Using Anterior Segment Optical Coherence Tomography (ASOCT) Parameters to Determine Pupillary Block Versus Plateau Iris Configuration

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Précis: The potential parameters for differentiating pupillary block (PB) from plateau iris configuration (PIC) on anterior segment optical coherence tomography (ASOCT) are lens/pupil size parameters and angles. Further study is needed to determine a landmark peripheral to the centroid of the iris.

Purpose: Investigate anterior segment parameters to distinguish between 2 mechanisms of angle closure, PB and PIC, using swept-source Fourier domain ASOCT.

Patients and Methods: Retrospective ASOCT images from narrow angle eyes were reviewed. PIC was defined either by ultrasound biomicroscopy and/or clinically when an iridoplasty was performed. Images were read by a masked reader using Anterior Chamber Analysis and Interpretation software to identify scleral spur landmarks and calculate anterior chamber, peripheral angle, iris size, iris shape, and lens/pupil size parameters. ASOCT parameters were summarized and compared using the 2-sample t test. Thresholds and area under receiver operating characteristic curve were calculated using regression analysis.

Results: One hundred eyes (66 PB and 34 PIC) of 100 participants were reviewed. Of all ASOCT parameters, iris length in each quadrant, pupil arc, lens/pupil parameters (pupil arc, lens vault, and pupil diameter), all pupillary margin-center point-scleral spur landmark (PM-C-SSL) parameters, and all except superior central iris vault parameters were significantly different between PB and PIC. On threshold evaluation, lens/pupil parameters had the greatest area under receiver operating characteristic curve values (0.77 to 0.80), followed by PM-C-SSL angles (0.71 to 0.75).

Conclusions: We propose that the pupil size parameters and PM-C-SSL angle are the most reliable novel ASOCT parameters to distinguish between PB and PIC eyes. These parameters do not rely on the visibility of the posterior iris surface, which is difficult to identify with ASOCT, but may be ambient lighting dependent.

Key Words: anterior segment optical coherence tomography, plateau iris, pupillary block, angle closure

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The primary angle closure spectrum of disease (PACSD) occurs as a result of predisposing anatomical structures in the anterior chamber, including a narrow anterior chamber angle, a thick peripheral iris, and a thick and anterior lens. There are 2 common mechanisms in PACSD: pupillary block (PB) and plateau iris configuration (PIC). In PB, contact between the iris and lens at the pupillary margin (PM) increases resistance to the flow of aqueous into the anterior chamber. When the pressure in the posterior chamber exceeds that in the anterior chamber, the peripheral and mid-peripheral iris moves forward and contacts the trabecular meshwork (TM), causing additional aqueous blockage at the TM. This can be prevented by creating a patent iridotomy or iridectomy. In PIC, the ciliary body is anteriorly positioned or rotated, resulting in anterior displacement of the peripheral iris into the angle and blocking aqueous from exiting the anterior chamber through the TM, despite the absence of PB. Several studies have shown that while PB can be effectively eliminated by laser peripheral iridotomy (LPI),1,2 the peripheral angle remains occludable after LPI in eyes with PIC,3 thereby, requiring an additional treatment to correct the angle anatomy. Therefore, the choice of treatment is different between these 2 mechanisms.

Classic teaching is that PIC cannot be diagnosed without first performing an iridotomy or iridectomy to rule out PB. Although gonioscopy remains the clinical gold standard for examining anterior chamber angle structures, it is subjective, descriptive, and a difficult skill to learn, which results in only moderate agreement on angle grading between examiners.3,4 In addition, there is no definitive criteria for diagnosing PIC on gonioscopy without a patent iridotomy or iridectomy present.

Alternatively, ultrasound biomicroscopy (UBM) is an imaging tool that enables objective and quantitative examination of anterior chamber structures as well as structures behind the iris, such as the position of the ciliary processes. However, the technique is performed under contact with the eye, making it difficult to obtain reproducible images. Thus, the diagnosis of PIC is usually based on the subjective interpretation of anteriorly positioned ciliary processes obliterating the ciliary sulcus.

Advances in imaging have resulted in our ability to evaluate the anterior chamber quantitatively. Dedicated
anterior segment optical coherence tomography (DASOCT) uses a 1310 nm central wavelength, reducing light scatter through tissue such as the sclera and iris, and allowing deeper image penetration of the peripheral angle as compared with the 840 to 870 nm wavelength used with commercially available devices not dedicated to imaging the anterior segment. The newer generation Fourier domain DASOCT uses swept-source technology, which provides higher image acquisition speed (30,000 A-scans per second) compared with time-domain DASOCT (2048 A-scans per second). The dramatic improvement in image speed reduces motion artifacts, increases image resolution, and allows for rapid anterior chamber angle assessment 360 degrees.

It is important to develop a diagnostic tool for PIC so it can be identified without having eyes first undergoing iridotomy or iridectomy, as this could potentially prevent the patient from having to undergo an unneeded procedure. More recent diagnostic definitions have included ultrasonic biomicroscopic findings of anterior rotation and flattening of the ciliary body and the lack of a ciliary sulcus. Unfortunately, UBM is not widely available and is a difficult, technician-dependent imaging modality. As DASOCT has become more accessible, its simplicity of use and less dependence on technician skill might make it a viable imaging alternative to differentiate the 2 mechanisms of angle closure without iridotomy or iridectomy.

The purpose of this study is to investigate potential anterior segment optical coherence tomography (ASOCT) parameters that can be used to distinguish between PB and PIC before iridotomy or iridectomy.

PATIENTS AND METHODS

This retrospective cohort study reviewed 4 prospective cohort studies previously conducted at the Robert Cizik Eye Clinic of the Ruiz Department of Ophthalmology and Visual Science at the McGovern Medical School at The University of Texas Health Science Center at Houston (UTHSCH). The UTHSCH Committee for the Protection of Human Subjects determined that this study was exempt from review and approved it. All research adhered to the Declaration of Helsinki and was HIPAA compliant, and data collection conformed with all relevant laws.

Participants

Participants enrolled in the 4 previous IRB-approved prospective studies were reviewed. Participants were 18 years of age and older. All eyes were phakic and underwent DASOCT imaging and gonioscopic examination within 2 weeks before imaging. Eyes were excluded if they had (1) open angles as determined by gonioscopic examination; (2) anterior segment abnormalities that could affect the quality of images such as significant corneal opacity; (3) lid obstruction or eye movement artifact that prevented proper imaging; and (4) been dosed with any medication that may have affected angle anatomy within a month before imaging (ie, pilocarpine or atropine). When both eyes qualified, 1 eye was randomly selected for the study.

Two of these 4 studies recruited only narrow angle participants for imaging before receiving laser iridotomy (26 eyes) or cataract extraction (16 eyes). Patients with nanophthalmos (axial length <18 mm) were excluded from Melese and colleagues. From the third study of 86 participants, all 24 narrow angles were included. The fourth study recruited both open and narrow angles eyes, and all 34 narrow angle eyes were included in the current study.

Demographics (age, race, and sex), intraocular pressure (IOP), and number of IOP-lowering medications were recorded for each eligible patient. IOP was measured by Goldmann applanation tonometry.

Gonioscopy Examination

Gonioscopy was performed by 1 of 3 experienced glaucoma specialists (RMF, NPB, LSB) using a Posner 4-mirror lens at high magnification (×10), with the eye in the primary position of gaze under the lowest possible ambient lighting conditions by turning off all ambient light sources and closing the door of the exam room. Gonioscopic examination was first performed without indentation, with care taken to minimize light from the slit lamp beam from entering the pupil. Peripheral angles were graded using the Spaeth grading system.

All study eyes had narrow angles (A or B) based on the deepest structure visible. For angles graded as C, where the scleral spur was partially visualized, the classification as narrow or open was based upon the clinical decision of whether treatment was required. Criteria clinically invoked to determine if a grade C eye needed treatment were presence of peripheral anterior synechiae, pigment smudging anterior to the TM, or clinical symptoms suggestive of intermittent angle closure.

Classification of PB and PIC

PB was defined as a narrow angle with the presence of ciliary sulcus and space between the iris and lens on UBM. PIC was defined either by a continued narrow angle with a patent LPI or UBM images that demonstrated a forward (anterior) rotation of the ciliary body or absence of ciliary sulcus.

Anterior Segment Optical Coherence Tomography and Image Reading Procedure

Instrument details for the CASIA SS-1000 (Tomey, Nagoya, Japan) have been previously reported.9,10,13 Software and image analysis procedures have also been previously described.9,10,13,14 Briefly, eyes were imaged using 3D mode with the angle analysis scan option in a dark room with an only light source from the computer monitor. The raw image files were imported into the Anterior Chamber Analysis and Interpretation software (ACAI; Houston, TX). The ACAI software divides 128 2D images into 8 panels, 16 images per panel (11.25 degrees between 2 consecutive angles). The images were read by an experienced reader (A.Z.C.) whose reliability has been previously reported.13 The reader was masked to the gonioscopic grading. The reader marked the scleral spur landmarks (SSLS) on each image in the first panel (this panel includes horizontal and vertical meridian images), and then the ACAI software automatically detected corneal and iris edges. If the edges of the cornea and iris were not accurate, the reader manually adjusted the intensity and, if that was not successful, manually adjusted the edge margins. Once the readers had completed and saved the interpreted results of the first panel, ACAI interpolated the SSLs in the remaining panels that may have affected angle anatomy within a month before imaging (ie, pilocarpine or atropine). When both eyes qualified, 1 eye was randomly selected for the study.

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TABLE 1. Definition of Anterior Chamber Structure Landmarks

| Landmark                  | Definition                                                                 |
|---------------------------|-----------------------------------------------------------------------------|
| Scleral spur landmark (SSL) | Point where there is a change in curvature in the corneoscleral-aqueous interface, often appearing as an inward protrusion of the sclera |
| SSL-to-SSL line           | Line connecting 2 SSLs on a meridian image                                   |
| Center point (C)          | Midpoint of SSL-to-SSL                                                     |
| Visual axis               | Line drawn from C perpendicular to SSL-to-SSL                               |
| Pupillary margin (PM)     | Point at the most inner border of the iris that forms the edge of the pupil |
| Centroid of iris (CI)     | Point at the centroid of iris cross-sectional area                          |
| Anterior lens surface (ALS) | Line draw along the anterior surface of lens between 2 PMs                  |
| Anterior iris surface (AIS) | Line draw along the anterior surface of iris                               |
| Posterior iris surface (PIS) | Line drawn along anterior surface of the demarcation line created by the reflection of the posterior layer of pigment epithelium |

ASOCT Parameters

The anterior chamber structure landmarks are defined in Table 1 and Figure 1. The landmarks include SSL, SSL-to-SSL line, center point of SSL-to-SSL line (C), PM, centroid of iris (CI), and others as pictured. The ASOCT parameters derived from these anterior chamber structure landmarks are described in Table S1, Supplemental Digital Content 1 (http://links.lww.com/IJG/A466) and illustrated in Figures 1–4. The anterior chamber parameters [anterior chamber depth (ACD), anterior chamber width, and anterior chamber volume] and angle parameters (angle opening distance, trabecular-iris space area, and trabecular-iris circumference volume) have been previously defined and widely used in previously published ASOCT and UBM studies. Some iris parameters (length, area, and volume), pupil diameter (PD), and lens vault (LV) have also been studied previously. The parameters newly defined in this study are length of central iris vault (CIV), pupillary margin vault (PMV), central iris thickness (CIT), inner iris plateau (IIP), pupillary arc (PA), and PA area, as well as angles from various iris landmarks, such as the angle between the PM-to-SSL line and the SSL-to-SSL line (PM-C-SSL angle), the angle between CI-to-SSL line and the SSL-to-SSL line (CI-SSL-C angle), the angle between the CI-to-SSL line and the PM-to-SSL line (CI-SSL-PM angle), and the angle between the PM-to-C line and the SSL-to-SSL line (PM-SSL-C angle).

These ASOCT parameters were calculated automatically by the ACAI software after performing a correction for refraction.

Data Analysis

Data collected were summarized by mean (± SD) or by frequency (%). All ASOCT parameters were compared between PB and PIC eyes using the 2-sample t test. As there were 60 ASOCT measurements studied and compared in this study, all P-values obtained from the 2-sample t test, P < 0.05 were adjusted by the Holm-Bonferroni method to control the error rate.

Logistic regression analysis with Youden optimal thresholds for each significant ASOCT parameter was performed to estimate the area under the receiver operating characteristic (AUROC) curve and determine the threshold cut off value and corresponding sensitivity and specificity.

An adjusted P-value (P*) <0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 for Windows (Cary, NC).

RESULTS

Participants

One hundred participants, 66 (66%) PB and 34 (34%) PIC, were included in the study. Seventy-nine (79%) were females, and the average age was 59.5 years (± 9.8; range, 39 to 82 y). Of 97 participants reporting race/ethnicity, 45 (46%) participants were white, 22 (23%) black, 16 (16%) Hispanic, and 14 (14%) Asian. There were no significant differences in sex (P = 0.55) between the PB and PIC groups (Table S2, Supplemental Digital Content 2, http://links.lww.com/IJG/A467). However, the PIC group was significantly younger than the PB group (P = 0.013). There were also race/ethnicity differences between the 2 groups (P = 0.027, Table S2, Supplemental Digital Content 2, http://links.lww.com/IJG/A467). All patients from these studies were phakic, and only 3 had previous PI.
Treated IOPs were similar between PB eyes [15.7 ± 3.7 mm Hg with 12 eyes (18%) on IOP-lowering medications] and PIC eyes [16.3 ± 4.3 mm Hg with 7 eyes (21%) on IOP-lowering medications] (P = 0.50, Table S2, Supplemental Digital Content 2, http://links.lww.com/IJG/A467).

Gonioscopy grading was significantly different between PIC and PB eyes (P = 0.001), with more eyes graded as C in the PIC group despite being considered clinically occludable.

Comparing ASOCT Parameters

Of 60 ASOCT parameters evaluated, only 16 parameters were statistically significant after adjusting for multiple tests: iris lengths (n = 4), PM-SSL-C angles (n = 4), pupillary parameters (PDs, PAs, and PA area, n = 5), and CIVs nasal, temporal, and inferior (n = 3, Table S3, Supplemental Digital Content 3, http://links.lww.com/IJG/A468).

Anterior Chamber and Peripheral Angle Parameters

None of the 4 anterior chamber and 9 peripheral angle parameters were significantly different between the 2 groups (*P ≥ 0.16, Table S3, Supplemental Digital Content 3, http://links.lww.com/IJG/A468).

Iris Size Parameters

When comparing 13 iris size parameters, including length, thickness, area, and volume, between the 2 groups, only the 4 iris lengths were significantly different between the 2 groups (*P < 0.022). Iris length in PIC eyes was significantly shorter than in PB eyes.

Pupil Size Parameters

All 5 pupil size parameters, including PD, PA, and PA area, were significantly different between the 2 groups (*P ≤ 0.001). Pupil size was significantly larger in PIC eyes compared with PB eyes.

Iris Shape Parameters

The CIV in PB eyes was significantly greater than in PIC eyes for all quadrants, except the superior quadrant (*P = 0.030 nasally, *P = 0.049 temporally, and *P = 0.027 inferiorly). As expected, mean IIPs were 45% to 52% smaller in PIC eyes nasally, superiorly, and temporally than in PB eyes. However, due to high variability (coefficient of variation range 109% to 267%), IIPs were not significantly different between the 2 groups (*P > 0.83). No differences were found for CI-SSL-C, PM-SSL-C, and CI-SSL-PM angles.

Lens Position Parameters

The PM-SSL-C angles were significantly different between the 2 groups in all 4 quadrants (*P ≤ 0.002). PM-SSL-C angles in PIC eyes were wider than PB eyes with a range of 33% inferiorly to 40% temporally. LV was not significantly different between the 2 groups (P = 0.17).

Threshold for Distinguishing PIC From PB

The estimated AUROCs and optimal threshold cutoff values for the 16 significant ASOCT parameters (*P < 0.05) are shown in Table S4, Supplemental Digital Content 4 (http://links.lww.com/IJG/A469). Lens/pupil size parameters had the greatest AUROC values (0.77 to 0.80), followed by

FIGURE 2. Anterior segment optical coherence tomography parameters. Illustration of anterior chamber structure parameters (see Table S1, Supplemental Digital Content 1, http://links.lww.com/IJG/A466 for further definition of angle parameters).

FIGURE 3. Anterior chamber measurements angle opening distance (AOD), trabecular-iris space area (TISA) at 750 μm from the scleral spur landmark (SSL).13
PM-SSL-C angles (0.71 to 0.75). At the optimal threshold cut off values, the sensitivity was high in iris size (0.85 to 0.97) and lens/pupil size (0.85 to 0.97) parameters. The specificity was generally low (≤0.7), with highest specificity found in PM-SSL-C angles (0.59 to 0.70) and lens/pupil size (0.58 to 0.68) parameters (Table S4, Supplemental Digital Content 4, http://links.lww.com/JIG/A469).

DISCUSSION

PACSD occurs by 2 different mechanisms: PB and PIC. Current diagnosis of PIC is made based on the degree of angle occludability despite absence of PB, which requires the patient to undergo a diagnostic surgical procedure that may or may not be therapeutic. Although gonioscopy is considered the gold standard for diagnosing occludable angles, it is subjective, descriptive, and difficult to perform, and examiners at most moderately agree on their findings.4 UBM has the advantage in that it can visualize behind the iris to determine anterior rotation of the ciliary body, thereby diagnosing PIC even in the presence of PB. However, UBM is a contact technique that is technician-dependent, thereby making reproducibility of images difficult.

DASOCT is a noncontact technique that results in highly reproducible images and quantitative results. Anterior chamber angle parameters obtained from DASOCT, including angle opening distance, trabecular-iris space area, and trabecular-iris circumference volume, have been studied in terms of repeatability, reproducibility, and agreement;5,7,13 and used to evaluate angle anatomy after LPI9 and lens extraction.10 Threshold values for these angle parameters have been determined and validated for discriminating narrow angles, which are more variable in the clinical setting than laboratory settings.

In previous studies by Moghimi and colleagues and Verma and colleagues,21-23 there was a significant difference in iris thickness 750 µm (IT750) between the PB and PIC groups but not the IT2000 using ASOCT. Similarly, CIT, which is ∼1700 to 1800 µm from SSL (approximately half of iris length), was not significantly different between the 2 groups. This is probably because the hump in plateau iris is in the peripheral, rather than center, of the iris. However, in our experience we have found that the IT750 measurement is not a reliable measurement to use with ASOCT imaging, because the posterior layer of the pigmented epithelium of the peripheral iris is often not well defined or visualized, especially when the posterior iris is in contact with ciliary processes.

Moghimi and colleagues investigated iris curve (I-curve), defined as “the perpendicular distance from a line between the most central (equivalent to PM) to the most peripheral points of the iris pigment epithelium to the

Anterior Chamber Parameters

Our study did not demonstrate a difference in ACD between PB and PIC. There are conflicting reports on comparing ACD between PB and PIC: some studies showed that PIC eyes were shallower24,25 some deeper,26 and others no difference.20-23 The conflicting results reported may be due to some of the eyes being classified as PIC by UBM having not had a prior LPI and due to a mixed mechanism of angle closure. Detecting this mixed mechanism is the topic of current studies.

Iris Size, Pupil, and Lens Position Parameters

This is the first study to report quantitative iris shape, lens, and pupil parameters distinguish between PB and PIC using ASOCT imaging. Previously studied ASOCT parameters have been useful for distinguishing between open and closed angles but have been unable to distinguish between PIC and PB.21 These newly defined ASOCT parameters that are able to distinguish between PIC and PB include a smaller PM-SSL-C angle, iris length, and CIV in 3 quadrants, as well as larger lens/pupil size, measured by PD, pupil arc, and pupil arc area under standardized lighting conditions. Pupil and iris length measurements are dependent on ambient lighting conditions, which are more variable in the clinical setting than laboratory settings.

The diagnostic abilities of DASOCT for PB and PIC have not been determined and compared with gonioscopy and UBM. Our study evaluated DASOCT parameters to distinguish between PB and PIC in PACSD eyes.
posterior iris surface at the point of greatest convexity." They found that the I-curve was unable to distinguish between the 2 groups.27,25 This could be because the I-curve only measures the maximum iris convexity without specifying the location where this convexity occurred. For example, the greatest iris convexity may be similar between the 2 groups, but if it occurs at the central iris for PB and the peripheral iris for PIC, it would not be differentiated. A similar parameter which attempts to describe the shape of central half of iris in our study is the IIP (difference of the CIV and PMV), which was also not significantly different between groups, confirming this finding.

The central LV showed no difference between groups. However, CIV at certain quadrants could differentiate between PIC and PB eyes. Perhaps a better measure would be the lens thickness, but this cannot be performed by the ASOCT instrument used in this study and was therefore not evaluated.

The CIV measurements have more to do with the shape, size, and insertion of the iris and, thus, are more likely to be impacted by the differences in the structure of PB and PIC eyes. It is interesting that 3 CIVs were significantly different but not their corresponding angles, CI-SSL-Cs. This is likely due to the angle depending not only on the vault parameters but also on their location, which is related to the shape and size of the iris. If the CIVs are located more peripherally in the iris, then the vault angles are also altered. There was also a difference in the location of these vault parameters in PB and PIC eyes. Thus, the vault angle parameters are similar between the 2 groups.

We propose that the pupil size parameters and PM-C-SSL angle are the most reliable, 2 novel ASOCT parameters to help distinguish between PB and PIC eyes. These parameters do not rely on the visibility of the posterior iris surface, which is difficult to identify with ASOCT. In addition, the pupil size parameters might have a higher sensitivity to detect the presence of PIC eyes. We propose that the 2 mechanisms, PB and PIC, are often found in combination. Sensitivity is related to our ability to detect a partial PIC. This threshold should not be used as a differentiator, but more as an identifier of the presence of PIC. It does not rule out the presence of PB; it identifies a component of ciliary body rotation.

Pupil size can be affected by such factors as lighting conditions, age, and pilocarpine use. We used standardized lighting conditions, and none of our patients were using pilocarpine. Although pupillary size does decrease with age, the age differences between the PIC and PB groups were within 5 years. With a 10-year age difference, pupillary size does not change by as big of a difference found between the PB and PIC groups.27 It is unknown whether other technology that measures pupil size would provide the same results.

Limitations

Limitations of this study include its retrospective nature, the ability to visualize the posterior layer of pigment epithelium with ASOCT at the peripheral iris, exclusion of axial length measurements, and the small sample size. The inability to visualize the posterior layer of pigment epithelium affects all ASOCT machines, which is why we propose using the pupil size parameters and PM-SSL-C angle as the most reliable measurements to distinguish between the 2 conditions. Although axial length may be an interesting parameter, data were only available for 1 subgroup of eyes and not measured with an ASOCT and outside the scope of this paper. Despite finding that lens/pupil size parameters had the greatest AUROC values (0.77 to 0.80), followed by PM-SSL-C angles (0.71 to 0.75), the corresponding optimal threshold values for these parameters should be verified by an independent data set.

CONCLUSIONS

The potential parameters for differentiating PB from PIC on ASOCT are lens/pupil size parameters and PM-C-SSL angles. Further study is needed to determine a landmark peripheral to the centroid of the iris. The iris may plateau peripheral to this centroid in both groups, so identifying a new peripheral landmark may allow for further differentiation between the groups.

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