of the cases not presentable.
- The infrared light will be absorbed on its way through the sclera. As a matter of this, the area of the ciliary body is not visible entirely.

Thus ASOCT using 1.3 µm wavelength is a very helpful tool for noncontact anterior segment evaluation. Its measurements correlate well with ultrasound biomicroscopy with various advantages over UBM. Various interventions can be performed on slit lamp with simultaneous guidance by OCT in SLOCT. Among the limitations of ASOCT are it provides limited visualization of the ciliary body and behind the iris. It may be used as the standard modality for anterior segment imaging in clinical practice.

**REFERENCES**


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“On patience: I remember one morning when I discovered a cocoon in the bark of a tree just as the butterfly was making a hole in its case and preparing to come out. I waited awhile but it was too long appearing and I was impatient. I bent over it and breathed on it to warm it. I warmed it as quickly as I could and the miracle began to happen before my eyes, faster than life. The case opened, the butterfly started slowly crawling out, and I shall never forget my horror when I saw how its wings were folded back and crumpled, the wretched butterfly tried with its whole trembling body to unfold them. Bending over it, I tried to help with my breath, in vain. It needed to be hatched out patiently and the unholding of its wings needed to be a gradual process in the sun. Now it was too late. My breath had forced the butterfly to appear, all crumpled, before its time. It struggled desperately and few seconds later, died in the palm of my hand.”

—Zorba the Greek