Title: Optical Coherence Tomography (OCT) of the Anterior Eye Segment

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DESCRIPTION
Optical coherence tomography (OCT) is a high resolution method of imaging the ocular structures. OCT for the anterior eye segment is being evaluated as a non-invasive diagnostic and screening tool for the detection of angle closure glaucoma, to assess corneal thickness and opacity, evaluate pre-surgical and postsurgical anterior chamber anatomy, calculate intraocular lens power, guide laser-assisted cataract surgery, assess complications following surgical procedures, and to image intracorneal ring segments. It is also being studied in relation to pathologic processes such as dry eye syndrome, tumors, uveitis, and infections.
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Background
OCT is a non-invasive method that creates an image of light reflected from the ocular structures. In this technique, a reflected light beam interacts with a reference light beam. The coherent (positive) interference between the 2 beams (reflected and reference) is measured by an interferometer, allowing construction of an image of the ocular structures. This method allows cross-sectional imaging at a resolution of 6 to 25 microns. The Stratus OCT™ (Carl Zeiss Meditec), which uses a 0.8-micron wavelength light source, was designed for evaluating the optic nerve head, retinal nerve fiber layer, and retinal thickness. The Zeiss Visante OCT™ and AC Cornea OCT (Ophthalmic Technologies) use a 1.3-micron wavelength light source designed specifically for imaging the anterior eye segment. Light of this wavelength penetrates the sclera, allowing high-resolution cross-sectional imaging of the anterior chamber angle and ciliary body. The light is, however, typically blocked by pigment, preventing exploration behind the iris. Ultrahigh resolution OCT can achieve a spatial resolution of 1.3 microns, allowing imaging and measurement of corneal layers.

An early application of OCT technology was the evaluation of the cornea before and after refractive surgery. Since this is a non-invasive procedure that can be conducted by a technician, it has been proposed that this device may provide a rapid diagnostic and screening tool for the detection of angle closure glaucoma. The classification of glaucoma (primary open angle or angle closure) relies heavily on knowledge of the anterior segment anatomy, particularly that of the anterior chamber angle. Angle closure glaucoma is characterized by obstruction of aqueous fluid drainage through the trabecular meshwork (the primary fluid egress site) from the eye's anterior chamber. The width of the angle is one factor affecting the drainage of aqueous humor. A wide unobstructed iridocorneal angle allows sufficient drainage of aqueous humor, whereas a narrow angle may impede the drainage system and leave the patient susceptible to angle closure glaucoma. The treatment for this condition is a peripheral iridotomy (laser) or peripheral iridectomy (surgery).

Slit lamp biomicroscopy is used to evaluate the anterior chamber; however, the chamber angle can only be examined with specialized lenses, the most common of these being the gonioscopic mirror. In this procedure, a gonio lens is applied to the surface of the cornea, which may result in distortion of the globe. Ultrasonography may also be used for imaging the anterior eye segment. Ultrasonography uses highfrequency mechanical pulses (10-20 MHz) to build up a picture of the front of the eye. An ultrasound (US) scan along the optical axis assesses corneal thickness, AC depth, lens thickness, and axial length. US scanning across the eye creates a 2-dimensional image of the ocular structures. It has a resolution of 100 μm but only moderately high intraobserver and low interobserver reproducibility. US biomicroscopy (≈ 50 MHz) has a resolution of 30 to 50 μm. As with gonioscopy, this technique requires placement of a probe under topical anesthesia.
Regulatory Status
The Visante OCT received marketing clearance through the U.S Food and Drug Administration (FDA) 510(k) process in 2005, listing the Stratus OCT and Orbscan™ II as predicate devices. The 510(k) summary describes the Visante OCT as “a non-contact, high resolution tomographic and biomicroscopic device indicated for the in vivo imaging and measurement of ocular structures in the anterior segment, such as corneal and LASIK flap thickness.”

The RTVue (Optovue) is a commercially available Fourier-domain OCT system with a resolution of 5 microns that received marketing clearance from the FDA in 2010. Although indicated for posterior segment imaging, a lens is available to allow imaging of the anterior segment.

The Slit-Lamp OCT (SL-OCT, Heidelberg Engineering) received marketing clearance through the FDA’s 510(k) process in 2006. The SL-OCT is intended as an aid for the quantitative analysis of structures and the diagnosis and assessment of structural changes in the anterior segment of the eye. “The SL-OCT examination system is not intended for the analysis of the cross-sectional images to obtain quantitative measured values. Neither the obtained measured values nor the qualitative evaluation of the images should be used as the sole basis for therapy-related decisions.”

Three commercially available laser systems, the LenSx (Alcon), Catalys (Optimedica), and VICTUS (Technolas Perfect Vision), include OCT to provide image guidance for laser cataract surgery.

Ultrahigh resolution OCT devices include the Bioptigen Envisu (Bioptigen) and the SOCT Copernicus HR (Optopol Technologies). Custom-built devices, which do not require FDA approval, are also used.

The AC Cornea OCT from Canada is not cleared for marketing in the United States.

POLICY
Scanning computerized ophthalmic (e.g., OCT) imaging of the anterior eye segment is considered experimental / investigational.

RATIONALE
A search of the MEDLINE database was initially performed in December 2007 and updated periodically using the MEDLINE database. The most recent literature review was performed through January 8, 2015. Recent literature searches have found numerous studies that use optical coherence tomography (OCT) to evaluate the anatomy of the anterior segment (AS) and report qualitative and quantitative imaging and detection capabilities. Although these studies provide evidence for the technical performance of OCT, assessment of a diagnostic technology typically focuses on 3 categories of evidence:
• Technical performance. Technical performance refers to how well the technology measures and records the parameter(s) that it is purported to evaluate. Evaluation of technical performance may include various measures of validity (e.g., criterion validity, construct validity, etc) and reliability (e.g., test-retest reliability, agreement among multiple reviewers, etc).

• Diagnostic accuracy. Diagnostic accuracy is the ability of a test to accurately diagnose a clinical condition in relevant populations of patients, in comparison with a reference standard. Measures of diagnostic accuracy include sensitivity, specificity, predictive values, likelihood ratios, and area under the curve analysis.

• Impact on health outcomes. Demonstration that the diagnostic information can be used to improve patient outcomes is essential to determining the utility of a diagnostic technology. Direct evidence on the impact of the diagnostic technology on health outcomes may be available if controlled trials have been performed. In most cases, an indirect chain of evidence needs to be constructed to determine whether there is a tight linkage between the diagnostic technology and improvement in health outcomes.

Technical Performance
Reproducibility of Measurements
Maram et al (2014) assessed the reproducibility of angle metrics using the Visante OCT. The anterior chamber (AC) angle from 20 eyes of 20 healthy subjects (open angle) were measured 1) by masked expert graders on 2 occasions, 1 week apart, to assess intraobserver reliability, and 2) by 2 independent reviewers to assess interobserver reliability. Intraobserver reproducibility was high (intraclass correlation coefficients [ICC], ≥0.93), although the interobserver reproducibility was modest (ICC, 0.49-0.82) for measurements of the angle-opening distance, trabecular iris space area, and scleral spur angle. The percentage error ranged from 9.29% for the scleral spur angle to 21.18% for the trabecular iris space area.

Diagnostic Accuracy
OCT Versus Gonioscopy
Several studies have compared OCT with gonioscopy for the detection of primary angle closure. For example, Nolan et al (2007) assessed the ability of a prototype of the Visante OCT to detect primary angle closure in 203 Asian patients. The patients, recruited from glaucoma clinics, had been diagnosed with primary angle closure, primary open-angle glaucoma, ocular hypertension, and cataracts; some had previously been treated with iridotomy. Images were assessed by 2 glaucoma experts, and the results compared with an independently obtained reference standard (gonioscopy). Data were reported from 342 eyes of 200 individuals. A closed angle was identified in 152 eyes with gonioscopy and 228 eyes with OCT; agreement was obtained between the 2 methods in 143 eyes. Although these results suggest low specificity for OCT, it is noted that gonioscopy is not considered to be a criterion standard. The authors suggest 3 possible reasons for the increase in identification of closed angles with OCT: lighting is known to affect angle closure, and the lighting conditions were different for the 2 methods (gonioscopy requires some light); placement of the gonioscopy lens on the globe may have caused distortion of the AS; and landmarks are not the same with the 2 methods. The authors noted that longitudinal studies will be required to determine whether eyes classified as closed by OCT, but not by gonioscopy, are at risk of developing primary angle closure glaucoma.

Narayanaswamy et al (2010) conducted a community-based cross-sectional study of glaucoma screening. The study population consisted of individuals 50 years or older who underwent AS
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OCT by a single ophthalmologist and gonioscopy by an ophthalmologist who was masked to the OCT findings. Individuals were excluded if they had a history of intraocular surgery, any evidence of aphakia/pseudophakia, or penetrating trauma in the eye; previous AS laser treatment; a history of glaucoma; or corneal disorders such as corneal endothelial dystrophy, corneal opacity, or pterygium, all of which could influence the quality of angle imaging by OCT. The angle opening distance (AOD) was calculated at 250, 500, and 750 μm from the scleral spur. Of 2047 individuals examined, 28% were excluded due to inability to locate the scleral spur (n=515), poor image quality (n=28), or software delineation errors (n=39). Of the remaining 1465 participants, 315 (21.5%) had narrow angles on gonioscopy, defined as having a narrow angle if the posterior pigmented trabecular meshwork was not visible for at least 180 degrees on nonindentation gonioscopy with the eye in the primary position. Of those who had an acceptable image, the area under the receiver operating characteristic curve was highest at 750 μm from the scleral spur in the nasal (0.90) and temporal (0.91) quadrants. A noted limitation of this quantitative technique for screening of angle closure glaucoma was the inability to define the scleral spur in 25% of the study population.

A 2009 publication also examined the sensitivity and specificity of the Visante OCT when using different cutoff values for the AOD measured at 250, 500, and 750 μm from the scleral spur.(5) OCT and gonioscopy records were available for 303 eyes of 155 patients seen at a glaucoma clinic. The patients were asked to look at prepositioned targets to prevent image distortion with low- and high-resolution OCT. The parameters analyzed could not be measured by commercially available software at the time of the study, so the images were converted to a format that could be analyzed by ultrasound (US) biomicroscopy software. Blinded analysis showed sensitivity and specificity between 70% and 80% (in comparison with gonioscopy), depending on the AOD and the cutoff value. Correlation coefficients between the qualitative gonioscopy grade and quantitative OCT measurement ranged from 0.75 (AOD=250) to 0.88 (AOD=750). As noted by these investigators, “a truer measure of occludable angles is whether an eye develops angleclosure glaucoma in the future.” Long-term follow-up of patients examined with these 2 methods would be informative.

A 2007 prospective observational study (N=26) evaluated imaging of the anterior angle chamber with the Stratus OCT, which had been developed for retinal imaging.(6) Ten eyes with normal open angles and 16 eyes with narrow or closed angles or plateau iris configuration, as determined by gonioscopy, were assessed. The OCT image was rated for quality, ability to demonstrate the AC angle, and for ability to visualize the iris configuration; patients were classified as having open angles, narrow angles, closed angles, or plateau iris configuration. Ultrasound biomicroscopy (UBM) was performed for comparison if plateau iris configuration was diagnosed. The investigators reported that the Stratus OCT provided high-resolution images of iris configuration and narrow or closed angles, and imaging of the angle was found to be adequate in cases of acute angle-closure glaucoma, in which the cornea was too cloudy to enable a clear gonioscopic view. Open angles and plateau iris configurations could not be visualized with the 0.8-μm wavelength Stratus OCT.

**OCT Versus UBM**

Garcia and Rosen (2008) evaluated the diagnostic performance of AC Cornea OCT (Ophthalmic Technologies, Toronto, ON, Canada) by comparing image results with UBM in patients with conditions of the AS.(7) The patients were recruited from various specialty clinics, and imaging with OCT and US was performed sequentially after obtaining informed consent. Eighty eyes with...
pathologic conditions involving the anterior ocular segment were included in the study: 6 cases were reported in detail to demonstrate the imaging capabilities of OCT and UBM. Comparison of OCT and UBM images showed that while the AC Cornea OCT has high resolution for the cornea, conjunctiva, iris, and anterior angle, UBM images are also clear for these areas. In addition, UBM was found to be superior at detecting cataracts, anterior tumors, ciliary bodies, haptics, and posterior chamber intraocular lenses. OCT was found to be superior at detecting a glaucoma tube and a metallic foreign body in the cornea when imaging was performed in the coronal plane.

Mansouri et al (2010) published a study that compared the accuracy in measurement of the AC angle by AS OCT and UBM in European patients with suspected primary angle closure (PACS), primary angle closure (PAC), or primary angle-closure glaucoma (PACG).(8) In this study, 55 eyes of 33 consecutive patients presenting with PACS, PAC, or PACG were examined with OCT, followed by UBM. The trabecular-iris angle was measured in all 4 quadrants. The AOD was measured at 500 μm from the scleral spur. In this comparative study, the authors concluded that OCT measurements were significantly correlated with UBM measurements but showed poor agreement with each other. The authors did not believe that AS OCT can replace UBM for the quantitative assessment of the AC angle.

Several retrospective studies have compared OCT with UBM for AS tumors. Bianciotto et al (2011) reported a retrospective analysis of 200 consecutive patients who underwent both AS OCT and UBM for AS tumors.(9) When comparing image resolution for the 2 techniques, UBM was found to have better overall tumor visualization.

OCT Versus Slitlamp Biomicroscopy
Jiang et al (2012) reported a cross-sectional, observational study of the visualization of aqueous tube shunts by high-resolution OCT, slitlamp biomicroscopy, and gonioscopy in 18 consecutive patients (23 eyes).(10) High-resolution OCT demonstrated shunt position and patency in all 23 eyes. Compared with slitlamp, 4 eyes had new findings identified by OCT. For all 16 eyes in which tube entrance could be clearly visualized by OCT, growth of fibrous scar tissue could be seen between the tube and the corneal endothelium. This was not identified in the patient records (retrospectively analyzed) of the slitlamp examination.

Effect on Health Outcomes
The literature indicates that OCT is being evaluated to assess AC angle, measure corneal thickness and opacity, evaluate presurgical and postsurgical AC anatomy, calculate intraocular lens power, guide surgery, assess complications following surgical procedures (e.g., blockage of glaucoma tubes, detachment of Descemet membrane, disrupted keratoprosthesis-cornea interface), image intracorneal ring segments, and evaluate pathologic processes such as dry eye syndrome, tumors, uveitis, and infections. Evidence for the effect of AS OCT on health outcomes follows.

Two-year results from the prospective PIONEER (Prospective Intraoperative and Perioperative Ophthalmic ImagIng With Optical CoherEncE TomogRaphy) study were published by Ehlers et al in 2014.(11) Intraoperative scanning was performed with a microscope-mounted portable OCT system. In the first 24 months, 531 eyes were enrolled, including 275 AS cases. A surgeon feedback form, which was part of the study protocol, indicated that intraoperative OCT (iOCT) informed surgical decision making by visualizing fluid in the graft/host interface in 48% of lamellar keratoplasty cases. This group has also reported preliminary results with a prototype
Optical Coherence Tomography (OCT) system (RESCAN 700) that is integrated with a microscope and has a heads-up display, video display, and foot pedal control of the OCT scanner. AS images in this initial phase included iOCT evaluation of corneal incisions, scleral closure, phacoemulsification groove depth, and intraocular lens position.

Cauduro et al (2012) provided a retrospective review of 26 eyes of 19 pediatric patients (age range, 2 months to 12 years) who presented with a variety of AS pathologies. OCT was used to clarify the clinical diagnosis. No sedation was needed for this noncontact procedure, and only 1 eye of a 2-month-old patient required topical anesthesia. The impact of the procedure on patient care was not reported.

Angle-Closure Glaucoma
There are no studies that provide direct evidence on the clinical utility of OCT for diagnosing narrow angle glaucoma. The clinical utility of OCT for diagnosing glaucoma is closely related to its ability to accurately diagnose glaucoma, because treatment is generally initiated on confirmation of the diagnosis. Therefore, if OCT is more accurate in diagnosing glaucoma than alternatives, it can be considered to have clinical utility above that of the alternative tests. While the available evidence does suggest that OCT is more sensitive than US or gonioscopy, specificity and predictive value cannot be determined.

Cataract Surgery
As of 2013, studies that compare the risk-benefit of OCT-laser assisted cataract surgery versus traditional phacoemulsification are ongoing. AS OCT is also being studied for preoperative evaluation of intraocular lens power, and postoperative assessment of intraocular stability of phakic lens and optic changes related to intraocular lens or ocular media opacities.

Endothelial Keratoplasty
Use of OCT is being reported for intraoperative and postoperative evaluation of graft apposition and detachment in endothelial keratoplasty procedures. In 2011, Moutsouris et al reported a prospective comparison of AS OCT, Scheimpflug imaging, and slit-lamp biomicroscopy in 120 eyes of 110 patients after Descemet membrane endothelial keratoplasty (DMEK). All slit-lamp biomicroscopy and OCT examinations were performed by the same experienced technician, and all images were evaluated by 2 masked ophthalmologists. From a total of 120 DMEK eyes, 78 showed normal corneal clearance by all 3 imaging techniques. The remaining 42 eyes showed persistent stromal edema within the first month, suggesting (partial) graft detachment. Biomicroscopy was able to determine the presence or absence of a graft detachment in 35 eyes. Scheimpflug imaging did not give additional information over biomicroscopy. In 15 eyes, only OCT was able to discriminate between a “flat” graft detachment and delayed corneal clearance. Thus, of the 42 eyes, OCT had an added diagnostic value in 36% of cases. This led to further treatment in some of the additional cases. Specifically, a secondary Descemet stripping automated endothelial keratoplasty (DSAEK) was performed for total graft detachment, while partial graft detachments were rebubbled or observed for corneal clearing. There were no false negatives (graft detachment unrecognized) or false positives (an attached graft recognized as a graft detachment).

Steven et al (2013) published a retrospective analysis of the use of intraoperative microscope mounted OCT to improve DMEK. Intraoperative OCT improved visualization of all steps of the procedure (graft preparation, localization of the endothelial side of the graft, graft unfolding,
apposition of the graft to the stroma and detection of interface fluid) and reduced AC air-filling time from 60 to 90 minutes to 4 minutes. OCT has also been reported to predict primary failure in DSAEK.(17)

Additional studies are needed to further evaluate these results and to demonstrate the clinical utility of using OCT in these situations.

**Neoplastic Disease**

The criterion standard for the diagnosis of ocular surface tumors such as squamous neoplasia (OSSN) is histologic examination of tissue specimens from excisional biopsy.(18) In a 2014 review, Thomas et al noted that noninvasive methods of diagnosing OSSN will be increasingly important as treatment moves toward medical therapy, although future studies will be needed to evaluate technical performance and diagnostic accuracy for this indication.(19)

**Uveitis of the AS**

In a study from India, Agarwal et al (2009) evaluated the AC inflammatory reaction by AS high-speed OCT.(20) This was a prospective, nonrandomized, observational case series of 62 eyes of 45 patients. Hyperreflective spots suggesting the presence of cells in the AC from the OCT images were counted manually and by a custom-made automated software package and correlated with clinical grading using Standardization of Uveitis Nomenclature criteria. Of 62 eyes, grade 4 aqueous flare was detected by OCT imaging in 7 eyes and clinically in 5 eyes. The authors concluded that AS OCT can be used as an imaging modality to detect inflammatory reaction in uveitis and also in eyes with decreased corneal clarity. Additional studies are needed to further evaluate these results and to demonstrate the clinical utility of using OCT in this situation.

**Ongoing and Unpublished Clinical Trials**

DISCOVER (Determination of feasibility of Intraoperative Spectral domain microscope Combine/integrated OCT Visualization during En face Retinal and ophthalmic surgery) is an ongoing study to assess the utility of iOCT.(12) Intraoperative imaging in the initial phase of the study was performed with RESCAN 700, a prototype iOCT system that is integrated with a microscope and has a heads-up display, video display, and foot pedal control of the OCT scanner.

**Clinical Input Received through Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 3 academic medical centers while this policy was under review in 2011. There was general, but not unanimous, agreement that this technique is investigational. Some reviewers commented that this technique may have application in specific conditions such as globe perforation, anterior segment (iris) tumors, and in the postoperative care of endothelial keratoplasty cases.
Summary
Ideally, a diagnostic test would be evaluated based on its technical performance, diagnostic accuracy (sensitivity, specificity, predictive value), and effect on health outcomes. Current literature consists primarily of assessments of qualitative and quantitative imaging and detection capabilities. Technically, the anterior segment OCT has the ability to create high-resolution images of the anterior eye segment. In addition, studies indicate that the anterior segment OCT detects more eyes with narrow or closed angles than gonioscopy, suggesting that the sensitivity of OCT is higher than gonioscopy. However, because of the lack of a true gold standard, it is not clear to what degree these additional cases are true positives versus false-positives, and therefore the specificity and predictive values cannot be determined. Evaluation of the diagnostic performance depends, therefore, on evidence that the additional eyes identified with narrow angle by OCT are more likely to progress to primary angle closure glaucoma. OCT imaging may be less sensitive in comparison with ultrasound biomicroscopy for other pathologic conditions of the anterior segment, such as cataracts, anterior tumors, ciliary bodies, haptics, and posterior chamber intraocular lenses.

Evaluation of the clinical utility of anterior segment OCT depends on demonstration of an improvement in clinical outcomes. For example, outcomes will be improved if OCT detects additional cases of primary angle closure glaucoma, which represent true cases of glaucoma and not false positives, and if these cases are successfully treated for glaucoma. It is not currently possible to determine the frequency of false-positive results with OCT, therefore it cannot be determined whether health outcomes are improved. For other potential indications (e.g., to aid in diagnosis of AS pathology or guide surgical procedures), evidence is currently limited.

Because the impact on health outcomes of anterior segment OCT for angle closure glaucoma, as well as for other disorders of the anterior chamber, is not known, this procedure is considered investigational.

CODING
The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS
92132 Scanning computerized ophthalmic diagnostic imaging, anterior segment, with interpretation and report, unilateral or bilateral

DIAGNOSIS
Experimental / investigational for all diagnosis.

REVISIONS
03-28-2011 Policy added to the bcbsks.com web site.
07-13-2012 Medical Policy Title has been updated from "Anterior Eye Segment Optical Imaging" to "Optical Coherence Tomography (OCT) of the Anterior Eye Segment"
REFERENCES


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**Other References**

2. Blue Cross and Blue Shield of Kansas Optometry Liaison Committee, June 2011; May 2012; May 2013; May 2014.