Published in final edited form as:

Expert Rev Ophthalmol. 2006 October 1; 1(1): 63–76. doi:10.1586/17469899.1.1.63.

Explaining The Current Role Of High Frequency Ultrasound In Ophthalmic Diagnosis (Ophthalmic Ultrasound)

D. Jackson Coleman, MD, Ronald H. Silverman, PhD, Mark J. Rondeau, Harriet O. Lloyd, MS, and Suzanne Daly, BSN

Margaret M. Dyson Vision Research Institute, Department of Ophthalmology, Weill Medical College of Cornell University, New York, NY

Summary

Ultrasound has become as indispensable as indirect ophthalmoscopy or slit lamp in evaluation of the eye. It is an important adjuvant for the clinical assessment of a variety of ocular and orbital diseases. Advances in instrumentation, higher frequencies and more sensitivity and resolution have resulted in continuous improvement in image quality.

Very high frequency ultrasound uses frequencies in the range of 35 to 100 MHz to show greater detail of the anterior segment. Penetration is limited for these higher frequencies to only a few millimeters and thus only the anterior vitreous behind the ciliary body and lens can be imaged. High frequency ultrasound in the range of 20 to 30 MHz has a penetration of about 10 mm and can be used for posterior pole evaluation of the retina and choroid.

Keywords

Ocular Ultrasound; Ophthalmic Ultrasound; High Frequency Ultrasound; UBM; Artemis; Anterior Segment Imaging; Refractive Surgery

INTRODUCTION

Imaging in ophthalmology is needed to complement visual and optical techniques for evaluating the normal, traumatized or diseased eye¹. Of the optical techniques, indirect ophthalmoscopy and slit lamp are the classical means of evaluation of the anterior segment and of the retina. Occult areas behind the iris and behind the retina can be evaluated only with ultrasound. Even newer imaging modalities such as optical coherence tomography (OCT) cannot image these areas². High frequency ultrasound offers an indispensable tool for diagnosis, and in recent years, has found a critical role in precise measurement of anterior segment for refractive surgery and determination of intraocular lens design and size in phakic eyes. Thus, there are two primary areas of development for both existing and new clinical applications that must be considered in discussions of ophthalmic ultrasound:

- Diagnosis
- Refractive surgery

Corresponding Author: D. Jackson Coleman, MD, Professor and Chairman, Department of Ophthalmology, Weill Medical College of Cornell University, 1300 York Avenue, Box 112, New York, NY 10021, Tel: 212-746-6106, Fax: 212-746-8850.

Proprietary Interests: Drs. Coleman and Silverman have a financial interest in Ultralink, LLC.

DIAGNOSIS

Instrumentation

At present, conventional ultrasound uses probes with frequencies of 7–15 MHz for routine B- and A-scan diagnosis (Figure 1). Instrumentation uses a quantifiable A-scan (Figure 2) in order to differentiate tissue types. The dimensions of the eye dictate that the imaging of the posterior globe wall and the orbit require frequencies of 10–15 MHz (Figure 3), although the upper theoretical limit when sound does not pass through the lens can be in the 20–30 MHz range³. Very high frequency transducers have been developed for higher resolution imaging of the anterior segment. These very high-resolution probes range from 35 MHz to 100 MHz, with penetration depths of about 10 mm to 3 mm. The Ultrasound BioMicroscope (UBM) was the first commercially available high frequency scanner to demonstrate the potential of frequencies of 50 MHz for examining the anterior segment of the eye⁴, although there are now several such systems available. Commercially available high frequency ultrasound instruments specifically for use in ophthalmology include:

- Artemis2, Ultralink LLC, St Petersburg, FL
- HF35-50 High Frequency Ultrasound system, Ophthalmic Technologies Inc., Toronto, Canada
- VUMAX™ UBM 35/50 Ultrasonic Bio-Microscope system, Escalon-Sonomed Inc., Lake Success, NY
- P60 UBM, Paradigm Medical Industries, Salt Lake City, UT
- CineScan A/B, Quantel Medical, Bozeman, MT
- HiScan, Optikon, Rome, Italy

The Artemis is an arc scanner, which can show the entire anterior segment in one pass and has maximum resolution, as it also utilizes radiofrequency (rf) and digital processing techniques. The other ultrasound scanners are analog sector scanners.

The anterior segment can be shown most easily with some form of immersion ultrasound, since the proximity of these structures to the transducer in contact techniques makes them difficult to display. An immersion standoff can be comprised of either saline or methylcellulose gel, with isotonic saline preferred in order to prevent swelling of the cornea. The Artemis 2 uses a novel reverse-immersion technique. The patient sits, and positions his or her chin on a three-point forehead and chin rest, while placing the eye into a soft rimmed eye-cup resembling a swimming goggle. The sterile saline fills the compartment in front of the eye and the scanning is performed via an ultrasonically transparent (sterile) membrane, without the need for a speculum. Thus, there is no contact by the scanner probe with the eye. Other very high frequency scanners use eye cups which are filled with methylcellulose gel as an immersion standoff; this method produces some pressure on the eye, which may distort the angle. It is also possible to use a sterile sheath filled with water or saline as a standoff. This is the preferred method when dealing with trauma or possible infection, which otherwise might preclude examination by ultrasound.

Anterior Segment

Very high frequencies of 35 MHz and higher provide superb imaging of the cornea and anterior segment. Resolution on the order of 30 microns or less can be achieved and reproducibility with digital signal processing can approach 5 microns for corneal thickness. The short wavelength of very high frequency systems allow resolution of Bowman's membrane, and hence provide a means for layered corneal biometry, as well as the capability of visualizing the interface between the flap and residual stroma following laser in situ keratomileusis (LASIK). For

corneal measurements, analysis of digitized ultrasound data involves detection of peaks associated with the anterior and posterior surfaces, Bowman's and the flap, where present. By applying digital signal processing techniques, the exact positions of each interface can be determined⁵. Such corneal measurements are useful in diagnosing keratoconus, where the cornea is thinned over the steepest part of the stroma; this thinning pattern can be an early sign of this condition. VHF ultrasound can also be used to characterize corneal haze or scarring. Loss of corneal transparency is a consequence of disruption of the regular arrangement of collagen fibers of the stroma, which causes scattering of light. This change in stromal microanatomy can also cause increased backscatter of ultrasound, and can be analyzed using power spectrum analysis⁶. This provides quantitative information that can be used to track changes associated with treatment or progression and qualitatively allows visualization of information including scar depth.

VHF ultrasound provides superbly detailed images of anterior segment structures, even in the presence of optical opacities such as hyphema or corneal scarring, and allows imaging of structures such as the ciliary body that are otherwise hidden by the sclera or iris. The iris, which has good reflectivity from the melanin in the pigment epithelium, can be imaged well. The anterior surface of the iris is usually discernible, but the echoes from the posterior iris surface usually merge with those from the anterior lens surface, and the posterior curvature of the lens can be imaged, but the equator is not seen because of its oblique orientation to the ultrasound beam.

Glaucoma

The iris is of interest largely for congenital anomalies, for physiologic studies, in trauma, for evaluation of tumors and in differentiation of glaucoma⁷. The most common form is open-angle glaucoma. In angle closure glaucoma, there will be a shallow anterior chamber and narrow angles. Pupillary block is the most common cause of angle closure following cataract surgery and intraocular lens (IOL) implantation. The pupil can become occluded by any surface that lies behind or in front of the iris⁸. Plateau iris is caused by an anatomically anterior position of the ciliary processes which supports the peripheral iris and prevents it from moving backward to open the angle following iridotomy. This syndrome occurs in eyes with shallow anterior chambers, similar to those in which pupillary block occurs⁹. Pigment dispersion syndrome occurs as a result of the proximity between the posterior iris pigment epithelium and the zonular fibers. VHF ultrasound can demonstrate anatomic differences in the angles of some patients with pigmentary glaucoma, indicating a posterior bowing of the peripheral iris which produces zonular touch.

Blood Flow

A variety of techniques has been used to study ocular blood flow¹⁰ including scanning laser ophthalmoscopy (SLO)¹¹, laser-Doppler flowmetry^{12,13} (LDF), ultrasound-Doppler¹⁴ and swept-scan¹⁵. SLO measures the filling of the retinal vasculature by use of dyes such as fluorescein or indocyanine green, but is limited to study of the visible fundus and does not allow study of pulsatility. LDF uses a beam of coherent light, which is directed into a perfused tissue and mean flow velocity and flow volume estimated from the spectrum of the backscattered light, but is limited in its ability to penetrate optically opaque tissues (under 1 mm). Ultrasound Doppler involves measurement of the frequency shift resulting from acoustic scattering by moving blood particles. Pulsed Doppler provides images in which flow is presented in a color scale superimposed on a gray-scale B-mode image of stationary tissue structures, while continuous wave (CW) Doppler can be used to measure pulsatile flow characteristics, providing high sensitivity, but low spatial resolution. Power Doppler produces a color-flow image with improved sensitivity and spatial resolution but involves discarding of flow speed and direction information. The principal limitation of ultrasound Doppler has been

its comparatively low spatial resolution, which is a consequence of the low frequencies used in diagnostic instruments, typically 7.5 MHz. Swept-scan, a very high frequency ultrasonic visualization and measurement of blood flow, involves time-domain measurement of change in scatterer range as a function of time¹³. This technique provides maximum spatial resolution in imaging and measuring slow-flow, although sensitivity is somewhat lower than pulsed or CW Doppler.

Trauma

Most ocular trauma results in bleeding within the eye (that precludes visual examination) and a certain degree of inflammation that requires lower frequencies for complete evaluation of the globe. Ultrasound is used to relate the position of a foreign body to the retina and lens and identify coexisting structural changes, for example, retinal detachment. In patients with recent ocular trauma, every attempt should be made to maintain sterile technique. A sterile latex sheath can be placed over the end of a transducer (which provides a cushion so that no significant pressure is placed on the eye) or an antibiotic solution can be instilled in the sterile water bath if immersion is used. With a severely traumatized globe, clinical judgment would determine whether immersion B-scan or contact A- or B-scan is indicated. Diagnosis must include the globe outline, hemorrhagic changes in both the vitreous (Figure 4) and choroid, presence of subretinal fluid or retinal detachment (Figure 5) and possible detection of foreign bodies (Figure 6). Very high frequency ultrasound examination is indispensable for evaluation prior to primary repair and for assessment prior to secondary repair^{16–20}. The evaluation for an intraocular foreign body can be accomplished with ultrasound alone, but the examination time can be shortened if a CT or X-ray has been obtained to indicate the presence of one or more foreign bodies. MR imaging should be avoided if there is a possibility of magnetic foreign bodies.

Tumors

Tumors are generally located in the iris, ciliary body, choroid or retina. Tumors of the anterior segment can be measured most accurately with frequencies as high as 50 MHz (Figure 7)^{21–29}. VHF ultrasound is useful in detecting iris and ciliary body tumors, as well as determining the possible extension of an iris tumor into the ciliary region. Cysts are seen ultrasonically as rounded, clear areas and may be differentiated from tumors, which appear solid. Tumors of the posterior uvea, such as malignant melanoma (Figure 8), metastatic carcinoma, hemangioma (Figure 9), lymphoma or retinoblastoma require lower frequency examination in order to adequately image and measure the tissue. Tissue characterization (Figures 10· 11· 12) is possible using power spectrum analysis, which has been demonstrated to improve diagnostic differentiation, not only of melanoma from simulating lesions, but also allows subclassification of melanomas to two distinct classes based on the presence of extravascular matrix patterns, that appear to correlate to degree of lethality^{30–32}. Widespread use of tissue characterization has been limited by availability of suitably advanced diagnostic instruments that are capable of rf data acquisition, which is necessary for tissue characterization using the power spectrum technique. Future trends for tissue characterization are use of higher frequencies and broader spectral sensitivities. Currently, some clinicians use “standardized echography”, a diagnostic technique which emphasizes the quantification of echo amplitudes using a tissue standard and “s” shaped amplification of the A-scan, to characterize tissue³³.

REFRACTIVE SURGERY

The use of laser in situ keratomileusis (LASIK) to correct vision by reshaping the cornea has popularized refractive surgery (Figure 13). As the technology has improved, the need for improved imaging has also increased. Very high frequency ultrasound has resolution on the order of a few microns, allowing individual corneal layers to be distinguished, and internal

corneal lamellar interfaces (such as the LASIK flap) to be detected, even years after surgery, despite optical transparency^{34–42}. B-scan, particularly with rf and digitally deconvoluted A-scan enhancement permits accurate measurements within 2–3 microns, thus allowing not only selection of surgical modality and plane, but also for evaluation of complications of such surgery, where the depth of flap, healing problems and analysis of unexpected results can be obtained (Figure 14). With a series of ultrasound scans taken in different meridians, corneal pachymetric maps can be constructed as a means for rapidly conveying layer thickness information. During post-processing of the ultrasound data, the range to each interface of the cornea is determined along each vector. This is accomplished by enhancement of resolution (deconvolution), generation of the optimal signal envelope (analytic signal magnitude detection) and automated or semiautomated detection of the echo peaks. By determining corneal interface position at each vector of each scan along each meridian, a 3D representation of the topography of each layer is produced. The thickness of each layer at any point can be found by generating an interpolated surface for each layer from the measurement points, and finding the shortest distance between the point of interest and the layer of interest. Accurate layered pachymetry of the postoperative cornea may enable safer surgical planning, particularly in the correction of higher refractive errors.

VHF ultrasound is useful in providing accurate determination of the anterior chamber depth, angle to angle and sulcus to sulcus measurements, which enhances selection of dioptric correction with an intraocular lens. The diameter of the cornea-iris angle and of the ciliary body sulcus is not uniform⁵². Meridional scans allow the axis of maximum diameter to be measured (Figure 15). The angle to angle and sulcus to sulcus measurements can be critical for sizing of IOL placement. These measurements may be very useful for placement of surgical incisions for presbyopia surgery (Figure 16), or for lens haptic size and placement (Figure 17). The position of the haptics can be a major source of persistent complications, whether eroding into the ciliary body, producing pain or hemorrhage, or folded back on the iris (Figure 18). Certainly “sizing” is the critical element in developing better lens designs, and VHF ultrasound is the preferred method for its accuracy in measuring all anterior ocular anatomies⁵³. Anterior segment OCT is able to provide excellent measurement where media are clear, but the iris angle, retroiridal areas and post-surgical tissue planes are better imaged with very high frequency ultrasound.

Intraocular lenses have also undergone significant advances in materials and design, e.g. accommodating lenses, multifocal lenses and intraocular lenses for phakic eyes as a means of correcting refractive errors^{43–53}.

Scan modalities of linear scan, sector scan and the arc scan provide the necessary detail to allow these improved lens design and lens materials to be suitably matched with the anatomic dimensions of the recipient. The most accurate system is the Artemis arc scan method, which also utilizes the radiofrequency and deconvolution digital imaging software developed at Weill Cornell Medical College by Ronald Silverman and Mark Rondeau.

Physiologic Evaluation of Macular Degeneration and Drug Delivery Systems

The present era of retinal diagnosis was significantly advanced by optical coherence tomography (OCT), which provides exquisite definition of the retina^{54–56}. This has allowed evaluation of age-related macular degeneration (AMD), adding to the information from indocyanine green (ICG) and fluorescein angiography, and certainly more important in evaluation of cystoid macular edema, pigment epithelial detachments and macular holes. That has improved not only their diagnosis, but directed appropriate surgical techniques and evaluated the effectiveness of these techniques. While ultrasound cannot approach the imaging definition of OCT for the retina, it can enhance imaging of the choroid, the optic nerve sheaths and tenon's capsule (Figure 19). The evaluation of the choroid is possible by using new

technologies of wavelet analysis⁵⁸ (Figure 20), flow measurement in the choroid by swept scan analysis¹⁵ (Figure 21) and harmonic imaging⁵⁹ (Figure 22). The analytical mathematical modeling technique for imaging the choroid using wavelet analysis increases the definition of the choroidal thickness and appreciation of vascular channels, as outlined by the the scattering elements that surround them. Swept scan imaging allows vascular patterns and flow characteristics to be both demonstrated and measured. The advantage of swept-mode in comparison to Doppler is that flow information is obtained at the same high resolution as the underlying B-mode data. Harmonic ultrasound imaging represents a potential means for improving resolution and image quality due to reduced noise. Improved imaging of the macular region, in particular, may provide significant improvements in diagnosis of retinal disease.

The increasingly important detection of inflammation is, at present, almost exclusively the purview of high frequency ultrasound. These inflammatory changes in the choroid are hallmarks of early onset and often occult manifestations of diseases such as diabetes, graves disease, optic neuritis and AMD. Evaluation of pharmacologic agents that can modify blood flow in the choroid and perhaps benefit pigment epithelial damage in macular degeneration are being studied using the wavelet and swept scan technologies.

Future Developments

The evolution of ultrasound will move in several areas. Scanning instrumentation will become cheaper and more widely available. Transducer technology will evolve to allow greater depth of field and spatial orientation, perhaps obviating mechanical scanning entirely. Higher frequencies will improve definition of the anterior segment of the eye, but limitations on frequency expansion posed by tissue absorption will prevent dramatic improvement in resolution at the posterior pole. Software for tissue classification and enhancement will improve evaluation of tumors and the anatomic changes in the choroid related to both aging and pharmacologic delivery methodologies. A concern in the development of new technologies will always be the limitations on funding for improved health care delivery and imaging systems. The positive side is the ever evolving improvement in transducer technology and digital enhancement and modulation of the reflected sound.

Expert Commentary

New and exciting refractive surgery techniques are dependent on accurate anatomic measurement. Corneal thickness accuracy relates to LASIK surgery as well as improving the accuracy of pressure measurements necessary for optimal control of glaucoma with drugs and/or surgery.

Accurate anterior segment measurements are required for lens support and placement (surgery) as well as for determination of lens power. (The old “white-to-white” estimate is clearly outmoded.)

Very high frequency ultrasound demonstrates the anatomic landmarks that correlate with the Coleman Catenary theory of accommodation that optimizes surgical placement of scleral relaxation implants or clefts for presbyopic surgery. Measurement of the posterior pole of the eye with VHF ultrasound will allow quantitative measurements to be used for testing of new drugs such as anti-VEGF and choroidal vasodilating drugs to treat age related macular degeneration.

Key Issues

- The posterior segment of the eye can be imaged using high frequency transducers in the 10–30 MHz range, with penetration depths of about 10 mm.

- Very high frequency transducers, ranging from 35–100 MHz with penetration depths of about 10 mm to 3 mm, are used for imaging the anterior segment.
- Very high frequency ultrasound provides excellent definition of the cornea and anterior segment, including iris and ciliary body tumor detection, and can provide precise measurement of ocular dimensions. Corneal thickness changes are utilized for standardization of intraocular pressure measurements.
- Very high frequency has significant impact concerning refractive surgery planning and analysis; it can be used to produce accurate 3D corneal thickness measurements for surgical planning; it can be used to diagnose complications in corneal refractive surgery; it can provide customization of refractive surgical intra-ocular phakic lens implants via accurate determination of internal ocular dimension (anterior chamber angle and sulcus-to-sulcus dimensions); and can provide a more accurate measurement for power selection of the intra-ocular lens replacement in cataract surgery.
- Ultrasound can be used to non-invasively classify tumors into high- and low-risk groups by detecting the presence of extracellular matrix patterns. This classification is useful as a tool for stratification of patient populations for tumor treatment evaluation.
- Age-related macular degeneration is the leading cause of blindness in the industrialized world. Choroidal changes that relate to progressive AMD can be studied using wavelet analysis of the back of the eye.

Five Year View

Despite almost a half century of development, the field of diagnostic ultrasound continues to develop new technologies that will offer new capabilities for imaging of the eye. Following are several areas of research and development that are likely to become available within the next five years.

Annular and Linear Arrays—Prototype annular arrays have been demonstrated at frequencies from 20 to 40 MHz. This type of array is relatively simple in design and offers a major improvement in the depth-of-field, which is otherwise quite limited for focused transducer. Linear arrays are also under development. Although more challenging to fabricate and control, such arrays offer the advantage of very high frame rates as a result of electronic beam steering instead of mechanical scanning.

Tissue Harmonic Imaging—Nonlinear propagation of ultrasound results in generation of harmonics of the emitted center frequency. Diagnostic ultrasound systems utilized in other clinical specialties where frequency is significantly lower than that used in ophthalmology have incorporated tissue harmonic imaging for several years. This modality, which makes use of the nonlinear effect, offers improved resolution and delineation of tissue boundaries.

High Resolution Color Flow Imaging—Color flow Doppler has long been available in non-ophthalmic specialties. Very high frequency ultrasound offers the capability of visualizing and measuring flow in the microvasculature of the choroid and ciliary body. The application of advanced signal processing methods, such as swept-mode, will bring this capability to widespread clinical practice, offering new diagnostic tools to be applied to study of perfusion physiology and disease. In addition, research is currently underway on ultrasound contrast agents suitable for frequencies of 20–40 MHz. Such agents will prove invaluable for enhancing the sensitivity of color flow methods to slow-flow within the uveal microvasculature.

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Figure 1.
A-scan and B-scan of an eye at 10 MHz with a sector scanner representative of a usual B-scan of an eye. The front of the eye is too close to the transducer to be imaged without a fluid standoff.

Figure 2.

An A-scan can be taken from the B-scan or with a separate transducer. Best results with the A-scan require either “quantification” from a glass plate and a logarithmic amplifier, or with a tissue standard (“standardization”) in order to help identify tissue type, i.e. tumor type or hemorrhage. Routine use of the A-scan also is for axial length measurements to determine appropriate lens power for intraocular lens implants.

Figure 3. Posterior globe wall and orbit on B-scan show better definition with higher frequencies, but the usual 10MHz is best because of lens attenuation or other absorption due to pathology. a) 10 MHz B-scan of a normal eye using a sector scanner. b) 10 MHz B-scan of an eye using an arc scanner.

Figure 4. Vitreous hemorrhage in an eye precludes visual examination in order to determine other pathology such as underlying tumor or if a retinal detachment is present.

Figure 5.

Retinal detachment shows a strongly reflective echo producing surface that can resemble blood along a detached vitreous (PVD) or indicating a choroidal detachment. Landmarks, such as the retina, always remaining attached at the optic nerve and the choroid showing a smooth convex surface due to pressure in the supra choroidal space exceeding that of the vitreous help to distinguish the pathology.

Figure 6.

Intraocular foreign bodies are typically higher reflection due to their density and surface orientation. Ringing artifacts are a hallmark of glass, metal and even air bubbles or gas. In this scan, the foreign body (arrow) appears in the anterior lens with ringing artifacts, serving as a pointer to the foreign body.

Figure 7. High frequency (50 MHz) shows an anterior segment demonstrating a solid tumor of the ciliary body. Transillumination can be helpful, but this is an optically occult area of the eye.

Figure 8.

a) B-scan of a melanoma, a solid tumor of the posterior pole. The A-scan is typical, demonstrating a rapidly decreasing amplitude due to tissue homogeneity. b) 20 MHz B-scan of a different melanoma, demonstrating improved resolution of the anatomic relationship of the tumor to the scleral wall.

Figure 9.

a) Hemangiomas of the eye are filled with vascular channels and fluid spaces that give a uniformly high amplitude A-scan through the tumor. b) 20 MHz B-scan of a different hemangioma, demonstrating improved resolution. Metastatic carcinomas can also show uniformly high amplitude, but if only moderate amplitude compared to the vitreoretinal surface.

Figure 10.

A representative low power histological section with color overlay (a,c). Areas in green denote tumor regions with the presence of arc and arc with branching features. Areas in red denote the presence of closed loop and network features. Companion spectral parameter images of acoustic concentration (b,d) given in db per mm³.

Figure 11.

The ROC (Receiver Operating Characteristic) curve analysis for the linear discriminant analysis and support vector machine in terms of retrospective performance. The area under the curve, a measure of the performance of a classifier, was .866 for the linear discriminant analysis and .983 for the support vector machine.

Figure 12.

B-scans at 20 MHz of small suspicious melanoma measuring less than 2 mm in thickness. Figure (a) shows a solid lesion with no evidence of subretinal or intraocular fluid, as seen in figure (b). These fluid spaces indicate a propensity for increased lethality.

Figure 13.

Ultrasound arc scan of post-LASIK cornea. In this case, the image is displayed without geometric correction, allowing better appreciation on internal anatomy. Note keratome interface (L), Bowman's membrane (B), which in this case shows several discontinuities consistent with breaks formed during surgery. Also shown in one line of radiofrequency echo data (RF) and its envelope, as determined from the deconvolved analytic signal of the RF data, which is accurate to 3 microns.

Figure 14.

A complicated LASIK flap demonstrating breaks in Bowman's membrane. Also shown are corneal thickness maps of reconstructed layers through multiple meridional planes.

Figure 15.

An overall single B-scan of the anterior segment with the Artemis2 arc scanner permits angle to angle (a) and sulcus to sulcus (s) measurements in order to select the appropriate lens size. Lens sizing is a critical element for new lens designs.

Figure 16.

The walls of the sclera adjacent to the equator of the lens are measurable in order to optimally place laser relaxing cuts or scleral implants in order to treat presbyopia surgically.

Figure 17.
An IOL in proper position in the capsular bag.

Figure 18.
An IOL with misalignment due to rupture of the supporting capsular bag and zonule.

Figure 19.

An optic nerve outline showing separation of the nerve (N) and sheath (S) by inflammation in optic neuritis. This may be the only objective sign in these cases.

Figure 20. Swept scan of region of the retina and choroid to demonstrate choroidal blood flow. This technique can be used to quantify flow with different pharmacologic agents, such as sildenafil or niacin.

Figure 21.

Wavelet imaging of the choroid in a human eye to demonstrate both thickness and microarchitecture. Comparison studies of normal and pathologic states, such as myopia or age-related macular degeneration can be used to document variations in the in vivo eye.

Figure 22.
20 MHz fundamental (left) and harmonic (right) image of the posterior segment of a normal human eye in the region of the optic nerve.