Anterior segment imaging in angle-closure disease

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Introduction

Angle-closure disease (both primary and secondary) is a spectrum of disorders characterized by iridotrabecular contact obstructing aqueous outflow. Anterior segment imaging plays an important role in understanding the pathophysiology of angle closure, diagnosis, and monitoring the treatment, especially in challenging cases. Indirect gonioscopy, the gold standard for visualizing the anterior chamber angle (ACA) is a subjective technique with moderate agreement among experts and inability to visualize structures posterior to the iris. It is affected by room illumination, pressure on the globe, clinicians’ skill, and patient cooperation. With advances in technology, many instruments are available for imaging the anterior segment. Each comes with its own advantages and limitations which the clinician must consider while making decisions.

Ultrasound biomicroscopy

Ultrasound biomicroscopy (UBM), developed by Pavlin et al., provides high-frequency (50–100 MHz) in vivo B-scan ultrasonography images of the anterior segment of the eye up to a depth of 4 mm with 25 µm axial and a 50 µm lateral resolution. In angle-closure disease, where more than one mechanism often coexists, UBM helps us to understand the dynamics and mechanism involved. Sound penetrates both opaque media and iris. Thus, retro-iridal structures like the ciliary body can be imaged. Images can also be obtained in the presence of corneal scars, hyphema, or corneal oedema providing invaluable information in secondary angle-closure disease.

In pupillary block glaucoma, UBM demonstrates a peripherally shallow anterior chamber, iridotrabecular contact, convex iris configuration (Fig. 1) and a well-formed posterior chamber. Pavlin et al. described reproducible quantitative information in the form of indices like angle opening distance (AOD), trabecular-ciliary process area, and iris thickness at specific positions (Fig. 2). However, this assumes the iris surface to be a straight line. To overcome this, Ishikawa and Schuman defined angle recess area (ARA), taking into account the iris irregularities (Table 1). They developed a semi-automated software to provide these parameters after identification of the scleral spur (SS). These parameters document the change with time or with treatment and help us to classify angle-closure disease into subtypes. Marchini et al. found a shorter axial length, a shallower anterior chamber depth (ACD), a thicker lens, more anteriorly located lens, a narrower ACA, a shorter trabecular-ciliary process distance (TCPD), and a smaller AOD500 in eyes with PACG as compared to normal. Guzzard et al. showed peripheral ACA widening and a reduction in iris convexity following laser peripheral iridotomy (LPI) (Fig. 3). Nonaka et al. reported angle widening and alteration in ciliary process configuration following cataract surgery. UBM can also be used to assess the adequacy and patency of LPI. Ramani et al. predicted the risk of development of PAC in eyes post-LPI. They found that 28% of patients who progressed to PAC had smaller ARA. UBM demonstrated a shallower ACD, narrow chamber angle, greater LV and a more anteriorly rotated ciliary body in eyes with acute primary angle closure (APAC). UBM can show residual appositional angle-closure post-LPI due to a more anteriorly positioned ciliary body, larger lens, and a thicker peripheral iris predisposing to progressive angle closure. UBM is the preferred imaging modality in plateau iris where it demonstrates a flat central iris plane, a steep rise in iris root from the point of insertion, an anteriorly positioned ciliary body (Fig. 4), absence of ciliary sulcus, large and long ciliary processes causing iridotrabecular contact impairing aqueous outflow despite patent LPI. It also helps in identifying pseudo-plateau iris produced by irido-ciliary cysts (Fig. 5), ciliary body edema, tumours or infiltration. UBM can also show iris flattening and subsequent angle opening post laser iridoplasty.

In aqueous misdirection syndrome or malignant glaucoma, UBM shows swelling or anterior rotation of the ciliary body with forward movement of the lens-iris diaphragm, uniform shallowing of AC and angle closure by the iris pushing against the trabecular meshwork (Fig. 6). UBM has been used to differentiate malignant glaucoma...
from pupillary block glaucoma and to classify it into two groups (with and without supraciliary effusion) and planning the clinical management. It demonstrates a shallow AC and thicker lens in eyes with pseudo-exfoliation presumably due to zonular weakness. It can also be used to determine the mechanism of unilateral or secondary angle-closure glaucoma, e.g. pupillary block in pseudophakic eyes, nanophthalmos, uveal effusion syndrome, Vogt Koyanagi Harada syndrome, and drug-induced uveal effusion (Fig. 7). UBM can be used to demonstrate a large, intumescent lens with forward movement leading to due narrowing of ACA in phacomorphic glaucoma.

Table 1  Parameters for quantitative measurement of anterior segment with UBM and ASOCT.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
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<tbody>
<tr>
<td>Angle opening distance (AOD 500/750)</td>
<td>Perpendicular distance from the trabecular meshwork at a specified distance (500 microns or 750 microns), anterior to SS to anterior iris surface</td>
</tr>
<tr>
<td>Trabecular iris surface area (TISA)</td>
<td>Area bounded anteriorly by the AOD, posteriorly by a line drawn from the SS perpendicular to the plane of inner scleral wall to the opposing iris, superiorly by the inner corneoscleral wall and inferiorly by the iris surface</td>
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<tr>
<td>Trabecular iris angle (TIA)</td>
<td>Defined in degrees as the angle formed from angle recess to points 500 micm from SS on trabecular meshwork and perpendicular on the surface of iris</td>
</tr>
<tr>
<td>Iris thickness 1 (IT1)</td>
<td>Measured along the line extending from corneal endothelium at 500 micm from SS perpendicular through the iris</td>
</tr>
<tr>
<td>Iris thickness 2 (IT2)</td>
<td>Iris thickness at 2 mm from the iris root</td>
</tr>
<tr>
<td>Iris thickness 3 (IT3)</td>
<td>Maximum iris thickness near the pupillary margin</td>
</tr>
<tr>
<td>Trabecular iris contact length (TICL)</td>
<td>Linear distance of contact between iris and cornea / sclera beginning at the SS</td>
</tr>
<tr>
<td>ARA</td>
<td>The area of triangle between angle recess and iris and cornea 500 / 750 micm from the SS</td>
</tr>
<tr>
<td>AC depth (ACD)</td>
<td>Distance from corneal endothelium to anterior surface of the lens</td>
</tr>
<tr>
<td>AC width (ACW)</td>
<td>Distance of a horizontal line joining the two SSs</td>
</tr>
<tr>
<td>Iris cross-sectional area (ICSA)</td>
<td>The average of cross-sectional area of both nasal and temporal and nasal sides</td>
</tr>
<tr>
<td>Iris curvature (ICurv)</td>
<td>Maximum perpendicular distance between iris pigment epithelium and line connecting most peripheral to most central point of epithelium</td>
</tr>
<tr>
<td>Scleral thickness (ST)</td>
<td>Measured perpendicular from the scleral spur to the episcleral surface</td>
</tr>
<tr>
<td>Lens vault (LV)</td>
<td>Perpendicular distance between anterior pole of crystalline lens and line joining the two scleral spurs</td>
</tr>
<tr>
<td>TCPD*</td>
<td>Distance between trabecular meshwork and ciliary process 500 microns anterior to the SS.</td>
</tr>
<tr>
<td>ICPD*</td>
<td>Distance between iris and ciliary process along the line of ICPD</td>
</tr>
<tr>
<td>IZD*</td>
<td>Distance between iris and zonules along the line of ICPD</td>
</tr>
</tbody>
</table>

*Can be measured with UBM only.
Mansouri et al. showed a significant correlation of UBM with ASOCT in the measurement of ACA in eyes with angle-closure disease but poor agreement. Kaushik et al. and Radhakrishnan et al. found angle widening following LPI to be better appreciated by UBM as compared to gonioscopy. More than 90% agreement with gonioscopy when done in a dark room has been reported.

Continuing advances in technology aim at providing better speed, sensitivity, and depth of focus. High-frequency annular arrays, linear arrays for imaging without probe movement, are under investigation. An 80-MHz UBM (iScience, iUltrasound) has been used to image the Schlemm’s canal.

Challenges

UBM is a contact procedure, requires an eyecup with a coupling medium (saline or methylcellulose) and supine positioning of the patient. This can influence the angle configuration and AC depth. Inability to indent makes it difficult to differentiate between appositional and synechial angle closure. To overcome these limitations, some investigators have used special eyecups which allow corneal compression and probes with bag/balloon covers or bubble tips enabling UBM in sitting position without a waterbath. Despite this, the procedure is more time consuming and requires a skilled operator. Moreover, the SS used as a reference for quantitative parameters needs to be marked manually. Good intraobserver but moderate interobserver agreement has been reported. Lin et al. found increased interobserver variation with respect to UBM parameters involving ciliary processes and recommended measurement by the same observer. Radhakrishnan et al. reported good correlation, similar reproducibility and sensitivity with UBM and ASOCT in eyes with narrow angles.

The UBM’s ability to visualize the ciliary body, zonules and posterior chamber, regardless of media opacities, good agreement with gonioscopy outweigh its limitations. It provides qualitative and quantitative information regarding the pathophysiology of angle-closure disease which supplements clinical examination.

Anterior segment optical coherence tomography

Anterior segment optical coherence tomography (ASOCT), introduced in 2003, is a non-contact method which uses a 1310 nm diode laser to provide cross-sectional, three-dimensional, high-resolution images (18 µm) images of the anterior chamber. It allows qualitative and quantitative assessment of the anterior segment structures involved in the pathogenesis of glaucoma. The main advantage over UBM is the fact that it is a...
non-contact procedure that can be performed in a sitting position. High-definition and three-dimensional imaging of anterior segment structures with SD OCT provides a definition of ocular tissues comparable to histology.

ASOCT permits optimal visualization of angle structures, including the iris root, angle recess, anterior ciliary body, scleral spur and sometimes the Schlemm’s canal (Fig. 8). Quantitative data provided by ASOCT (Fig. 9) can determine the mechanism of angle-closure disease by revealing the relationship between peripheral iris and trabecular meshwork, configuration of peripheral iris and its level of insertion. Polarization-sensitive OCT with its additional tissue-specific contrast has been used to visualize trabecular meshwork. A variety of ASOCT machines are currently available (Table 2). The scleral spur, used as a landmark, may not always be visible. Sakata et al. reported that scleral spur was detected in 72% of the ASOCT images with difficulty in localization in the superior, inferior quadrants and in quadrants with a gonioscopically closed angle. Algorithms to detect angle parameters independent of scleral
spur have been developed. Various parameters available to quantify the iridocorneal angle are listed in Table 1.

Narayanaswamy et al.14 assessed the diagnostic performance of angle measurements using ASOCT for eyes with narrow angles and found the AOD at 750 µm to be the most useful parameter. Studies have shown good repeatability and reproducibility for measurement of AOD, TISA, ARA and TIA with ASOCT. Apart from AC depth, ASOCT parameters associated with angle closure include decreased ACD, smaller AC width, ACA, ACV, larger lens vault, greater iris thickness, curvature and area. Angle parameters in fellow normal eyes of unilateral APAC had significantly shallower AC, smaller angles, shorter AOD, marked iris root curvature and a greater degree of closure. Nongpuir et al.14 found eyes with angle closure to have thicker lenses with a greater lens vault. Aptel et al.14 reported an increase in iris volume after pharmacological mydriasis in eyes with narrow angles. A reduction in AOD and TISA with physiological mydriasis under low-light conditions has been seen with ASOCT, especially in eyes with narrow ACD.

ASOCT has shown a change in angle parameters following LPI, the patency of LPI, and the detection of extent and location of peripheral anterior synechiae.14 It can document secondary angle closure from a subluxated or dislocated lens. Phacomorphic glaucomas have shallower anterior chamber in the periphery than centrally, with iridotrabecular contact associated with the cataractous lens.

In malignant glaucoma, a uniform shallowing of anterior chamber, marked displacement of anterior segment structures with peripheral iridocorneal touch and forward displacement of lens beneath the iris can be visualized. ASOCT can demonstrate ciliochoroidal detachment and anterior rotation of ciliary body in drug-induced bilateral secondary angle closure. It can image PAS and iridocorneal adhesions in eyes post penetrating keratoplasty with corneal scars.

Radhakrishnan et al. has reported excellent reproducibility of anterior segment parameters with repeated images obtained in the same session with greatest reproducibility for ACD (intraclass correlation coefficient 0.93) in nasal and temporal quadrants (ICC 0.67–0.90). Inferior quadrant showed lower values, whereas the superior quadrant was not imaged. The long-term reproducibility (measured 24 hours apart) showed very good to excellent reproducibility (ICC 0.56–0.93).

Sakata et al.18 revealed a fair agreement (Kappa 0.40, 95% CI 0.35–0.45), whereas Park et al. showed good agreement between van Herrick’s and gonioscopy, but poor agreement with ASOCT. Lavanya et al. using gonioscopy as the reference standard demonstrated a sensitivity and specificity of 0.88 and 0.63, respectively. The low specificity has raised concerns in screening for PAC. Nolan et al.19 showed that gonioscopy detected 44.4% of eyes with angle closure, whereas ASOCT detected 66.7% eyes. High percentage detected by ASOCT could be related to the ability of ASOCT to evaluate angles in dark.

**Swept source OCT**

Swept source OCT (SSOCT) uses a monochromatic tunable fast scanning laser (1310 nm) with scan dimensions of 16 mm × 16 mm × 6 mm achieving high-resolution images of 10 µm (axial) by 30 µm (transverse). With an improved high-speed scanning of 30,000 A scans/second the ACA can be imaged 360° in 128 cross sections (each with 512 A scans) in 2.4 seconds. A three-dimensional display of iris and ACA can be generated with a three-dimensional reconstruction of individual frames.

It measures biometric parameters similar to those measured using ASOCT (Fig. 10). It can visualize both the SS and Schwalbe’s line in a high-resolution scan mode improving the precision of measurements and detection of angle closure. TISA was found clinically superior to AOD and ARA, as it includes the entire iris contour and excludes area posterior to SS, thus representing the angle filtering area. The iridotrabecluar contact index (ITC) is a quantitative measure of the extent of angle closure across 360° of the.
angle expressed as a percentage.\textsuperscript{20} It has a moderate agreement and good diagnostic performance for angle closure with gonioscopy as reference.

**Challenges**

Inability of the ASOCT to visualize ciliary sulcus and posterior border of ciliary body limits its use in plateau iris and opaque media. Poor identification of SS has been noted in 25% of images. ASOCT is less likely to obtain a good image of superior and inferior angles due to eyelids. Differentiation between appositional and synechial angle closure is not possible due to the inability to perform indentation. Advantages include non-contact technique, higher image resolution, and more precise localization of the position of interest for evaluation compared with UBM. The major differences between the two imaging modalities are highlighted in Table 3.

**Goniophotography**

The advantage of gonioscopy includes low cost, visualization of the angle details, ability to indent to differentiate appositional from synechial closure. Goniophotography using a slit lamp-mounted camera can be used to obtain direct images of the angle. However, it is challenging to obtain good-quality images. Gonioscopes with automated 360° goniophotography are under development.

**EyeCam**

EyeCam provides high-resolution colour images of the ACA using 120° and 130° wide-field lenses. It has a good degree of agreement with clinical gonioscopy, with moderate sensitivity and specificity for detecting angle closure.\textsuperscript{21} Limitations include cost, inability to perform indentation, effect of illumination, non-visualization of corneal wedge or lightly pigmented trabecular meshwork, learning curve and gravity due to supine position. It has moderate to poor reproducibility. Multiphoton lasers and Axicon system (bessel beam microscopy) are under investigation and have been used in porcine eyes to obtain high-resolution images of the ACA.

**Scanning peripheral ACD analyser**

Scanning peripheral ACD analyser (SPAC), using slit lamp-based photography, measures ACD at various points in 0.67 seconds at 0.4 mm intervals with a reported sensitivity and specificity of 0.89.
and 0.80, respectively, for identifying PAC and PACS in a population-based screening. Measurements correlate strongly with angle assessment by modified van Herick (sensitivity and specificity of 0.85 and 0.73), UBM and ASOCT for identifying narrow angles. It has a similar sensitivity and specificity as slit lamp-based ASOCT for identifying subjects at risk for PAC in a hospital-based population.22, 23

However, it provides information only about peripheral ACD.

**Pentacam**

Pentacam allows non-contact quantification of the AC parameters using a rotating Scheimpflug camera to create a three-dimensional image. It can measure ACD (corneal endothelium to anterior lens surface), ACA, ACD and ACV, respectively, with a correlation coefficients of 0.65, 0.85, and 0.81 with gonioscopy. However, this was less than correlation of UBM with gonioscopy.0.81 with gonioscopy. However, this was less than correlation of UBM with gonioscopy. However, this was less than correlation of UBM with gonioscopy. However, this was less than correlation of UBM with gonioscopy.24, 25

Limitations include inability to identify the SS in many cases due to light scattering affecting angle reproducibility, no direct visualization of ACA, and difficulty in obtaining images in children, elderly, and patients with nystagmus.

**Conclusion**

Advances in imaging technology provide invaluable information for the assessment of the anterior segment of the eye aiding in both diagnosis and management of angle-closure disease. However, neither technique is a substitute for detailed clinical examination but a useful adjunct providing information which complements gonioscopy.

**References**

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