

Ultrasound Biomicroscopy Dark Room Provocative Testing: A Quantitative Method for Estimating Anterior Chamber Angle Width

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Purpose: To describe a quantitative method for measuring the iridocorneal angle recess area, and, using this, to evaluate factors associated with appositional angle-closure during dark room provocative testing using ultrasound biomicroscopy (UBM).

Methods: All patients (178 patients, 178 eyes) with clinically narrow angles referred for UBM dark room provocative testing between September 1996 and March 1998 were enrolled in this study. Images of the inferior quadrant of the angle taken under standardized dark and light conditions were analyzed. The angle recess area (ARA) was defined as the triangular area demarcated by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium drawn from a point 750 μm anterior to the scleral spur to the iris surface. ARA, and acceleration and y-intercept of the linear regression analysis of the ARA were calculated. In the linear regression formula, $y = ax + b$, the acceleration a describes the rate at which the angle widens from the scleral spur; the y-intercept b describes the distance from the scleral spur to the iris.

Results: Under dark conditions, the angles in 99 patients (55.6%) showed evidence of appositional angle-closure during testing. ARA (0.11 ± 0.04 vs. 0.15 ± 0.05 mm^2 , $P < .0001$, Student t -test), acceleration a (0.22 ± 0.15 vs. 0.26 ± 0.17 , $P = .068$), and y-intercept b (66 ± 46 vs. 92 ± 47 μm , $P = .0003$) were smaller in eyes that were occluded. In the eyes that were not occluded, y-intercept b showed no significant difference between light and dark conditions ($P = .1$, paired t -test), while acceleration a did ($P < .0001$). In the eyes that were occluded, both decreased significantly under dark conditions ($P < .0001$).

Conclusions: The ARA linear regression formula provides useful quantitative information about angle recess anatomy. The more posterior the iris insertion on the ciliary face, the less likely the provocative test will be positive. **Jpn J Ophthalmol 1999;43:526–534** © 1999 Japanese Ophthalmological Society

Key Words: Angle-closure, glaucoma, provocative test, quantitative method, ultrasound biomicroscopy.

Introduction

Eyes with appositional angle closure are at risk for progressive trabecular damage, elevated intraocular pressure (IOP), peripheral anterior synechiae, and acute angle-closure glaucoma. It is generally agreed that eyes with occludable iridocorneal angles should undergo laser iridotomy.^{1,2}

Gonioscopy has been the most important step in assessing the iridocorneal angle. Accurate assess-

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ment of the potential for occlusion requires gonioscopy in a completely darkened room to allow the pupil to dilate physiologically. Nevertheless, being a subjective examination, gonioscopy does not guarantee determination of whether an angle is occludable, and even glaucoma subspecialists have disagreed as to the grading of a particular angle and its occludability.³ To compensate for this, a variety of provocative tests have been described for the detection of potential appositional angle closure in patients with normal vision and asymptomatic narrow angles.

Nonpharmacologic tests have been regarded as more accurately reproducing natural conditions than those that involve stimulating the sphincter and dilator muscles. Dark-room and prone dark-room provocative tests, considered the most physiologic of the provocative tests, have been much less frequently used since the advent of laser iridotomy. These tests require a dedicated room, and still rely on gonioscopy. An objective test for angle occludability would be useful and desirable.

With high frequency ultrasound biomicroscopy (UBM), high resolution imaging of the anterior segment in vivo can be attained, and this method is ideally suited for evaluation of the anatomy and pathophysiology of anterior segment diseases.⁴ In 1995, Pavlin et al reported the use of UBM as a helpful method in dark-room provocative testing to demonstrate angle occludability in a small series of patients.⁵ Sakuma et al⁶ performed UBM under dark-room conditions and reported two anatomic patterns of appositional angle closure. They subsequently found the topology of the iris root to be related to the pattern of the appositional angle closure.⁷

We have developed a software program to measure the iridocorneal angle recess area quantitatively, taking into account the topographic configuration of the anterior iris surface. We have used this program to evaluate factors associated with appositional angle closure during UBM dark-room provocation testing.

Materials and Methods

All patients with clinically narrow angles referred for UBM dark-room provocative testing at the New York Eye and Ear Infirmary between September 1996 and March 1998 were enrolled in this study. We defined clinically narrow angles as those angles regarded by the examiner as being grade 1 or 2 using the Shaffer grading system. Patients who had undergone intraocular surgery, including laser treatment; who used topical drugs affecting pupillary diameter;

and who had a history of ocular diseases (except for cataract) or trauma that may have changed the configuration of the angle were excluded. If both eyes qualified for the study, the right eye was tested. All eyes had open iridocorneal angles on both gonioscopy and UBM under light conditions.

Written informed consent was obtained from all subjects using a consent form approved by the Institutional Review Board of the New York Eye and Ear Infirmary.

Ultrasound biomicroscopy (Paradigm Medical Industries, Salt Lake City, UT, USA) was performed with a 50 MHz transducer, lateral and axial physical resolution of approximately 50 μm and 25 μm , respectively, and penetration depth of 4–5 mm. Scanning was performed in the supine position and the probe was manually moved perpendicular to the structure to be scanned. Fixation and accommodation were held constant by having the patient fixate with the fellow eye on a ceiling target.

Initial image acquisition was performed under bright illumination. For each patient in this study, one image taken of the inferior quadrant of the angle, which is usually wider than the superior quadrant of the angle, was saved and used for the analysis. The process was repeated under dark illumination following 3 minutes of dark-room adaptation. A positive provocative test was defined as the presence of iris apposition to the trabecular meshwork under dark conditions.

Captured image files were transferred as PCX formatted data via floppy disks into an IBM PC. Images were analyzed using a software program of our own design that was developed for this study and is used with Microsoft Windows 95.

The position of the scleral spur was defined as the innermost point of a line separating the ciliary muscle and scleral fibers, and localized on the UBM image by the observer. The angle recess area (ARA) was defined as the triangular area bordered by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium drawn from a point 750 μm anterior to the scleral spur to the iris surface (Figure 1).⁸ ARA was automatically calculated following localization of the scleral spur by the observer.

During the calculation of ARA, the program measures the angle opening distance (AOD) from the base of the angle recess to 750 μm anterior to the scleral spur, along the entire endothelial length. This series of contiguous parallel AOD measurements was used to perform linear regression analysis of the sequential AOD measurements. As a result of this linear

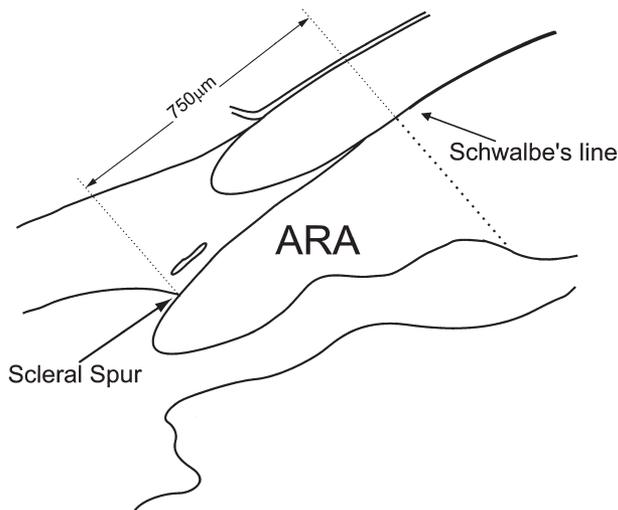


Figure 1. Angle recess area (ARA) was defined as triangular area bordered by anterior iris surface, corneal endothelium, and line perpendicular to corneal endothelium drawn from point 750 μm anterior to scleral spur to iris surface.

regression analysis ($y = ax + b$), we can obtain two data, acceleration and the y-intercept, where a is the acceleration and b is the y-intercept (Figure 2).

The Student t -test and paired t -test, respectively, were used to compare each parameter between the two groups, the eyes that occluded during testing and the eyes that did not, before and after dark-room provocation.

The reproducibility of the ARA measurement was assessed by evaluation of the proportional relationship of the standard deviation of the repeated measurements to the mean of those measures [ie, coefficient of variation (CV)]. A $\text{CV} < 10\%$ was considered indicative of good reproducibility. Two observers performed independent ARA measurements 10 times on each image of 10 subjects (5 narrow-angle and 5 open-angle subjects) in random order on 10 separate occasions. A measurement of intraobserver reproducibility was then obtained by calculating the CV of the results for each of the two observers. Interobserver reproducibility, obtained by evaluation of the differences in the mean between observers, was evaluated by the Student t -test.

Results

All 178 eyes tested had anatomically open angles during UBM under light conditions. During dark-room provocation, 99 eyes (55.6%) were occluded (Group I) and 79 eyes (44.4%) were not (Group II eyes) (Table 1). Age, race, gender, refractive error, and axial length were similar in both groups.

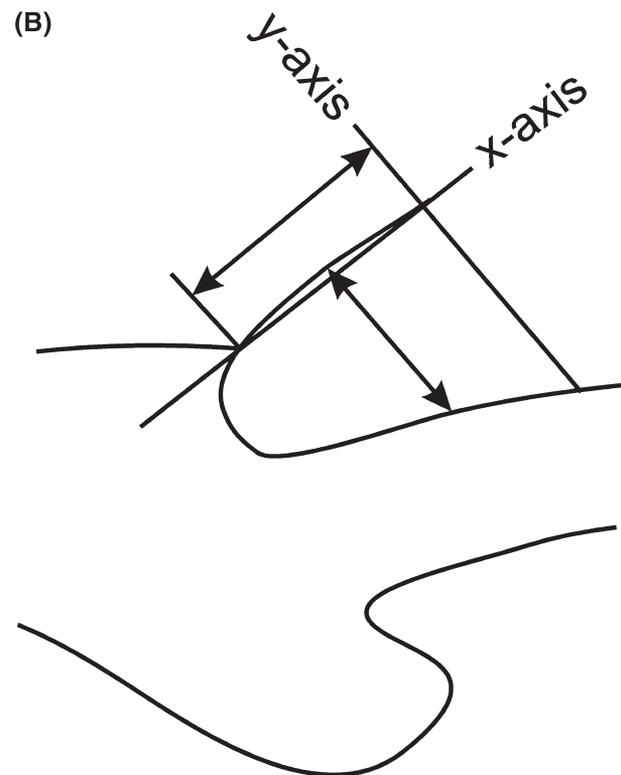
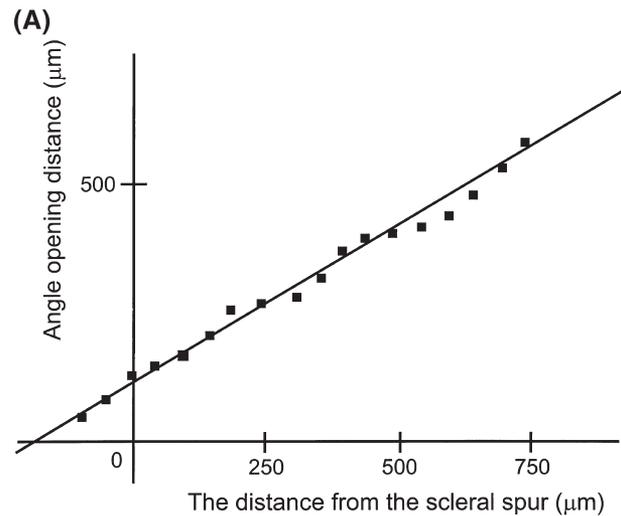


Figure 2. (A) Linear regression analysis plot graph has distance from scleral spur along corneal endothelial surface as x-axis and measurement of angle opening distance as y-axis. (B) Interpretation of meaning of linear regression analysis onto schematic image of angle.

ARA and y-intercept b were significantly smaller in group I eyes than in group II eyes under light conditions (Table 2). The difference in acceleration a between the two groups under light conditions did not reach significance ($P = .068$).

Table 1. Demographic Data

Parameters		Group I	Group II	<i>P</i>
Gender	Male	23	27	.12*
	Female	76	52	
Race	White	86	66	.11*
	Black	5	5	
	Hispanic	2	7	
	Asian	6	1	
Age (y)		63.8 ± 12.1	65.7 ± 11.2	.31 [†]
Range		36 – 94	43 – 92	
RE (D)		1.15 ± 1.81	0.82 ± 2.05	.34 [†]
Range		–4.25 – 6.75	–3.75 – 6.50	
AL (mm)		22.69 ± 1.02	23.21 ± 1.25	.21 [†]
Range		21.54 – 25.71	21.64 – 25.48	

RE: refractive error, AL: axial length.

*Chi-square.

[†]Student *t*-test.

ARA, acceleration *a* and y-intercept *b* of group I decreased significantly under dark conditions (*P* < .0001, paired *t*-test). ARA and acceleration *a* of group II decreased significantly under dark conditions (*P* < .0001), whereas the y-intercept *b* decreased, but not significantly (*P* = .10) (Table 3). Representative images show angle narrowing in both groups in the dark, but for group II, the y-intercept *b* did not change (Figure 3).

Reproducibility Study

Mean intraobserver measurement reproducibility was high for any single image (mean coefficient of variation, 2.47%, 1.67%, and 5.42% for ARA, acceleration, and y-intercept) (Table 4). Interobserver reproducibility was high for two subjects, but less so for the remaining subjects and was related to the small standard deviation of both observers (Table 5). The actual number of measured cross-sectional areas was similar for each observer.

Discussion

A predictive and objective provocative test to elicit angle closure has been a long-sought goal.

Table 2. Comparison of Variables Between Groups I and II

Variables	Group I	Group II	<i>P</i> *
ARA (mm ²)	0.11 ± 0.04	0.15 ± 0.05	<.0001
Acceleration <i>a</i>	0.22 ± 0.15	0.26 ± 0.17	.068
Y-intercept <i>b</i> (μm)	66 ± 46	92 ± 47	.0003

ARA: angle recess area.

*Student *t*-test.

Table 3. Comparison of Variables Under Light and Dark Conditions

Group	Variables	Light	Dark	<i>P</i> *
Group I	ARA (mm ²)	0.11 ± 0.04	0.03 ± 0.03	<.0001
	Acceleration <i>a</i>	0.22 ± 0.15	0.07 ± 0.15	<.0001
	y-intercept <i>b</i> (μm)	66 ± 46	8 ± 47	<.0001
Group II	ARA (mm ²)	0.15 ± 0.05	0.11 ± 0.04	<.0001
	Acceleration <i>a</i>	0.26 ± 0.17	0.15 ± 0.15	<.0001
	y-intercept <i>b</i>	92 ± 47	84 ± 46	.10

*Paired *t*-test.

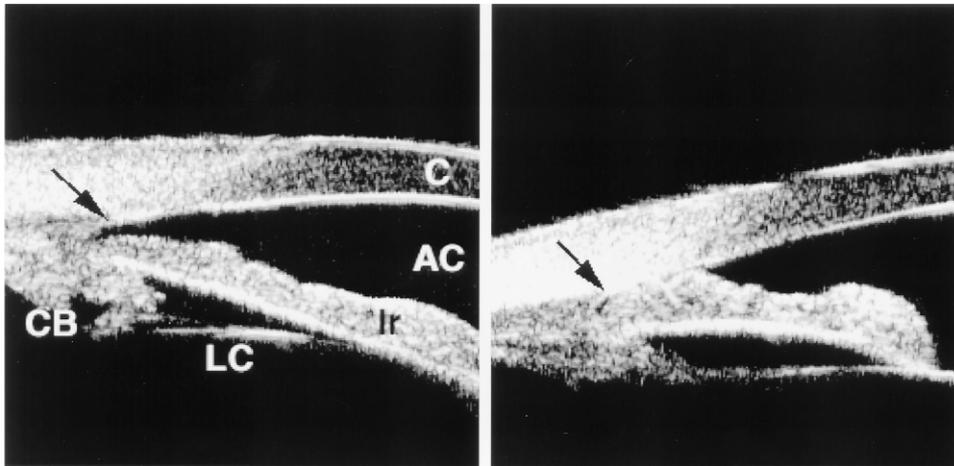
Elimination of the potential complications of intraocular surgery, particularly cataract formation, has created a de facto liberalization of criteria for performing iridotomy.¹ Nevertheless, laser iridotomy is not entirely without complications.^{9–33}

To perform laser iridotomy in all eyes with narrow angles would be an overapplication of the procedure. In a survey of 947 eyes of patients of all ages, Spaeth³⁴ judged as many as 6% of angles to be capable of occlusion, but that only 5%–10% of these would develop angle-closure glaucoma. In an era of cost management, the development of reliable predictors for the development of anterior chamber angle closure has re-emerged.

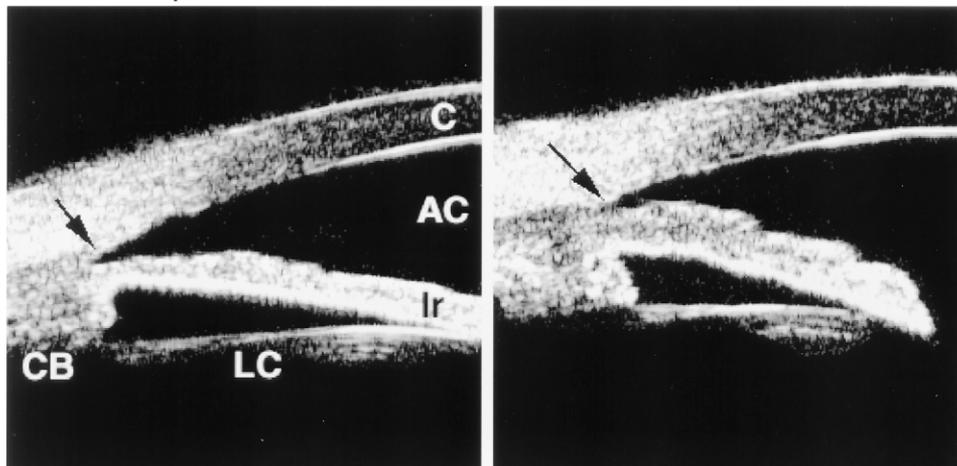
A variety of tests have been developed to attempt to determine whether or not a narrow angle is actually occludable.³⁵ A rise in IOP of 8–10 mm Hg is considered positive when verified by detecting angle closure on gonioscopy. Nonpharmacologic tests have been regarded as more accurately reproducing natural conditions than pharmacologic ones. In the dark-room test, the patient is placed in a dark room for 1 to 2 hours. In the prone provocative test, the patient sits or lies face down for 1 hour without sleeping. Performing the prone provocative test in a darkened room significantly increases the yield of positive tests.³⁶ Mydriatic and combined mydriatic-pilocarpine tests have also been advocated.

Although qualitative image analysis is easy to perform, quantitative analysis of angle configuration remains largely to be developed. Pavlin et al^{37,38} proposed an objective, quantitative method of estimating angle width by UBM. They selected a point on the corneal endothelium 500 μm anterior to the scleral spur and drew a perpendicular from that point to the iris surface. They defined the length of this perpendicular as the angle-opening distance (AOD 500) and the angle whose apex is the scleral spur as angle theta (θ). This method does not take iris contour into account, because it treats the iris surface as a straight line. This assumption cannot be generally applied to

A: Group I



B: Group II



Under lighted condition

Under dark condition

Figure 3. Ultrasound biomicroscopy images of both groups. (A) Images show angle open under light conditions (left), which was closed under dark room conditions (right) (in light: $a = 0.23$, $b = 104$, in dark: $a = 0$, $b = 0$). (B) Images show angle open under both light and dark conditions (in light: $a = 0.42$, $b = 60$, in dark: $a = 0.26$, $b = 61$). C: cornea, Ir: iris, AC: anterior chamber. CB: ciliary body, LC: lens capsule, arrow: scleral spur.

eyes with narrow angles or angle closure, since irregularities of iris contour and curvature play important roles in pathophysiology.⁸ For example, Figure 4 shows two schema of the anterior chamber angle demonstrating exactly the same value for the AOD 500 and angle theta. However, it is evident that the angle on the left is gonioscopically narrower and is more likely to be occludable than the apparently normal angle on the right. This is also presented clinically (Figure 5).

In our study, 55.6% of the eyes with narrow an-

gles, which were considered to have a high possibility of occludable angles, occluded during dark-room testing. UBM was performed in a supine position, which allows the lens to fall backward. Koeppel gonioscopy, performed in this position, provides a wider view of the iridocorneal angle than does Goldmann or four-mirror gonioscopy.³ It is possible that, had the test been performed in the prone position, a greater proportion of the angles would have closed, since forward lens movement can contribute to or exacerbate pupillary block.³⁹

Table 4. Intraobserver Reproducibility (Coefficient of Variation)

Variables	Operator 1	Operator 2	Mean
ARA	1.76 ± 0.69	3.18 ± 1.18	2.47
Acceleration <i>a</i>	1.12 ± 1.30	2.21 ± 1.67	1.67
Y-intercept <i>b</i>	4.56 ± 4.59	6.28 ± 5.33	5.42

ARA: angle recess area.

Our method of ARA determination yields high intraobserver reproducibility of measurement of cross-sectional angle area. Observer input is limited to the identification of the scleral spur, while irregularity of iris contour is reflected in the final calculation of ARA. The high intraobserver reproducibility confirms the consistent localization of scleral spur by each examiner. Although the actual ARA measurement differences between observers was clinically insignificant, a statistical difference could be detected between the observers in 3 cases because the standard deviation within each group of measurements for each observer was extremely small. Potential sources of error include patient factors, mechanical error, and observer error. External factors such as room illumination, accommodative stimuli, and mechanical errors can be reduced by using experienced examiners, standardizing illumination, and controlling accommodation. Minimizing observer interaction with measurement programs decreases the likelihood of incorporating bias into image analysis and measurement.

The measurement of ARA has theoretical limitations similar to those described above, because angles with different clinical appearances may have similar ARAs. For example, a normal angle and a closed angle that widens rapidly to a deep anterior

chamber may have the same or very similar ARAs. To account for these conditions, we also calculated the coefficient and intercept values based on a linear regression analysis of the continuous trabecular-iris distances from the iris insertion to a point 750 μm anterior to the scleral spur. Acceleration describes how rapidly the angle widens from the iris root. The basic concept of this value is similar to the trabecular-iris angle described by Pavlin et al. However, instead of using degrees as units, acceleration uses the tangent of the angle. The y-intercept refers to the distance between the scleral spur and the iris surface along a perpendicular line to the plane of the trabecular meshwork. This is similar to AOD at the scleral spur level.

In spite of these similarities, acceleration and the y-intercept have unique characteristics. Since these values are calculated from linear regression analysis, they can be negative numbers, which is impossible for routine on-screen measurements. A negative number for acceleration implies that the angle has a fairly normal configuration peripherally and becomes very shallow or is apposed to the cornea more centrally (eg, angle closure at Schwalbe’s line with some space at the bottom of the angle recess) (Figure 6). A negative number for the y-intercept means that the angle recess is very shallow or attached to the cornea very peripherally (usually within 150–200 μm from the scleral spur), while it has a relatively wide angle approach more centrally (Figure 7).

By virtue of the characteristics of these measurements, the use of ARA, acceleration, and y-intercept makes it possible to describe the angle configuration very precisely.

Our results suggest that the angles that occluded tended to have smaller ARA and y-intercept. In other

Table 5. Interobserver Reproducibility

Case	ARA (mm ²)			Acceleration <i>a</i>			Y-intercept <i>b</i> (μm)		
	Op. 1	Op. 2	<i>P</i> *	Op. 1	Op. 2	<i>P</i> *	Op. 1	Op. 2	<i>P</i> *
1	0.17	0.16	<.0001	0.48	0.50	<.0001	49.8	22.7	<.0001
2	0.24	0.23	<.0001	0.15	0.16	.005	198.6	191.7	<.0001
3	0.17	0.16	.002	0.35	0.35	.002	88.6	84.2	.028
4	0.42	0.41	.42	0.79	0.75	<.0001	225.6	227.1	.83
5	0.34	0.34	.64	0.40	0.40	.006	220.8	219.9	.78
6	0.11	0.11	.01	0.28	0.29	.01	38.2	29.8	.0001
7	0.23	0.22	<.0001	0.37	0.37	.18	157.0	141.5	<.0001
8	0.09	0.09	.02	0.09	0.09	.07	80.5	81.7	.07
9	0.12	0.11	<.0001	0.12	0.13	<.0001	95.7	85.0	<.0001
10	0.10	0.09	<.0001	0.18	0.18	1.0	59.7	49.5	<.0001

Op.: operator.

*Student *t*-test.

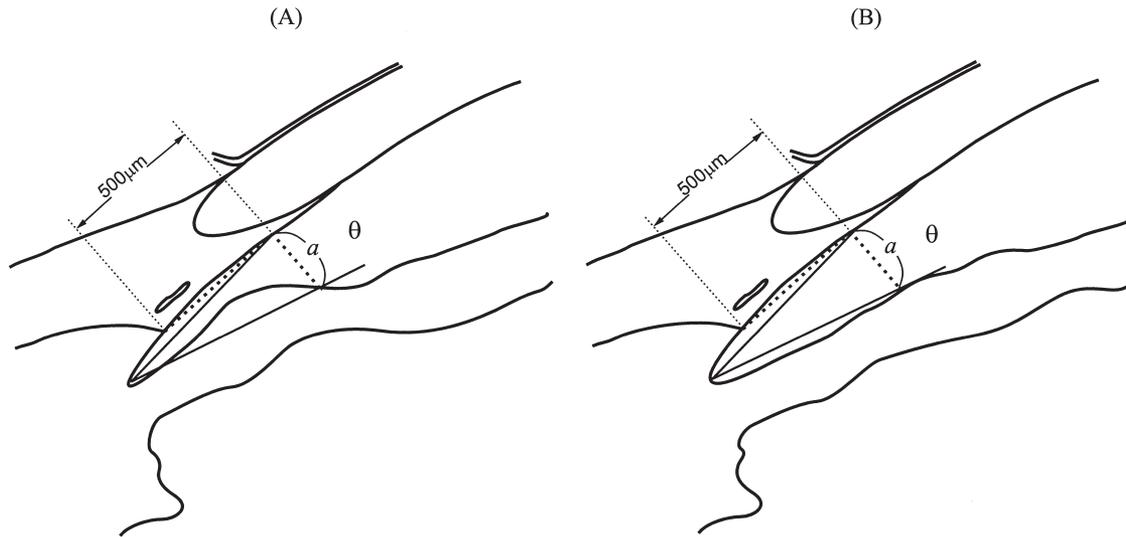


Figure 4. Although angle opening distance is equal in both these patients, (A) angle is more likely to close than (B) angle.

words, close placement of the iris surface to the trabecular meshwork plane from the very bottom of the angle recess to the vicinity of Schwalbe's line is a risk factor for appositional angle closure, as one would expect. Our quantitative evidence supports the clinical impression.

In group I (angles that closed), both the acceleration a and the y-intercept b decreased significantly under dark conditions. This suggests that the peripheral part of the iris, including the iris root, moved toward the trabecular meshwork plane evenly. More simply, the force that pushes the iris against the cor-

nea is applied to the iris equally and makes the peripheral part of the iris closer to the cornea.

On the contrary, in group II, the acceleration a decreased significantly, while the y-intercept b remained the same. This suggests that while the peripheral iris moved closer to the cornea, the iris root stayed at the same location. This implies an uneven distribution of force pushing the iris against the cornea or different rigidity at different locations in the iris. In this situation, the physical stability of the iris root may play an important role in keeping the iris away from the trabecular meshwork plane. The physical fragility of the

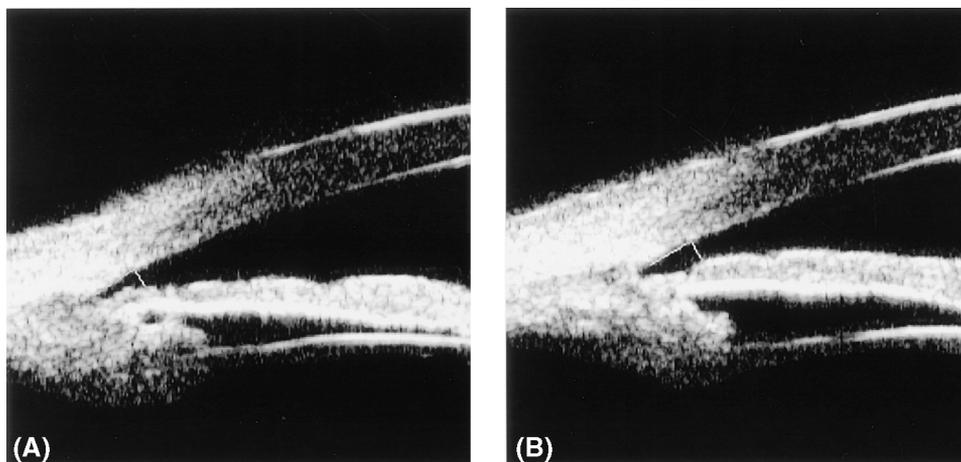


Figure 5. Clinical ultrasound biomicrographs corresponding to schema shown in Figure 4.

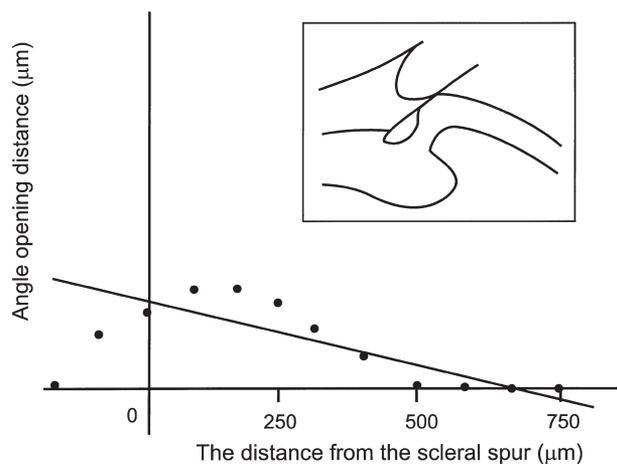


Figure 6. Linear regression analysis on plot graph of angle opening distance versus distance from scleral spur. Line of linear regression shows negative acceleration *a*. This means that angle has almost normal configuration at its peripheral part and become very shallow or is apposed to cornea at its central part (eg, the appositional angle closure started around point of Schwalbe's line with some space at bottom of angle like schema angle in box).

iris root may be a key determinant in the pathophysiology of the appositional angle closure. Even if the angle has a very fragile iris root, an initially large iris root-trabecular meshwork distance would prevent an-

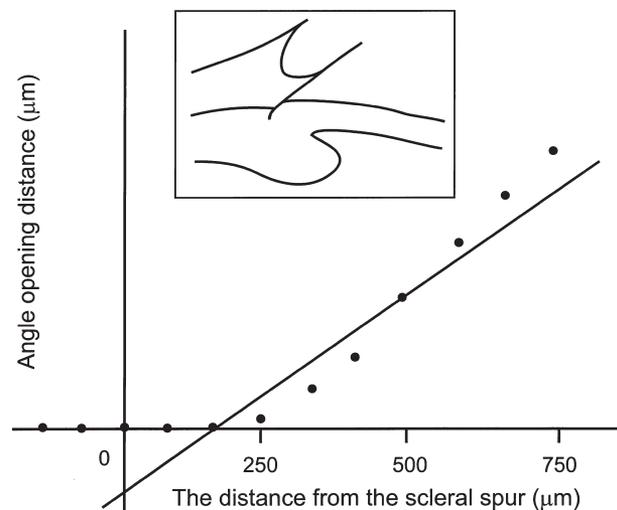


Figure 7. Another linear regression analysis on the graph of angle opening distance versus distance from scleral spur. Line of linear regression shows negative y-intercept *b*. This means that angle recess is very shallow or attached to cornea at its very peripheral part (usually within 150–200 µm from scleral spur) while it has relatively wide angle recess as its central part, like schema angle in box.

gle occlusion. Therefore, the fragility of the iris root and the location of the iris insertion can be the most important parameters to describe the mechanisms of the appositional angle closure.

In conclusion, the ARA measurement provides a useful and reproducible way to estimate the anterior chamber angle depth. The ARA linear regression formula provides useful quantitative information about angle-recess anatomy. The more posterior the iris insertion on the ciliary face and the more stable the iris root, the less likely the provocative test will be positive. The fragility of the iris root and the iris insertion location may be the key factors that affect the mechanism of angle-closure glaucoma.

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