

Anterior Segment Optical Coherence Tomography

Imaging the anterior chamber angle.

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Optical coherence tomography (OCT)¹ is a high-resolution, cross-sectional imaging modality that was initially developed for visualizing the retina.^{2,3} When first described in 1994, anterior segment imaging with OCT utilized a 0.8- μm -wavelength light source similar to that used in retinal OCT.⁴ This wavelength, however, is suboptimal for imaging the anterior chamber angle; 0.8- μm light cannot penetrate the sclera and thus prevents the visualization of the underlying angle structures.

OCT using 1.3- μm -wavelength light is better suited for imaging the anterior chamber angle due to two significant properties. First, the amount of scattering in tissue is lower at this wavelength, a difference that increases the penetration of light through scattering ocular structures such as the sclera and the iris so that the morphology of the anterior chamber angle is visualized with more detail (Figure 1). Second, because water in the ocular media strongly absorbs 1.3- μm -wavelength light, only 10% of the light incident on the cornea reaches the retina. This improved retinal protection allows the use of higher-powered illumination, which in turn enables high-speed imaging. The advantages of high-speed imaging include an elimination of motion artifacts, decreased examination time, and an ability to image dynamic ocular events. This article explores how anterior segment OCT works and its potential applications.

Anterior segment OCT has several advantages over gonioscopy

for the evaluation of the anterior chamber angle. The latter is subjective, requires a highly trained examiner, and involves ocular contact. In contrast, anterior segment OCT quantitatively measures the anterior chamber angle in a noncontact fashion, and the technology is easy to use after minimal training. Because it does not require contact with the eye, anterior segment OCT is safer and more comfortable for patients, and it avoids the mechanical distortion of the structures to be examined. A potentially significant advantage of this technology is that it may be used in complete darkness. Any changes in the angle configuration that are induced by ambient lighting are thus eliminated.

COMPARING MODALITIES

OCT has several advantages over other cross-sectional imaging modalities such as ultrasound biomicroscopy (UBM) and Scheimpflug photography. Compared with

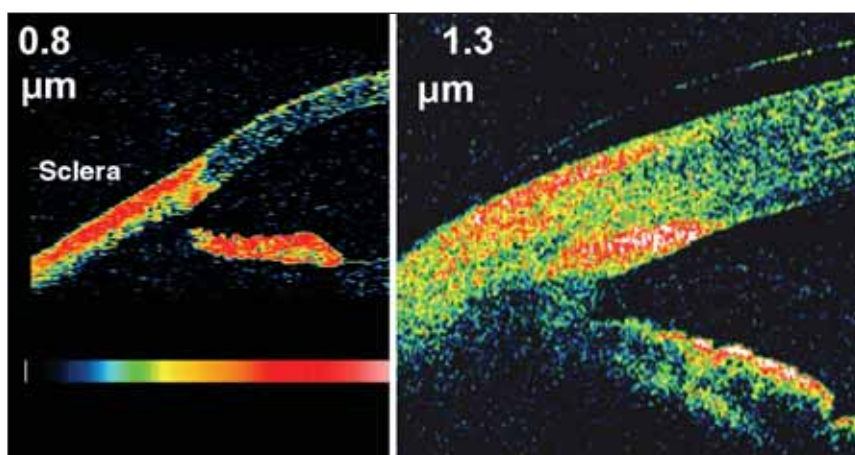


Figure 1. The difference in visualization with 0.8- μm - and 1.3- μm -wavelength anterior segment OCT is evident.

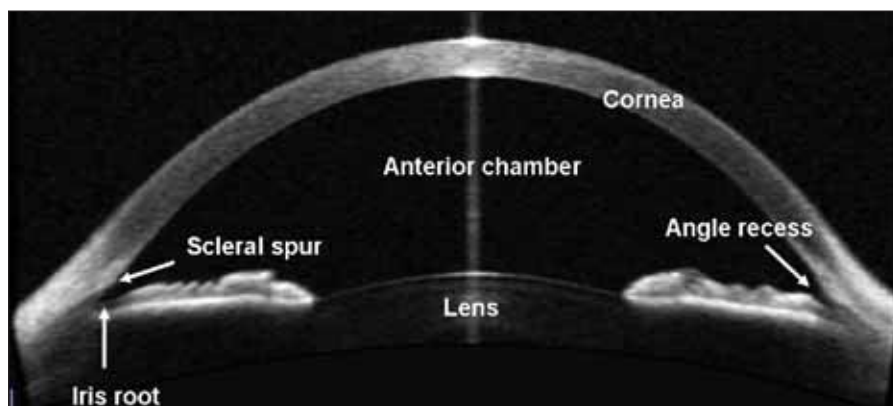


Figure 2. This OCT image of the anterior segment illustrates the anterior chamber angle anatomy. The scleral spur, ciliary body band, angle recess, and iris root are clearly identifiable. (Reprinted with permission from Radhakrishnan S, Huang D, Smith SD. Optical coherence tomography imaging of the anterior chamber angle. *Ophthalmol Clin North Am.* 2005;18:375-381.)

UBM, OCT provides a higher resolution, is completely noncontact, and is relatively easy to perform. Because Scheimpflug photography does not image the actual angle recess, it does not provide visualization of important structural detail. In contrast, OCT provides detailed direct imaging of the anterior chamber angle region.

PROTOTYPES

Several anterior segment OCT prototypes have been described in the literature,⁴⁻⁸ and an FDA-approved device (Visante; Carl Zeiss Meditec Inc., Dublin, CA) recently became commercially available. We have employed some of these prototypes in our studies. The system that we currently use was developed by Carl Zeiss Meditec Inc. It uses a 1.3- μm -wavelength light source and delivers 2,000 A-scans per second. The device acquires and displays eight image frames per second in real time, each with 500 axial scans. The geometry of the scan is telecentric with adjustable scanning widths of 1 to 16 mm and scanning depths of 1 to 8 mm. The axial resolution is 15 μm .

QUANTITATIVELY MEASURING THE ANTERIOR CHAMBER ANGLE

Structures in the anterior chamber angle are well delineated by 1.3- μm OCT (Figure 2). To perform quantitative measurements, the OCT image must first be processed⁹ to obtain correctly dimensioned images, with adjustments for the geometry of the scan and the refraction of the OCT beam at the eye's anterior surface. Highly reflective and easily identifiable in OCT images, the scleral spur is the landmark used for measuring the parameters of the anterior chamber angle. The quantita-

tive parameters that we have used in our studies include the angle-opening distance at 500 μm , the angle recess area at 500 and 750 μm , and the trabeculo-iris-space area at 500 and 750 μm (Figure 3).

CLINICAL STUDIES

In two recently published studies,^{8,10} the quantitative measurement of the anterior chamber angle with OCT correlated well with gonioscopy in terms of identifying occludable angles. In one of these studies,⁸ the investigators also acquired UBM measurements,

and they found that both the OCT and UBM parameters were comparable in terms of their reproducibility and correlation with gonioscopy. The best OCT parameters were slightly superior to UBM, with 100% sensitivity and 95.7% specificity for detecting gonioscopically occludable angles.

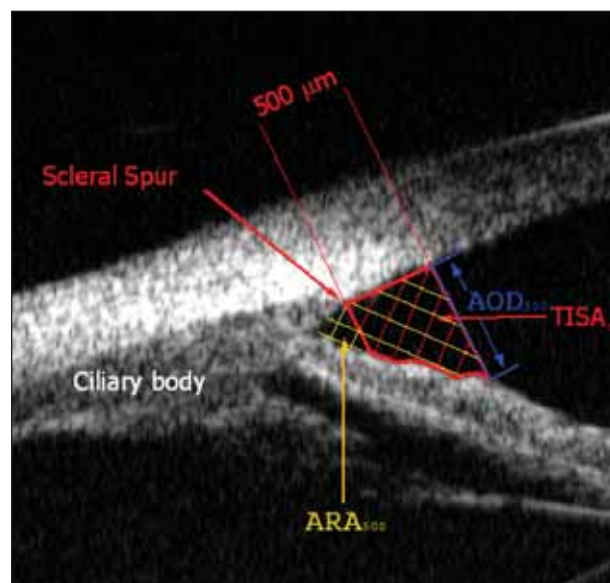


Figure 3. This anterior segment OCT image demonstrates the quantitative parameters of the anterior chamber angle. AOD represents the angle-opening distance, ARA signifies the angle recess area, and TISA stands for the trabeculo-iris-space area. (Reprinted with permission from Radhakrishnan S, Huang D, Smith SD. Optical coherence tomography imaging of the anterior chamber angle. *Ophthalmol Clin North Am.* 2005;18:375-381.)

Anterior segment OCT can quantify changes in the width of the anterior chamber angle due to various factors. A recent case report used a prototypic system to demonstrate the deepening of the anterior chamber angle after a laser peripheral iridotomy.¹¹ Preliminary data from an ongoing study to evaluate illumination-induced changes in the anterior chamber angle with OCT indicate a significant deepening of all anterior chamber parameters under conditions of bright illumination.¹²

CONCLUSION

Anterior segment OCT appears to be a promising tool for evaluating the anterior chamber angle configuration, including changes induced by illumination and laser peripheral iridotomy. As a rapid, easy-to-use, and completely noncontact modality, the device may be a useful screening tool for occludable angles. Ongoing clinical studies will help to evaluate its efficacy in this regard. The use of anterior segment OCT for evaluating trabeculectomy blebs is a future area of study. □

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- Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science* 1991;254:1178-1181.
- Swanson EA, Izatt JA, Hee MR, et al. In vivo retinal imaging by optical coherence tomography. *Opt Lett*. 1993;21:1864-1866.
- Hee MR, Izatt JA, Swanson EA, et al. Optical coherence tomography of the human retina. *Arch Ophthalmol*. 1995;113:325-332.
- Izatt JA, Hee MR, Swanson EA, et al. Micrometer-scale resolution imaging of the anterior eye in vivo with optical coherence tomography. *Arch Ophthalmol*. 1994;112:1584-1589.
- Koop N, Brinkman R, Lankenau E, et al. Optical coherence tomography of the cornea and the anterior eye segment. *Ophthalmology*. 1997;94:481-486.
- Hoerauf H, Wirbelauer C, Scholz C, et al. Slit-lamp-adapted optical coherence tomography of the anterior segment. *Graefes Arch Clin Exp Ophthalmol*. 2000;238:8-18.
- Radhakrishnan S, Rollins AM, Roth JE, et al. Real-time optical coherence tomography of the anterior segment at 1310nm. *Arch Ophthalmol*. 2001;119:1179-1185.
- Radhakrishnan S, Goldsmith J, Westphal V, et al. Comparison of coherence tomography and ultrasound biomicroscopy for detection of narrow anterior chamber angles. *Arch Ophthalmol*. 2005;123:1053-1059.
- Westphal V, Rollins AM, Radhakrishnan S, Izatt JA. Correction of geometric and refractive image distortions in optical coherence tomography applying Fermat's principle. *Opt Express*. 2002;10:397-404.
- Wirbelauer C, Karandish A, Haberle H, Pham DT. Noncontact gonioscopy with optical coherence tomography. *Arch Ophthalmol*. 2005;123:179-185.
- Chalita MR, Li Y, Smith S, et al. High-speed optical coherence tomography of laser iridotomy. *Am J Ophthalmol*. 2005;140:1133-1136.
- Radhakrishnan S, See J, Chew PT, et al. Illumination-induced changes in the angle configuration: an evaluation by anterior segment optical coherence tomography. *IOVS*. 2005;46:e-abstract 148.

INDICATIONS AND USAGE

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension who are intolerant of other intraocular pressure lowering medications or insufficiently responsive (failed to achieve target IOP determined after multiple measurements over time) to another intraocular pressure lowering medication.

CONTRAINDICATIONS

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% is contraindicated in patients with hypersensitivity to bimatoprost or any other ingredient in this product.

WARNINGS

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% has been reported to cause changes to pigmented tissues. These reports include increased pigmentation and growth of eyelashes and increased pigmentation of the iris and periorbital tissue (eyelid). These changes may be permanent.

LUMIGAN® may gradually change eye color, increasing the amount of brown pigment in the iris by increasing the number of melanosomes (pigment granules) in melanocytes. The long-term effects on the melanocytes and the consequences of potential injury to the melanocytes and/or deposition of pigment granules to other areas of the eye are currently unknown. The change in iris color occurs slowly and may not be noticeable for several months to years. Patients should be informed of the possibility of iris color change.

Eyelid skin darkening has also been reported in association with the use of LUMIGAN®.

LUMIGAN® may gradually change eyelashes; these changes include increased length, thickness, pigmentation, and number of lashes.

Patients who are expected to receive treatment in only one eye should be informed about the potential for increased brown pigmentation of the iris, periorbital tissue, and eyelashes in the treated eye and thus, heterochromia between the eyes. They should also be advised of the potential for a disparity between the eyes in length, thickness, and/or number of eyelashes.

PRECAUTIONS

General:

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface (see Information for Patients).

Patients may slowly develop increased brown pigmentation of the iris. This change may not be noticeable for several months to years (see Warnings). Typically the brown pigmentation around the pupil is expected to spread concentrically towards the periphery in affected eyes, but the entire iris or parts of it may also become more brownish. Until more information about increased brown pigmentation is available, patients should be examined regularly and, depending on the clinical situation, treatment may be stopped if increased pigmentation ensues. The increase in brown iris pigment is not expected to progress further upon discontinuation of treatment, but the resultant color change may be permanent. Neither nevi nor freckles of the iris are expected to be affected by treatment.

LUMIGAN® (bimatoprost ophthalmic solution) 0.03% should be used with caution in patients with active intraocular inflammation (e.g., uveitis).

Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost ophthalmic solution. LUMIGAN® should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

LUMIGAN® has not been evaluated for the treatment of angle closure, inflammatory or neovascular glaucoma.

LUMIGAN® should not be administered while wearing contact lenses.

Information for Patients:

Patients should be informed that LUMIGAN® has been reported to cause increased growth and darkening of eyelashes and darkening of the skin around the eye in some patients. These changes may be permanent.

Some patients may slowly develop darkening of the iris, which may be permanent.

When only one eye is treated, patients should be informed of the potential for a cosmetic difference between the eyes in eyelash length, darkness or thickness, and/or color changes of the eyelid skin or iris.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection) or have ocular surgery, they should immediately seek their physician's advice concerning the continued use of the multidose container.

Patients should be advised that if they develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice.

Contact lenses should be removed prior to instillation of LUMIGAN® and may be reinserted 15 minutes following its administration. Patients should be advised that LUMIGAN® contains benzalkonium chloride, which may be absorbed by soft contact lenses.

If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Carcinogenicity studies were not performed with bimatoprost.

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* mouse micronucleus tests.

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (approximately 103 times the recommended human exposure based on blood AUC levels).

Pregnancy: Teratogenic Effects: Pregnancy Category C.

In embryofetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 33 or 97 times, respectively, the intended human exposure based on blood AUC levels.

At doses 41 times the intended human exposure based on blood AUC levels, the gestation length was reduced in the dams, the incidence of dead fetuses, late resorptions, peri- and postnatal pup mortality was increased, and pup body weights were reduced.

There are no adequate and well-controlled studies of LUMIGAN® administration in pregnant women. Because animal reproductive studies are not always predictive of human response, LUMIGAN® should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether LUMIGAN® is excreted in human milk, although in animal studies, bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when LUMIGAN® is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients.

ADVERSE REACTIONS

In clinical trials, the most frequent events associated with the use of LUMIGAN® (bimatoprost ophthalmic solution) 0.03% occurring in approximately 15% to 45% of patients, in descending order of incidence, included conjunctival hyperemia, growth of eyelashes, and ocular pruritus. Approximately 3% of patients discontinued therapy due to conjunctival hyperemia.

Ocular adverse events occurring in approximately 3 to 10% of patients, in descending order of incidence, included ocular dryness, visual disturbance, ocular burning, foreign body sensation, eye pain, pigmentation of the periorcular skin, blepharitis, cataract, superficial punctate keratitis, eyelid erythema, ocular irritation, and eyelash darkening. The following ocular adverse events reported in approximately 1 to 3% of patients, in descending order of incidence, included: eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, and conjunctival edema. In less than 1% of patients, intraocular inflammation was reported as iritis.

Systemic adverse events reported in approximately 10% of patients were infections (primarily colds and upper respiratory tract infections). The following systemic adverse events reported in approximately 1 to 5% of patients, in descending order of incidence, included headaches, abnormal liver function tests, asthenia and hirsutism.

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