The Role of Diagnostic Testing in Corneal Disease
# The Role of Diagnostic Testing in Corneal Disease

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OVERVIEW

The cornea is a transparent organ with no blood vessels. It covers the iris, pupil, and anterior chamber of the eye. With a refractive power of about +45.00 diopters, the cornea's primary function is the refraction of light rays. Corneal focusing accounts for approximately 70% of the eye's optical power, while the remainder is provided by the lens. When distortions, irregularities, and diseases of the cornea exist, patients may experience major problems with their vision. Therefore it is important to understand the various abnormalities and diseases of the eye as well as the tools physicians use in diagnosing and treating corneal disease.

The cornea is comprised of five layers. The outermost layer, the epithelium, is five cell-layers thick. Because these cells slough and regenerate, the epithelium heals very quickly if injured and does not scar. From the outermost layer inward, the second layer is Bowman's layer. This thin layer consists of acellular collagen. The stroma is the center layer and comprises 90% of the cornea. The highly organized layers of collagen fibers and the level of relative dehydration of the stroma account for most of the transparency of the cornea. After injury, the repaired collagen is usually disorganized and therefore creates a hazy scar. The fourth layer is the Descemet's membrane, which is the basement membrane of the innermost fifth layer of endothelial cells. Together, these two layers regulate the flow of water in and out of the cornea; they are thin and generally viewed together during slit lamp examination unless there is pathology present that affects the Descemet’s membrane.

This course discusses many of the basic concepts and technologies used in corneal diagnostic testing. Descriptions of common corneal abnormalities are explored, as are the indications, purposes, and limitations of the testing process. Information is also provided on the role of the topographic image in detecting regular and irregular astigmatism and other corneal abnormalities.

The following sections of the course describe the diagnostic tools available in assisting the physician in the accurate diagnosis and treatment of corneal diseases.

ANTERIOR SLIT LAMP BIOMICROSCOPY

The first step in the evaluation of a cornea is performed with the slit lamp biomicroscope. The slit lamp is a fundamental instrument found in every eye care practice and is invaluable in diagnosing abnormalities of the cornea. This instrument is used to magnify and illuminate all of the anterior structures of the eye, which are those from the anterior portion of the vitreous forward. With additional lenses, the slit lamp can be focused to view the retina and optic nerve. The biomicroscope is unique because its light source can be directed in a myriad of ways and each is used for a specific purpose. These include:

- Diffuse Illumination: Diffuse illumination provides the observer with a comprehensive overview of the lids, puncta, conjunctiva, sclera, and cornea. Diffuse illumination typically is accomplished by the expansion of the light beam to 3mm and subsequent direction of the beam at the eye from an oblique (45°) angle. This form of illumination is useful in assessing the eye for gross abnormalities. Using the lesser amount of magnification on the slit lamp will provide the clinician with the broadest field. The slit lamp has several filters used to reduce the intensity of the light and to create a colored beam. When used to assess corneal integrity, the most important of these colors is the cobalt-blue filter. The deep blue color excites the fluorescein dye to fluoresce a yellow color. This is the same filter that is used during applanation tonometry, but diffuse illumination is also used with fluorescein dye to detect corneal epithelial defects, to examine the corneal tear film, and to assess the fitting characteristics of rigid contact lenses. If the corneal epithelium is compromised, the dye will pool in that area. The green filter is a red-free light causing hemorrhages or blood vessels to appear black. With its increased contrast, it is used to detect a Fleischer ring or the lymphocytes (white blood cells) that are indicative of an infection. A healthy cornea will appear smooth, lustrous, and transparent. Abnormalities seen on diffuse illumination include corneal scars, punctate keratopathy, and corneal erosions.
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- **Slit Illumination:** With the instrument on slit illumination, the observer uses a beam approximately 1mm or less in width. This beam of light creates a three-dimensional optical section of the cornea and the anterior segment. As the light beam passes through the cornea, the examiner can also visualize the anterior chamber, the crystalline lens, and the anterior portion of the vitreous. When the height of the narrow beam is reduced, the examiner can also identify the presence and amount of cell and flare in the anterior chamber. Discrete lesions and irregularities are made evident with slit illumination. The enhanced perception of depth due to a thin slit beam helps with evaluating clinically important issues such as the depth of a corneal opacity or the depth of the anterior segment. The location of lens opacities in a cataractous eye can also be identified. Abnormalities seen on slit illumination include corneal abrasions, microcystic edema, corneal infiltrates, and corneal foreign bodies. When abnormalities of the cornea are not visible with direct illumination, the scleral scatter technique is often employed. When using this method, the clinician focuses a narrow beam on the limbus temporally. The reflection details transparent changes not otherwise visualized.

- **Retroillumination:** A technique used less frequently in examination of the cornea is retroillumination from the fundus. In this method, the beam of light is directed through the pupil to the fundus, creating a shadow of the ocular abnormality. Because the light enters the pupil directly, constriction would normally occur. For this reason, this technique is limited to patients whose pupils have been dilated. When using this type of illumination, the light strikes a particular point from behind the object and is reflected back to the observer, much like a photographic silhouette. Light is reflected directly or indirectly from the iris or from the fundus, creating a red reflex. When direct illumination from the iris is the technique employed, a relatively wide beam is aimed toward the iris behind the corneal finding. As the light hits the iris, the pathology is highlighted for the viewer behind the biomicroscope. It is necessary to vary the beam for the best detail of the area in question. Like the direct illumination method described previously, the light is directed to the iris and to the area of the iris that falls directly behind the location of the corneal pathology. The ensuing shadow provides the clinician with additional contrast for viewing corneal opacity. Corneal abnormalities seen on retroillumination include corneal dystrophies and guttae, corneal ulcers, folds in Descemet’s membrane, and keratic precipitates. Use of the red reflex helps visualize some types of cataracts, the posterior capsule after cataract surgery, and the corneal distortion caused by keratoconus.

**SLIT LAMP EVALUATION OF THE CORNEA**

After the anterior structures have been carefully evaluated for gross abnormalities with diffuse illumination on a low light, the clinician begins examining the eye with slit illumination. The 1mm (or less) beam width helps identify any refractive index differences as the light rays pass through the cornea, the anterior chamber, and finally, the lens.

When performing a meticulous corneal evaluation, the tear meniscus is evaluated first, followed by the integrity of the epithelium, the outermost layer of the cornea. The Bowman’s layer and both the anterior and posterior stromal layers are examined for stromal opacities or edema. Examination of Descemet’s membrane is followed by a careful assessment of the endothelial mosaic for any sign of guttae, an indication of Fuch’s corneal dystrophy. (Ophthalmic trivia: These deposits are frequently but incorrectly called “guttata” because the condition, in medical Latin, is “Cornea guttata.” But “guttata” is an adjective, not a noun; therefore the noun “guttae” is correct.)

Slit lamp examination with staining is also used to detect irregularities of the conjunctiva and corneal epithelial lesions. Additionally, biomicroscopy is used to evaluate lacrimal impairment and tear production. The stains used in these examinations are fluorescein, lissamine green, and rose bengal. Each has a unique chemical structure. The specific uses are listed in the following table.
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<table>
<thead>
<tr>
<th>CORNEAL STAINING DYSES</th>
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<tbody>
<tr>
<td><strong>Fluorescein:</strong> This orange dye is used to show defects in the corneal epithelium when it fluoresces a green color when exposed to the cobalt-blue filter light of the biomicroscope. Available in two forms, fluorescein may be instilled as a drop when combined with a topical anesthetic or applied from an individually wrapped strip.</td>
</tr>
<tr>
<td><strong>Rose Bengal:</strong> This red dye is available only in strip form. This stain will adhere to damaged or non-viable corneal and conjunctival cells.</td>
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<tr>
<td><strong>Lissamine Green:</strong> This green stain works similarly to rose bengal and is less irritating.</td>
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**CORNEAL PACHYMETRY**

Pachymetry is the measurement of corneal thickness. The usual central corneal thickness is between 0.49 mm–0.60 mm. Corneal thickness gradually increases from the center out towards the limbus. Because corneal thickness affects applanation tonometry (a thicker cornea is less flexible and therefore gives a higher pressure reading with applanation tonometry), glaucoma patients will often have a baseline pachymetry reading. For the purposes of this course, only its uses as a diagnostic tool for corneal pathology will be discussed.

There are two types of pachymetry:

- **Corneal Optical Pachymetry:** This type of pachymetry measures the thickness of the optical cross section of the cornea viewed in a slit lamp. The slit lamp (using oblique illumination) observes an oblique slice of cornea. The apparent thickness is a physical measurement made by moving an optical marker from the front to the back of the cornea. The optical pachymeter produces two images of the oblique section. Rotating the top image (front surface) and aligning it to the bottom image (back surface) moves an optical marker from the front to the back of the cornea. The observation microscope is set at an angle with the illumination system, and the corneal thickness is derived using a geometrical formula. In a 2004 study “Comparison of Optical Coherence Reflectometry and Ultrasound Central Corneal Pachymetry,” A. Gillis and T. Zeyen found that the variability of the central corneal thickness measurements taken with the noncontact optical pachymeter is significantly lower and less accurate than those taken with the contact ultrasound pachymeter.¹

- **Ultrasonic Pachymetry:** Ultrasonic pachymetry is based on the speed of sound in a normal cornea. Audible sound is defined as mechanical vibrations within a solid or liquid that travel in a wave pattern at a frequency from 20–20,000 Hertz (20 Hz-20K Hz). The speed of sound is determined completely by the volume or thickness of the medium through which it passes. Sound travels faster through solids than through liquids. This is important to understand, because the eye is composed of both solids and liquids. Ultrasound has a frequency greater than 20,000 (20K Hz), which is inaudible to human ears.

The ultrasonic pachymeter has an applanator tip and is held perpendicular to the surface of the cornea. Rapid pulses of ultrasound are emitted, bounce off Descemet’s membrane on the posterior cornea, and return to the applanator tip, which detects the return pulse. The internal computer of the pachymeter measures the time the pulse is emitted from the tip to when it is returned, and then calculates the thickness of the cornea that creates the time delay. Ultrasonic pachymeters are typically portable. Topical anesthesia is required because the tip must be in contact with the cornea. As indicated above, it is widely believed that ultrasonic biometry is more accurate than corneal optical pachymetry.

Detecting Corneal Abnormalities with Pachymetry

This section discusses conditions that are detected and monitored by the use of corneal pachymetry.

- **Fuch's Dystrophy and Keratoconus**: A classic function of the pachymeter is in the management of corneal pathology. Corneal thickness measurement plays a key role in monitoring the progression of Fuch's dystrophy and keratoconus. Recording a baseline corneal thickness measurement for patients with endothelial dystrophy and early cataracts helps eye physicians assess corneal decompensation and evaluate for potential cataract surgery. If a patient has a corneal thickness of 530 microns as a base measurement, and the corneal thickness rises through the years to 600 microns, a physician can conclude that the corneal endothelium is compromised and may not withstand the stress of cataract surgery. It also is possible that corneal edema is contributing to the reduction in visual acuity. On the other hand, if the initial thickness is 600 microns and remains stable over time, it is evidence that the cornea is stable and cataract surgery may be less likely to cause decompensation of the cornea.

- **Corneal Edema**: Endothelial cells are hexagonal, tightly packed, and have a uniform density. The job of the corneal endothelium is to keep the cornea clear by acting as a leaky barrier for the aqueous humor. When functioning properly, this barricade permits aqueous humor to penetrate the posterior cornea and then pumps the water molecules back into the anterior chamber, leaving behind the nutrients necessary for maintaining the health of the cornea. When this barricade is not functioning properly, the aqueous seeps into the cornea faster than the remaining endothelial cells can pump it out. The cornea then becomes edematous and cloudy.

When the endothelium is functioning properly, the corneal stromal water content is maintained at approximately 78%, and corneal thickness measurements fall within the normal range. The primary job of the endothelium is to maintain proper hydration of the cornea to ensure the clarity and transparency of this structure. As people age, endothelial cells die and do not regenerate. Neighboring cells expand to fill in the space left by the dead cells. As a result, the endothelial cell counts drop, and the pumping mechanism becomes less potent. Chronic corneal edema is generally the cause of a deficient endothelial pump function. Because people are born with an excessive number of endothelial cells, the natural loss of endothelial cells does not usually reduce the residual pumping to the point of causing corneal edema. However, if disease, degeneration, dystrophy, or trauma damages too many pumping cells, the remaining cells are inadequate, and corneal edema occurs. Pachymetry remains a valuable instrument used in the measuring and monitoring of corneal edema and its subsequent progression.

- **Keratorefractive Procedures**: Pachymetry measurements must be captured prior to any keratorefractive procedures, such as laser-assisted keratomileusis (LASIK), photorefractive keratectomy (PRK), or astigmatic keratectomy (AK). Proving a normal corneal thickness in all meridians of the cornea prior to any refractive procedure involving the cornea is crucial. This helps eliminate the potential for corneal ectasia (abnormal bulging forward of a thinned cornea). Corneal ectasia occurs when the cornea becomes biomechanically unstable and begins to bulge due to excessive thinning. This condition is discussed in greater detail in other sections of this course.

- **Corneal Thinning**: Keratoconus, pellucid marginal degeneration, and corneal ectasia after refractive surgery are discussed in detail later in this module. Pachymetry plays a major role in monitoring the progression of these corneal disorders. Measurements of corneal thickness must be taken at each exam in order to properly evaluate potential advancement of disease.

INTRODUCTION TO CORNEAL TOPOGRAPHY (VIDEOKERATOGRAPHY)

The introduction of corneal topography to the field of ophthalmology has profoundly impacted the visual outcomes of corneal, cataract, and refractive surgery in a positive way. Without this revolutionary technology, the field of refractive procedures would not have evolved into the remarkable success story it has become.
Before the invention of corneal topography, the keratometer was the standard device used in ophthalmic practices for measuring the anterior curvature of the cornea and determining the amount of corneal astigmatism in the eye. Until the advent of refractive surgery, the keratometer provided an adequate amount of information for most clinical situations. However, since the keratometer measures only four points on the central 2.8–4mm of the central cornea, it does not provide sufficient information to determine whether or not a patient is a good candidate for refractive surgery. This assessment requires a corneal contour map.

The topographer measures and analyzes the radius, refractive power, and anterior curvature at thousands of points across the anterior cornea from the apex to the periphery. With this data, a contour map is generated. The color map that is generated illustrates the cornea’s shape and corneal curvature changes from the apex out to the periphery. This information is useful in determining whether a patient has a normal or abnormal amount of astigmatism, whether he or she has a normal-shaped cornea or an abnormally shaped cornea, and whether a patient is a good candidate for a refractive procedure.

Since the cornea is responsible for close to 70% of an eye’s refractive power, accurate contour mapping is crucial. A contour map of the cornea is much like a geographic contour map, with cooler colors representing flatter areas (like a valley) and warmer colors representing areas of steepness (like hills). It is important to pay close attention to the color scale to accurately follow what colors correspond to which dioptic powers. Many topographers use a sliding scale that varies from eye to eye. Therefore, the same color may have a different diopter value, even on the same eye measured on two different days.

All topographers gather the data by projecting light onto the cornea. The alteration of the projected light by the cornea is captured by a video system. After the information is analyzed by proprietary computer software, a contour map is constructed.

![Figure 1a: Normal axial view.](image1a)

![Figure 1b: Normal 4 view.](image1b)
TYPES OF CORNEAL TOPOGRAPHY

This section discusses the three fundamental concepts of corneal topography technology.

Placido-Based Devices: Placido disk imaging was the first technology to employ a computer to measure the dioptic powers of the anterior curvature of the cornea. A placido-based device projects alternating black and white rings (called mires) onto the cornea. The reflected images are then detected by a video camera. The computer measures the distance between each mire, and the data are expressed in a color contour map. The closer together the mires are, the steeper the area. The wider apart the mires are, the flatter the area. The mathematical calculations (also referred to as algorithms) used for placido-based devices assume that the cornea is spherical, and errors in interpretation can occur in diseased eyes or eyes that have undergone refractive surgery.

Figure 2: Normal placido image on eye.

Scanning Slit Technology: Scanning slit technology is a noncontact segment-analysis system that is integrated with an advanced placido-disc system. While a placido image is projected on the cornea all at once, the scanning slit sequentially captures cross-sectional scans of the cornea with a series of 40 slit beams (20 to the left and 20 to the right) angled at 45 degrees to the left and right of the video axis. The system captures over 9,000 data points in 1.5 seconds. Because this technology acquires cross-sectional scans of the cornea, elevation and curvature measurements can be captured on both the anterior and posterior view of the cornea. Additionally, full corneal pachymetry (out to the periphery) is captured by a computer analysis of the reflection of the scanning slit on both the anterior and the posterior surfaces of the cornea. Scanning slit instruments can also provide measurements of the white-to-white diameter, mesopic pupil size, anterior chamber depth, and angle kappa that are all displayed on the contour map.

Figure 3: Orbscan map of a normal cornea.
Rotating Slit/Scheimpflug: Several Scheimpflug topography devices provide a complete three-dimensional picture from the anterior surface of the cornea all the way through to the posterior surface of the lens. The Oculus Pentacam and Ziemer Galilei systems utilize a rotating Scheimpflug camera and are able to calculate a three-dimensional image of the anterior segment of an eye from as many as 25,000 true elevation points. It takes two seconds to generate a complete image, and any eye movement is detected by a second camera and corrected. A Scheimpflug image provides anterior and posterior corneal topography and pachymetry of the eye from limbus to limbus, calculation of the anterior chamber angle, chamber volume, chamber depth, and chamber height. There is also a manual measuring tool that can be used to measure any location within the anterior chamber of the eye. Like the scanning slit devices, the Scheimpflug instruments do not come in contact with the patient’s eye.

Figure 4: Pentacam basic capture screen of keratoconus patient. Scheimpflug image (black and white) is in upper left corner.

BASICS OF INTERPRETING TOPOGRAPHY MAPS

Each corneal topography model has its own user guide that should be studied and followed in order to gain the maximum value from the device. However, the basic concept of the topography color displays is relatively consistent among devices. The key display is the color map of corneal power, usually referred to as the “axial” or “keratometric” map. The calculated corneal power, in diopters, is displayed as a circle of colors. The colors correspond to a color bar at the side of the map, with the numerical power assigned to each color printed next to the color.

The color bar is adjustable in two major ways. The first is that it can be set to automatically adjust itself to cover the range of powers of an individual map. The advantage of the automatic setting is that an abnormally flat or steep cornea will not result with a broad area of the same color at the end of the color scale when the corneal power is beyond the range of that scale. The disadvantage is that the colors represent different diopter values on different eyes, or even the same eye on different days, making comparison of two scans difficult. A fixed scale avoids this problem but requires the user to recognize when a topography map is “off-scale” and intervene with an adjusted scale for that eye (see Figures 7d and 7e).

The other basic adjustment is the size of the steps represented by each color change. If the steps are too small, the topography becomes “noisy” with color changes that do not correspond to real differences. If the steps are too big, however, important changes can be masked. Most users will pick color steps of 0.5 or 1.0 diopter (D).

The newer generation of corneal topographers frequently gives color maps for anterior and posterior elevation (referred to as “float” by one device). Instead of dioptric power, the color scale is based on microns of elevation above or below a theoretical normal (usually a sphere). Similarly, corneal thickness values can be displayed on a color map, often with the numerical values printed over the map. In
principle, the anterior elevation map should correspond well with the power map, because a flatter, lower-power corneal area should be depressed relative to the reference sphere, and a steeper, higher-power area should be elevated above the reference sphere. Cross-checking the power and anterior elevation maps is a good way to determine whether the topography image is high quality or has artifact.

Figure 5a: Posterior elevation map of pellucid patient.

Figure 5b: Sagittal map of pellucid patient.

INTRODUCTION TO ASTIGMATISM

In the ensuing paragraphs, the discussion will focus on astigmatism, its mapping through various topographical techniques, and indications for use of each mapping technique.

A flawless cornea has a spherical shape and is steepest in the center with progressive flattening toward the periphery. At birth, the cornea is typically a perfect sphere but begins to lose its spherical properties by the age of four. Regular astigmatism occurs when the cornea begins to shift from a spherical shape to an oblong shape (like a football).

A cornea with regular astigmatism has a flat meridian and a steep meridian 90 degrees apart, thereby preventing light rays from focusing together to form a single point on the retina. This causes objects to be blurred and/or distorted at distance and near. When one focal line falls on the retina and the other focal line falls behind or in front of the retina, this condition is referred to as *simple astigmatism*. If both focal lines fall in front of the retina, this is called *compound myopic astigmatism*. If both focal lines fall behind
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the retina, this is referred to as compound hyperopic astigmatism. Mixed astigmatism is when one focal line lands behind the retina, and the other focal line lands in front of the retina.

Regular Astigmatism

On a topographical map, regular astigmatism has the appearance of a symmetrical bowtie, or hourglass pattern. Regular astigmatism occurs when the principle meridians are perpendicular, or at right angles to each other.

There are two separate categories within the regular astigmatism classification. The first is “with-the-rule” astigmatism (think of an American football lying on its side); the second is “against-the-rule” astigmatism (think of an American football being held straight up for a kickoff). A bowtie pattern of warm colors in the horizontal meridian is represents “against-the-rule” astigmatism, and a bowtie pattern of warm colors in the vertical meridian is represents “with-the-rule” astigmatism. (Remember: the warmer colors are the higher diopter powers of the steeper curvature.)

Irregular Astigmatism

Irregular astigmatism occurs if the cornea has been damaged by trauma, contact lens warpage, corneal surgery, scattering in the crystalline lens due to a cataract, developmental anomalies, post-inflammatory degenerative conditions, keratoconus, or other thinning disorders. Irregular astigmatism will appear as an asymmetric pattern on topography. For example, there may be superior steepening, inferior steepening, sagging bowtie patterns, or nonspecific irregularities.

Because of the lack of geometric symmetry of the corneal surface inherent in irregular astigmatism, this condition is not fully correctable with a cylindrical lens placed in a pair of spectacles. Hard contact lenses, such as rigid gas-permeable lenses or toric lenses, may be employed to optically neutralize the irregular astigmatism. A soft contact lens is not an option, because the soft contact lens will drape over the cornea, following the curvature of the irregular cornea. Corneal surgery may be necessary if inadequate optical performance, instability of the contact lens, or discomfort prevents the patient’s vision from being satisfactorily corrected with rigid lenses. This surgery includes collagen cross-linking treatments, implanted ring segments, custom excimer laser reshaping, and corneal transplantation.

Detecting Corneal Abnormalities with Corneal Topography

Corneal topography has become instrumental in detecting early keratoconus, pellucid marginal degeneration, and post-refractive ectasia. Corneal topography is not only invaluable in diagnosing...
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abnormal corneas, but it also allows the clinician to track the progression of the disease. A discussion of some of the common abnormalities of the cornea follows.

- **Keratoconus**: Keratoconus occurs in approximately 50 out of 100,000 individuals. Positive familial histories have been reported in approximately 6–8% of keratoconus cases. Patients with Down’s syndrome (trisomy 21) are predisposed to developing keratoconus, as are patients with Marfan’s syndrome, atopy, floppy eyelid syndrome, mitral valve prolapse, Leber congenital hereditary optic neuropathy, and other congenital abnormalities of the eye. A scissoring of the eye’s red reflex with retinoscopy, also called “Rizzutti’s sign,” is an early indication of keratoconus. There is also a phenomenon in which iron deposits appear at the base of the cone, and this is known as a Fleischer ring. A Fleischer ring appears brownish in color and can be seen at the slit lamp most easily with a cobalt-blue filter and a broad, oblique beam.

Corneal topography supplies clinicians with the final piece to the keratoconus diagnostic challenge by producing a color-coded map outlining, in diopters, the shape and amount of astigmatism. In keratoconus, the central or paracentral cornea experiences progressive thinning and bulging. It can occur bilaterally or unilaterally. On rare occasions, the thinning will progress to the point of a tear in Descemet’s membrane, which results in acute corneal edema known as acute hydrops. The topographical analysis of a keratoconus patient will display either an inferior steepening of the cornea or a substantial asymmetric bowtie pattern with the inferior bow appearing much larger and steeper than the superior bow on the contour map.

Patients with very mild keratoconus may have normal visual acuity and no visible signs of keratoconus on examination. When a suspicion of subclinical keratoconus is raised by the topographic pattern, the term “forme fruste” keratoconus is commonly applied. A refractive surgeon hopes to detect forme fruste keratoconus during the preoperative assessment so these patients can be excluded from excimer laser treatment of the cornea. Avoiding surgery on these patients can prevent a weakening of the cornea through the removal of tissue, possibly triggering clinical and progressive keratoconus (see upcoming section on corneal ectasia).

The early signs of keratoconus on topography are: 1) a steep central cornea, especially above 46-47D; 2) asymmetry of the corneal power vertically (typically, at a 3mm diameter, an inferior power that is 1.6D or more higher than the corresponding superior corneal power, referred to as the I-S disparity); 3) a sagging bowtie pattern; 4) a posterior corneal elevation higher than normal, usually central or inferior to center (normal values depend on the instrument); 5) a thin central cornea, especially under 470 microns; and/or 6) minimum corneal thickness located inferior to the corneal apex.

![Figure 7a: Mild keratoconus in 0.5D steps.](image)
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Figure 7b: Possible mild keratoconus in 1D steps.

Figure 7c: Severe keratoconus (auto scale) axial map.

Figure 7d: Severe keratoconus (off scale) 4 map.
• **Pellucid Marginal Degeneration**: Pellucid marginal degeneration is an uncommon disorder, and its etiology is unclear. Pellucid occurs bilaterally and is nonhereditary and may be a variant of the same corneal weakening disorder that causes keratoconus. The diagnosis of pellucid is typically made between the ages of 20–40. Pellucid marginal degeneration usually occurs inferiorly with severe thinning located within 1–2 mm from the limbus. Men and women are equally affected by pellucid. Cases of acute hydrops have been reported, and rare cases of spontaneous corneal perforation due to extreme corneal thinning also have been recorded.

On corneal topography, advanced pellucid appears as an inferior steeping that has a “crab claw” appearance to it. However, distinguishing between keratoconus and pellucid marginal degeneration on topography early in the disease process can be difficult.

To correct the irregular astigmatism induced by pellucid marginal degeneration, glasses should be tried first. If that option fails, an attempt at a contact lens fitting should be made. However, contact lens fittings for pellucid patients are typically more challenging than for keratoconus patients due to the location of the thinning. If the patient’s acuity is uncorrectable with glasses, and the patient is unable to tolerate or wear a contact lens, collagen cross-linking and corneal transplantation are the only other options. Because the thinning occurs very close to the limbus, performing corneal transplantation on these patients is challenging. The graft is very large and close to the inferior limbus, making the surgery technically difficult and the patient more vulnerable to graft rejection.
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**Corneal Ectasia:** Corneal ectasia (often called “keratectasia”) is a bulging of the cornea induced by a biomechanical weakening of the cornea as a result of a refractive surgical procedure. Ectasia is also referred to as iatrogenic keratoconus, or secondary keratoconus. This condition is a very serious long-term complication of corneal refractive surgery, as it is unstable and progressive.

Because of the necessity for the creation of a flap in LASIK, ectasia is primarily associated with LASIK. The theory is that the flap creation undermines the structural integrity of the cornea as a structural element, even years after the surgery. In ectasia, the loss of the structural support of the flap plus the stromal tissue removal by the laser optical correction does not leave enough remaining corneal tissue for structural integrity of the cornea. Over time, the cornea stretches, causing thinning and distortion similar to that caused by keratoconus.

Some specific circumstances contributing to ectasia include: 1) a cornea that is too thin for the flap and amount of laser tissue removal; 2) a flap that is cut thicker than expected; and 3) forme fruste (or subclinical) keratoconus not detected on corneal topography prior to surgery. However, a few patients with no identifiable risk factors have developed ectasia after corneal refractive surgery.

There are nonsurgical and surgical treatments for ectasia. The treatments are the same as a patient who has keratoconus or pellucid: glasses, rigid contact lenses, collagen cross-linking, implanted ring segments, and corneal transplantation.

**INDICATIONS FOR CORNEAL TOPOGRAPHY**

The following sections discuss the various medical indications for the use of corneal topography in the diagnosis and treatment of corneal abnormalities.

**Measuring and Managing Astigmatism in Postoperative Corneal Transplant Patients**

A clear corneal graft does not always translate into a visual success story. A graft that suffers from an excessive amount of regular and/or irregular astigmatism due to suture tension or wound misalignment is essentially an optical failure, regardless of its clarity. Corneal topography’s ability to provide color mapping and analysis for postoperative astigmatism makes it an extremely vital tool in improving the quality of a patient’s visual acuity after corneal transplantation.

Suture tension in a running suture can be adjusted postoperatively, guided by topographic analysis. If there is excessive tension (demonstrated by a steep meridian on topography) in one location of the
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running suture, the surgeon can use a jeweler’s forceps to tighten the suture in an area where it is looser (a flatter, lower-power area on topography with cool colors) and shift the lax suture in the direction of the steeper cornea (warm colors) in order to relax some of the suture tension. If a surgeon prefers to use an interrupted suture technique rather than a running suture technique, selective suture removal in an area of steepening assists in minimizing induced astigmatism.

Suture adjustment after corneal transplantation can considerably improve visual acuity outcomes. Without the use of computerized corneal topography, successful suture adjustments would not be possible, and patients would be unable to achieve their best potential visual acuity postoperatively.

Evaluate Potential Refractive Surgery Patients

It is critical to discover corneal abnormalities in patients who desire LASIK, PRK, or AK. Corneal topography has proved indispensable in uncovering subclinical corneal abnormalities that could adversely affect refractive surgery outcomes. In fact, it would be negligent to perform any refractive procedure without the careful capture and thorough review of topographical analysis.

Prior to LASIK, PRK, or AK, a topographical analysis should be performed to rule out keratoconus, forme fruste keratoconus, pellucid marginal degeneration, or other corneal abnormalities. Corneal ectasia can occur postoperatively if these abnormalities are not recognized on the preoperative topography.
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Evaluating Patients Receiving Presbyopia-Correcting Intraocular Lenses

A corneal topographic map is very useful in preoperative assessment of patient receiving presbyopia-correcting intraocular lenses (IOLs). In order to achieve the goal of good functional vision without glasses, these patients must not have pre-existing irregular astigmatism, and any significant amount of regular astigmatism must be taken into account and corrected during the cataract and implant surgery. Postoperatively, if a patient with a presbyopia-correcting IOL is complaining of low-quality postoperative vision, a corneal topography map is essential in the evaluation of possible causes and treatment. The ability to compare the corneal contour to the preoperative cornea also is helpful when assessing these patients during the postoperative period.

Evaluating Patients Having Astigmatism Surgery or Toric Intraocular Lenses

A preoperative corneal topography map greatly benefits the surgical correction of astigmatism, whether by incisions or with toric IOLs. The topography will identify potential problems such as asymmetric astigmatism and can guide the surgeon in placing different length incisions or placing the incisions slightly asymmetrical in cases of a mildly sagging bowtie-astigmatism pattern. For both incisional surgery and toric IOLs, the topographic map validates the accuracy of other measures like keratometry and provides a useful tool at surgery so the surgeon can visually confirm the correct placement of the astigmatism correction.

Evaluating Unexplained Loss of Vision

Corneal topography is a key tool in evaluating a patient with unexplained reduced visual acuity. The cornea may show irregularity from a number of causes not visible on direct examination. A common example is previously undiagnosed keratoconus. Another occasional problem is a higher degree of astigmatism than previously suspected. Conversely, a normal corneal topography will rule out many conditions and allow the clinician to pursue other causes of decreased vision.

LIMITATIONS OF CORNEAL TOPOGRAPHY

There are limitations to all medical devices, including the corneal topographer. These include:

- If a patient suffers from tear film defects, the light projected onto the cornea by the topographer will be severely distorted, thereby making it difficult for the video system to properly analyze the information captured. Sometimes instilling artificial tears and having the patient blink several times will result in a usable image.
Severe irregularities of the cornea pose difficulties in acquiring an accurate topographical map. The light projected onto a severely irregular cornea will be distorted due to the cornea’s lack of geometric symmetry, and the topographical software will be unable to analyze the information precisely.

Misalignment of the device could give a false impression of keratoconus or corneal apex decentration.

OTHER DIAGNOSTIC INSTRUMENTS USED IN EVALUATING CORNEAL DISEASE

There are several other instruments used in evaluating corneal disease. These include:

Anterior Segment OCT

Anterior segment optical coherence tomography (OCT) provides a two-dimensional, cross-sectional image of the tissue in focus. Prior to the introduction of this technology, the only way to obtain cross-sectional images of the anterior segment was with histological sectioning.

OCT is a noncontact technique that eliminates patient discomfort. Corneal OCT is also another means of providing corneal pachymetry maps out to the periphery. This diagnostic instrument provides the corneal surgeon with accurate measurements of the anterior chamber width, the anterior chamber depth, corneal thickness and curvature and the crystalline lens vault. When used prior to LASIK, it provides the surgeon with global corneal thickness measurements and a map feature that illustrates changes in postoperative corneal thickness. Secondly, after LASIK, anterior segment OCT provides a full visualization of the flap as well as residual bed thickness. This is helpful when considering LASIK enhancements.

Figure 11: OCT pachymetry map.
Specular Microscopy

Specular microscopes are used to view the corneal endothelium at a magnified level utilizing light that is angled to reflect off the endothelial cells. With the introduction of the specular microscope in 1974, the clinical evaluation of endothelial cells (in-vivo) was possible for the very first time. An average normal adult endothelial cell density is somewhere between 2500–3500 cells per square millimeter. As mentioned earlier in this module, cell density decreases with age, and endothelial cells have no ability for cell division or repopulation.

This documentation allows the analysis of the population, size, and shape of the endothelial cells. This can also be achieved using the biomicroscope after much practice. A narrow beam of light is placed on the cornea in position so the reflection of light shines brightly into the examiner’s eyes. The magnification is changed from low to high so the endothelium is visible. Contrast will be weak, making it difficult to count the endothelial cells. Specular microscopy is a far more accurate method and also provides a picture of the cells for the medical record.
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For a clinician to definitively evaluate the health of a patient’s endothelium prior to anterior segment surgery, specular microscopy may be performed. Any anterior segment surgery poses some risk to the endothelium. If there is any trauma, such as touching of instruments to the endothelium, cells will be lost.

There are both contact and noncontact specular microscopes available today. Noncontact specular microscopes are easier to use, do not require topical anesthetics, but may produce unreliable images when the patient’s corneal surface is abnormal.

Visualization of the endothelial cells through the use of specular microscopy also enables clinicians to identify and differentiate abnormalities such as Fuch’s dystrophy and posterior polymorphous membranous dystrophy (PPMD).

- **Fuch’s Endothelial Dystrophy:** Guttae are reflective small, round, whitish deposits seen on Descemet’s membrane when examined at the slit lamp. Fuch’s dystrophy is a progressive corneal condition that usually occurs after the age of 50, often afflicting more women than men. Fuch’s dystrophy can range from asymptomatic guttae to stromal edema with corneal decompensation. Symptomatic patients present with complaints of glare and blurred vision long before pain is present. Guttae are first seen centrally and eventually spread toward the periphery. On specular microscopy, guttae appear as dark roundish spots, making the endothelial cells invisible in that area.

- **PPMD:** This is a slowly progressive and uncommon dystrophy that presents early in life. PPMD is a dystrophy in which the endothelium becomes multilayered and appears and behaves like epithelium. PPMD is often hereditary.

**In-Vivo Confocal Microscopy (IVCM)**

The confocal microscope is a diagnostic tool that allows for a detailed, noninvasive, layer-by-layer examination of corneal disease and an improved understanding of corneal microstructure. IVCM utilizes refined imaging techniques in an attempt to capture information that normally requires the collection of dead tissue samples and pathology expertise.

There are currently two confocal microscope technologies in clinical practice today: the noncontact slit scanning confocal microscope (SSCM) and the contact laser scanning confocal microscope (LSCM). Even in cases of corneal scarring and swelling, both devices supply the clinician with a magnified, high-resolution view of corneal cell layers, structures, and organisms. Images captured with IVCM are in real-time; the speedy acquisition of these images is crucial due to microsaccades (fixational eye movements) and involuntary patient movements (such as respiration).

IVCM makes it possible to view the following in healthy corneas: superficial epithelial cells, intermediate (or wing) epithelial cells, basal epithelial cell layer, sub-basal nerve plexus, stromal keratocytes that increase in density as one moves from anterior to posterior, and endothelial cell layers.

In less healthy corneas, typical inflammatory cells appear as bright moderate-sized images. Macrophages, which play a pertinent role in the immune system, are larger and frequently have a distinct nucleus.

IVCM is a rapidly evolving diagnostic tool and its applications are still being explored. In corneas after refractive surgery, the IVCM has been used to evaluate the amount of stromal haze after PRK, image reflective particles found in the flap interface introduced by mechanical microkeratomes, determine the depth of epithelial ingrowth under a LASIK flap and the subsequent planning of its surgical management, and visualize hyperactivated keratocytes in postoperative LASIK and PRK. Other corneal abnormalities identified by IVCM include:

- **Acanthamoeba:** Acanthamoeba is a genus of amoebae, one of the most common protozoa in soil and is also frequently found in fresh water and other habitats. When found in the eye, Acanthamoeba can be preliminarily diagnosed with IVCM and then confirmed by a histological
examination of an epithelial biopsy specimen. Acanthamoeba cysts appear in the epithelium as round, hyper-reflective shapes with a thin wall and bright central core. Stromal nerves inflamed by the Acanthamoeba parasite (Acanthamoeba perineuritis) will also appear on IVCM, correlating with the slit lamp observation of "thickened corneal nerves." Although rare, the transmission of Acanthamoeba is most often related to poor contact lens hygiene. The patient presents in a great deal of pain and, like many infections, early diagnosis is important to a full recovery.

Figure 14: Confocal microscopy of an Acanthamoeba cysts.

- Fungal Infections: Fusarium is a large genus of filamentous fungi widely distributed in soil and in association with plants. Most species are harmless saprobes, and are relatively abundant members of the soil microbial community. Some species produce mycotoxins in cereal crops that can affect human and animal health if they enter the food chain. The main toxins produced by these Fusarium species are fumonisins and trichothecenes. Fusarium fungal infections can occur in the cornea and typically appear as hyper-reflective, branching strands on confocal microscopy. Thin, linear structures that branch at 45-degree angles are pathognomonic for Fusarium. Like Acanthamoeba, this infection is most common among contact lens wearers.

Figure 15: Confocal microscopy of Fusarium.

Less frequently observed fungi that may affect the ocular system include Aspergillus, which are also linear (but lack the 45 degree branching of Fusarium). Like Fusarium, these often infect the eye after an abrasion caused by organic matter. Candida, common to the northern and coastal
areas of the United States, are the most common yeast fungi and are often observed in debilitated patients or in patients who have engaged in chronic use of corticosteroids. They are imaged as bright round structures. They are smaller than Acanthamoeba cysts and do not have an external wall.

CONCLUSION

The cornea provides approximately 70% of the optical correction of the eye. Distortions and irregularities of the corneal contour often result in major degradation of vision; therefore, it is important to understand the various diagnostic tools available that assist physicians in the diagnosis and treatment of patients with corneal disease. The allied health care professional plays an important role in this process by effectively performing the diagnostic testing required by the physician. Diagnostic instrumentation is rapidly evolving, making it critical that the technology is utilized effectively in order to provide the eye care physician with better, more accurate data to diagnose and treat corneal disease.

NOTE: Additional helpful and informative resources might be available in the CLASS MATERIALS section of this course. The CLASS MATERIALS section is located in the menu on the course homepage.
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COURSE EXAMINATION

1. In a cornea with simple astigmatism:
   a. One focal line falls on the retina and the other focal line falls behind or in front of the retina.
   b. Both focal lines fall behind the retina.
   c. Both focal lines fall in front of the retina.
   d. One focal line falls behind the retina and the other focal line falls in front of the retina.
   e. The cornea is a perfect sphere and all light rays fall directly on the retina.

2. The most common refractive condition is:
   a. Hyperopia.
   b. Myopia.
   c. Compound myopic astigmatism.
   d. Compound hyperopic astigmatism.
   e. Regular astigmatism.

3. A keratometer measures only three points on the central 3.0mm to 5.0 mm of the cornea.
   a. True
   b. False

4. The cornea is responsible for approximately:
   a. 50% of the eye’s refractive power.
   b. 100% of the eye’s refractive power.
   c. 70% of the eye’s refractive power.
   d. 15% of the eye’s refractive power.

5. All topographers share a certain characteristic:
   a. The computer measures the distance between each mire.
   b. They are all integrated with a placido disc system.
   c. They all utilize a scanning slit to capture cross-sectional scans of the cornea.
   d. They all project light onto the cornea.
   e. They all capture an anterior and posterior view of the cornea.

6. A corneal topography is critical in determining a patient’s eligibility for a refractive procedure. Prior to a refractive surgical procedure it is critical to know:
   a. If a patient has simple astigmatism.
   b. If a patient has mixed astigmatism.
   c. If a patient has compound myopic astigmatism.
   d. If a patient has compound hyperopic astigmatism.
   e. If a patient has a normal-shaped cornea, an abnormally shaped cornea, a normal amount of astigmatism, or an abnormal amount of astigmatism.

7. With-the-rule astigmatism exhibits a bowtie pattern of warm colors in the horizontal meridian.
   a. True
   b. False
8. The key display of topographical devices is the:
   a. Pachymetry.
   b. Scheimpflug images.
   c. Axial or keratometric map.
   d. Simulated keratometry.
   e. Anterior chamber depth.

9. The newer topographers:
   a. Have color maps for anterior and posterior elevation.
   b. Have alternating black and white rings called “mires.”
   c. Employ a computer to measure the dioptric powers of the anterior curvature of the cornea.
   d. Measure the distance between each mire.
   e. Measure the central 2.8 to 4.0 mm of the central cornea.

10. An option for correcting irregular astigmatism is:
    a. A cylindrical lens placed in spectacles.
    b. A soft contact lens.
    c. Patching.
    d. An intraocular lens.
    e. Corneal surgery.

11. Corneal ectasia is a:
    a. Bulging of the cornea.
    b. Degenerative disease that occurs inferiorly with severe thinning located within 1 to 2 mm from the limbus.
    c. Steeping of the central cornea.
    d. Developmental anomaly.
    e. Result of a poorly fitted gas-permeable lens.

12. Corneal topography is instrumental in detecting:
    a. Glaucoma.
    b. Lenticular astigmatism.
    c. Keratoconus.
    d. Graft failure.
    e. Scattering of the crystalline lens due to a cataract.

13. A contour map of the cornea is much like a geographic contour map, with cooler colors representing flatter areas (like a valley) and warmer colors representing areas of steepness (like hills).
    a. True
    b. False

14. The limitations of corneal topography become evident:
    a. If a patient suffers from tear film defects.
    b. If there are severe irregularities of the cornea.
    c. If there is a misalignment of the device.
    d. With poor fixation and cooperation.
    e. All of the above.
15. Corneal topography is an important tool in evaluating a patient with unexplained diminished visual acuity.

  a. True
  b. False