# Prediction of accommodative optical response in prepresbyopic subjects using ultrasound biomicroscopy

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**PURPOSE:** To determine whether relatively low-resolution ultrasound biomicroscopy (UBM) can be used to predict the accommodative optical response in prepresbyopic eyes as well as in a previous study of young phakic subjects, despite lower accommodative amplitudes.

**SETTING:** College of Optometry, University of Houston, Houston, USA.

**DESIGN:** Observational cross-sectional study.

**METHODS:** Static accommodative optical response was measured with infrared photorefraction and an autorefractor (WR-5100K) in subjects aged 36 to 46 years. A 35 MHz UBM device (Vumax, Sonomed Escalon) was used to image the left eye, while the right eye viewed accommodative stimuli. Custom-developed Matlab image-analysis software was used to perform automated analysis of UBM images to measure the ocular biometry parameters. The accommodative optical response was predicted from biometry parameters using linear regression, 95% confidence intervals (CIs), and 95% prediction intervals.

**RESULTS:** The study evaluated 25 subjects. Per-diopter (D) accommodative changes in anterior chamber depth (ACD), lens thickness, anterior and posterior lens radii of curvature, and anterior segment length were similar to previous values from young subjects. The standard deviations (SDs) of accommodative optical response predicted from linear regressions for UBM-measured biometry parameters were ACD, 0.15 D; lens thickness, 0.25 D; anterior lens radii of curvature, 0.09 D; posterior lens radii of curvature, 0.37 D; and anterior segment length, 0.42 D.

**CONCLUSIONS:** Ultrasound biomicroscopy parameters can, on average, predict accommodative optical responses with SDs of less than 0.55 D using linear regressions and 95% CIs. Ultrasound biomicroscopy can be used to visualize and quantify accommodative biometric changes and predict accommodative optical response in prepresbyopic eyes.

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The ability to accommodate decreases progressively with age and is completely lost at around 50 years, resulting in the condition called presbyopia. Corrective options for presbyopia, such as bifocals, progressive addition lenses, monovision, multifocal contact lenses, and multifocal intraocular lenses (IOLs), provide functional far and near vision. However, these corrections do not provide the true dynamic continuous range of focusing ability present in young eyes. There is considerable interest in restoring accommodation to the presbyopic eye.[1–3] Previous studies show that presbyopia is caused by age-related stiffening of the lens[4,5] and that the ciliary muscle continues to contract in the presbyopic eye.[6] Attempts have been made to use the functional ciliary muscle activity to increase the optical power of the eye by producing a forward shift of an IOL,[7] by increasing the separation of dual-optic IOLs,[8,9] or by increasing the curvature of the IOL surfaces.[10] However, so far, these strategies have not reliably restored accommodation in all presbyopic patients.

To establish whether accommodation has been restored to the presbyopic eye, it is essential to use objective measurement methods that provide a true measure of the accommodative ability of an eye.

 
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Clinically, accommodation is measured objectively as an optical change in power of the eye or as biometric changes in the ocular anterior segment. Although commercially available autorefractors and aberrometers provide objective measurement of the accommodative optical changes in an eye, they do not allow for visualization and quantification of the anterior segment biometric changes that produce the optical change.[11] Visualizing and measuring accommodative biometric changes using imaging methods such as ultrasound biomicroscopy (UBM) or optical coherence tomography (OCT) enable the accommodative mechanism to be evaluated; however, these methods do not provide a quantitative measure of the ocular refractive changes. It is important to measure both the accommodative optical and biometric changes to fully evaluate the accommodative ability of an eye or of an accommodation restoration concept in vivo. At present, it is not possible to objectively measure the accommodative optical and biometric changes with a single clinical instrument. Previous studies[12–14] report that the accommodative optical and biometric changes are linearly related. Using these linear relationships, a study[15] of young human subjects showed that the accommodative optical response could be predicted from UBM-measured anterior segment biometry parameters with standard deviations of less than 0.50 diopter (D). This means that UBM can be used to visualize and quantify the accommodative changes in the ocular anterior segment and to predict the accommodative optical response in young phakic individuals with high accommodative amplitudes.

Although no single clinical instrument exists for performing simultaneous refraction and biometry measurements, photorefraction allows refraction to be measured in 1 eye while biometry is measured simultaneously in the contralateral eye.[13] In addition, because photorefraction uses a remotely positioned infrared video camera, it can readily be used on a supine subject, such as is required for a UBM examination. Photorefraction also offers the opportunity to perform dynamic refraction measurements at video frequencies of 30 to 60 Hz. The benefit of measuring the accommodative refractive changes and the corresponding ocular biometry changes simultaneously is that it is certain that both measurements originate from the same accommodative response and therefore are as closely coupled as possible. This is true even if measurements are done in contralateral eyes because of the close coupling of accommodation between the 2 eyes. If the accommodative optical response and the ocular biometry changes are measured sequentially, the accommodative amplitude might not be the same in both instances.

It would be of interest to know whether objective UBM measurements could be used to estimate the accommodative optical response in accommodation restoration concepts. However, before attempting to use UBM on accommodation restoration concepts, it is important to establish whether UBM can be used to estimate the accommodative optical response in older phakic eyes within clinically acceptable limits of variance. Older phakic eyes have lower accommodative amplitudes than younger eyes, and UBM has a relatively low axial resolution of approximately 60 μm relative to other imaging methods such as OCT and Scheimpflug (<20 μm). Thus, it is important to first establish the accuracy of UBM in measuring accommodative biometric changes in older phakic eyes and to then estimate the accommodative optical response from the measured biometry. Although a previous study did this in young subjects,[15] prepresbyopic subjects are a more appropriate study population because they have lower accommodative amplitudes, they are closer representative subjects to presbyopic subjects in age and ocular health, and they form part of the target patient population for accommodation-restoration concepts.

The goal of this study was to establish the accuracy of UBM to objectively measure accommodative biometric changes and estimate the accommodative optical response from the measured biometric changes in phakic prepresbyopic subjects with low accommodative amplitudes.

## SUBJECTS AND METHODS

### Subjects

This study of prepresbyopic subjects followed the tenets of the Declaration of Helsinki and was performed in

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accordance with an institutionally approved human subject protocol. Subjects were enrolled after passing a screening examination that included measurement of uncorrected baseline refraction, subjective refraction, and anterior segment evaluation using slitlamp biomicroscopy. Exclusion criteria included spherical refractive errors greater than ±6.0 D, astigmatism greater than 2.0 D, previous ocular surgery, ocular disease, and known sensitivities or contraindications to topical anesthetic (proparacaine hydrochloride). Subjects with less than 1.0 D of objectively measured accommodative amplitude were excluded. Refractive errors were corrected with spherical or toric soft contact lenses. A similar study of 26 young subjects (8 men, 18 women) aged 21 to 36 years (mean age 24.15 ± 3.03 years) was performed previously.[12,15] A comparison of data from young subjects and prepresbyopic subjects will be presented here.

## Autorefraction

An autorefractor (WR-5100K, Grand Seiko Co., Ltd.) was used to perform objective measurement of the static accommodative optical response as described previously.[15] Briefly, subjects viewed the near target monocularly with the left eye, with the right eye occluded. Plus 1.0 D was added to the subject's contact lens correction to facilitate near working distances. Emmetropic subjects wore a +1.0 D soft contact lens. Three refraction measurements were made for each stimulus demand from 0.0 D to 2.0 D in 0.25 D steps, 2.0 to 4.0 D in 0.50 D steps, and 4.0 to 6.0 D in 1.00 D steps (a total of 15 stimulus demands). High enough stimulus demands were used to ensure that each subject's maximum accommodative response was measured. Measurements were recorded in dim room illumination to maintain the largest pupil diameter possible. The stimulus demand that achieved a subject's maximum objectively measured accommodative optical response was recorded, and this served as the maximum demand to be presented for that subject for all subsequent procedures. The mean ± standard deviation (SD) of the sphere component of the refraction measurements for all stimulus demands were used for the analysis. The autorefractor did not have the ability to measure pupil diameters.

## Infrared Photorefraction

Accommodative optical response and pupil diameter were measured in the left eye with a custom-built photorefraction system as described previously.[15] The far and the near targets were aligned to ensure on-axis measurements. A photorefraction trial lens calibration was performed before accommodation measurements were performed.[15] Three 8-second photorefraction video sequences (each video containing 240 images) were recorded as the subjects accommodated to each stimulus demand from 0.0 D to the maximum demand determined previously, with the right eye occluded. Photorefraction videos were analyzed offline using custom Matlab automated image-analysis software (Mathworks, Inc.).[15]

## Ultrasound Biomicroscopy

Accommodative anterior segment biometry changes were imaged using UBM (Vumax, Sonomed Escalon) as described previously.[12] Briefly, the subject was supine, looking up, with the head stabilized with a gel headrest. Immediately in front of the viewing eye was a beam splitter oriented at 45 degrees. The subject viewed the far target through this beam splitter or the near target reflected off to the side of the beam splitter. Only 1 of the far or near targets was illuminated at 1 time, so only 1 target was visible. Above the beam splitter, a hot mirror was positioned. This allowed the photorefraction camera to image the subject's eye as reflected in the infrared light off the hot mirror, while the subject could view the far target in visible light through the hot mirror. Above the hot mirror was a front silvered mirror oriented at 45 degrees, which allowed the subject to view the far target that was projected on a screen on the wall. Before imaging, contact lenses were removed from the left eye. Two drops of proparacaine 0.5% (Eye Caine) were instilled in the left eye, and a scleral eyecup was inserted under the eyelids and filled with a warmed balanced salt solution. All UBM imaging was performed in dim room illumination. Three sequences each of 50 well-aligned UBM images of the left eye were captured over 8 seconds using a 35 MHz handheld transducer, while the right eye accommodated to each stimulus demand from 0.0 D to the maximum stimulus demand determined previously. The UBM transducer did not block the view of the near target to the subject's right eye. Subjects were encouraged to try to make the near target clear through their right eye. Because the UBM imaging required the left eye to be in primary gaze position, the angle of the near target attached to a meter stick was adjusted by the subject so that all the accommodative convergence was taken up by the right eye and the left eye remained in the primary gaze position for UBM imaging. All scans were captured along the horizontal meridian (3 to 9 o'clock).

Anterior segment parameters such as anterior chamber depth (ACD), lens thickness, corneal thickness, anterior and posterior lens radius of curvature, and anterior segment length (anterior segment length = corneal thickness + ACD + lens thickness) were measured objectively from UBM images using the custom automated image-analysis software (Figure 1, *A*). The measured lens surface radii of curvature (anterior and posterior) were found to be outside the range expected for lens anterior and posterior surfaces. It was determined that the measured radius of curvature was dependent on the *y*-position of the surface in the UBM image due to image distortion. To correct for this distortion, convex and concave calibration surfaces of known radii of curvature approximating the range of lens surface curvatures expected were imaged at various distances from the UBM transducer. Correction factors were calculated from the calibration surfaces to correct the measured anterior and posterior lens radii of curvature and measurements.[12]

## A-Scan Ultrasound

Axial accommodative biometric changes were measured using a 10 MHz A-scan ultrasound system (A-5500, Sonomed Escalon) as described previously.[12] One subject declined to have A-scan measurements recorded. Five A-scan measurements each were recorded by touching the transducer to the cornea while the subjects were accommodating to stimulus demands from 0.0 D to the maximum stimulus demand determined previously. Accommodative changes in ACD, lens thickness, vitreous chamber depth, and axial length (AL) were measured.

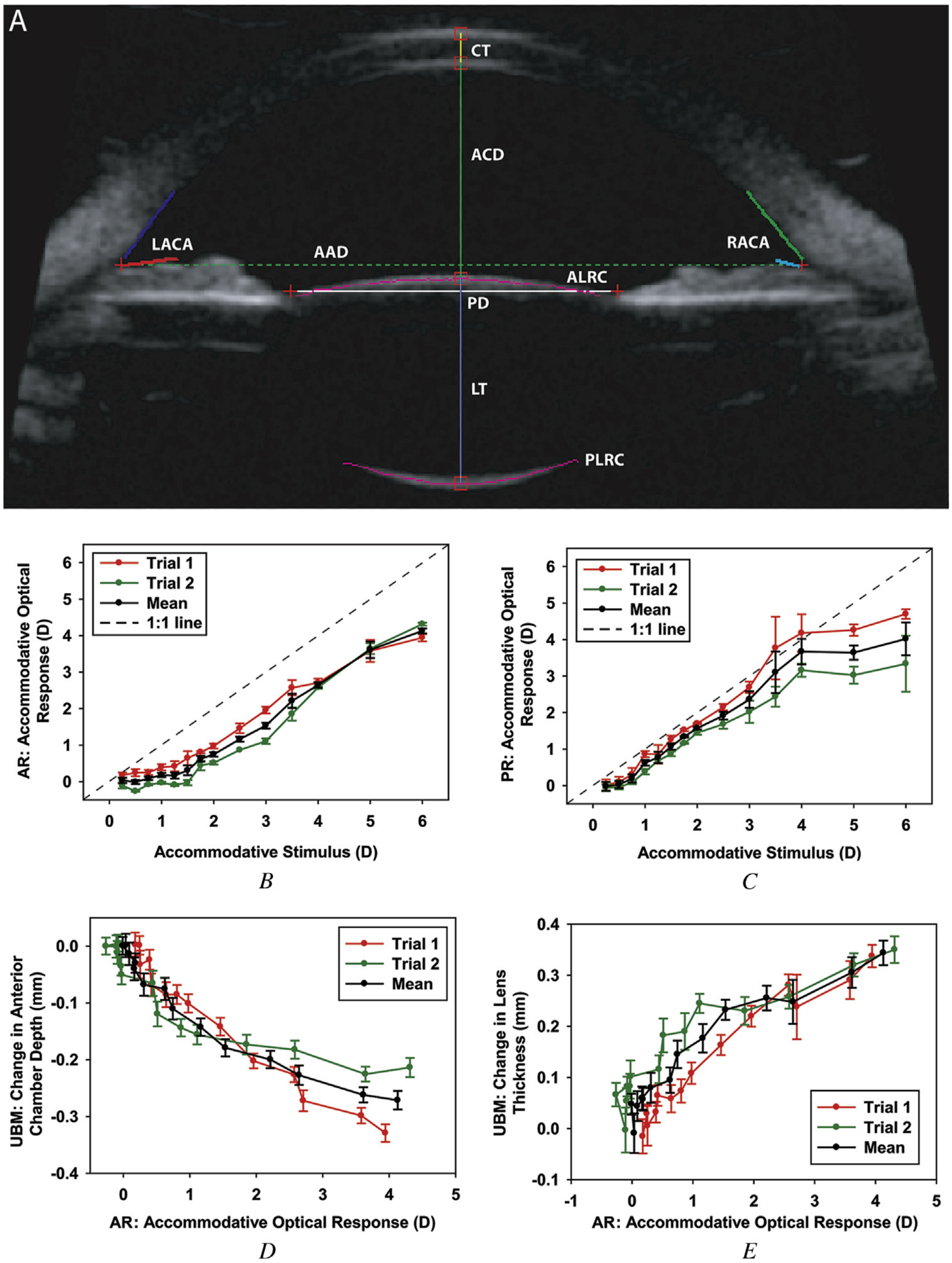



**Figure 1.** *A*: Ultrasound biomicroscopy (UBM) image with all analyzed measurements shown (AAD = angle-to-angle distance; ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; CT = corneal thickness; LACA = left anterior chamber angle; LT = lens thickness; PD = pupil diameter; PLRC = posterior lens radius of curvature; RACA = right anterior chamber angle). *B*: Autorefractor (AR) stimulus response function from a 36-year-old subject from 2 separate trials. *C*: Photorefraction (PR) accommodation stimulus response function from the same subject for the 2 separate trials. Comparison of UBM-measured change in ACD (*D*) and lens thickness (*E*) as a function of autorefractor measured accommodative optical response from 2 separate trials from the same subject. Error bars represent ± 1 SD from 3 measurements.

## Statistical Analysis

Data from each procedure were stored in Matlab arrays and saved as Matlab .mat files for data analysis. All UBM-measured and A-scan-measured biometric parameters were corrected for appropriate sound velocities for various ocular tissues: cornea, 1660 m/s; aqueous and vitreous humor, 1532 m/s; and lens, 1641 m/s. Accommodative optical and biometric changes from the prepresbyopic subjects in the current study were plotted with data from a previous study of young subjects[12,15] for comparison. To calculate repeatability (intrasession and intersession), 3 subjects had 2 repeats of the experiment at least 5 days apart. Intrasession repeatability analysis of the UBM-measured parameters (ACD, lens thickness, anterior and posterior lens radii of curvature, anterior segment length, and corneal thickness) from 3 video sequences from all prepresbyopic subjects for the 0.0 D stimulus demand was performed. Intersession repeatability analysis was performed for the 0.0 D stimulus demand from the 3 subjects who had 2 repeats of the experiment. Repeatability (intrasession and intersession) was evaluated in terms of the (1) coefficient of variation, which is the ratio of the SD of the measurements to the mean; (2) mean SD of the differences between the measurements; (3) coefficient of repeatability (CoR), which is 2 times the mean SD of the differences between the measurements; (4) CoR (%), which is the ratio of CoR to the mean of the measurements multiplied by 100; and (5) intraclass correlation coefficient as described previously. Other anterior segment parameters, such as angle-to-angle distance and left and right anterior chamber angles, were measured from UBM images; however, these parameters are not discussed further because they did not change significantly with accommodation.

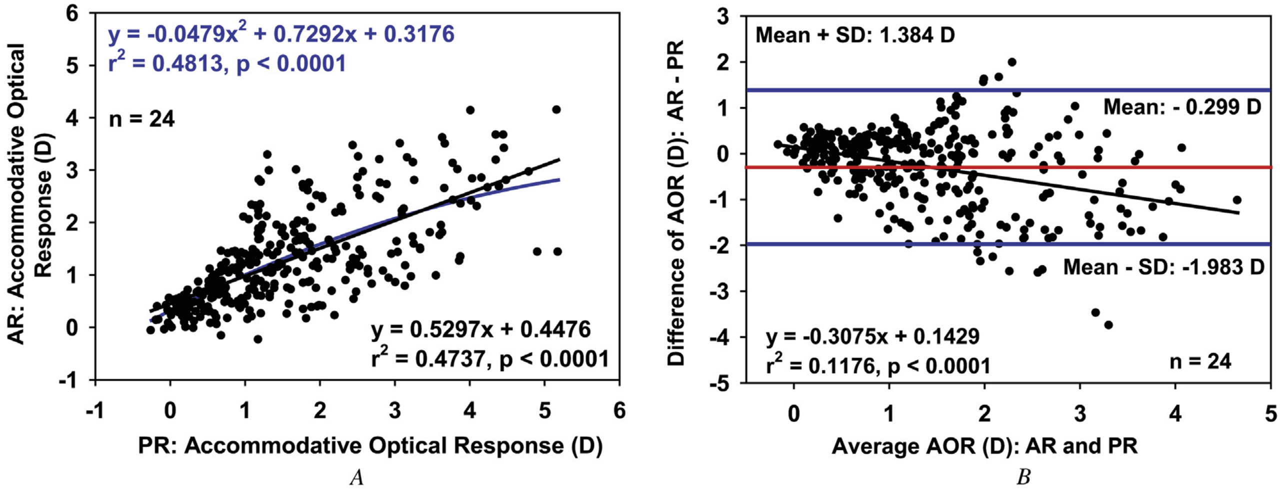
## RESULTS

Twenty-five prepresbyopic subjects participated. The mean age of the 8 men and 17 women was 40.80 years ± 3.08 (SD) (range 36 to 46 years). Of the 25 subjects, 13 had myopia and 3 had hyperopia with a mean refractive error −1.40 ± 1.98 D (range −6.00 to +0.50 D). The mean objectively measured accommodative amplitude using the autorefractor was 2.56 ± 1.01 D (range 1.00 D to 4.56 D). Figure 1 shows representative data from 2 repeated trials in 1 subject. Accommodative stimulus response functions recorded with the autorefractor and photorefraction were both repeatable but dissimilar to each other, with photorefraction tending to plateau in 24 of 25 subjects at higher stimulus demands (Figure 1, *B* and *C*). The autorefractor-measured accommodative optical response plotted against sequentially measured UBM biometry in the same subject showed a decrease in ACD (Figure 1, *D*) and an increase in lens thickness (Figure 1, *E*) with accommodation. The mean curves comparing biometry and autorefractor-measured accommodative optical response (*black lines*) for this subject (Figure 1, *D* and *E*) show statistically significant linear relationships (autorefractor accommodative optical response versus ACD: $r^2 = 0.9248$, $P < .0001$; autorefractor accommodative optical response versus lens thickness: $r^2 = 0.9180$, $P < .0001$) (regression lines not shown), although second-order functions were better fits and improved the $r^2$ values (autorefractor accommodative optical response versus ACD: $r^2 = 0.9871$, $P < .0001$; autorefractor accommodative optical response versus lens thickness: $r^2 = 0.9650$, $P < .0001$) (also not shown).

The relationship between the autorefractor-measured and photorefraction-measured accommodative optical response in all subjects was linear (Figure 2, *A*), although a second-order fit to the data marginally improved the $r^2$ value. In the individual data from each subject, a second-order function provided a better fit in most subjects (22 of 25). Only 1 subject did not have a statistically significant relationship between accommodative optical response measured with autorefraction and photorefraction (data not shown). A Bland-Altman plot of the data from all subjects shows that photorefraction overestimated the autorefractor-measured accommodative optical response with a mean difference of −0.30 D and more so at higher stimulus demands (Figure 2, *B*). As a result of this difference, the autorefractor-measured accommodative optical response was used in all subsequent analyses. Photorefraction measurements showed an accommodative decrease in pupil diameter as a function of autorefractor-measured accommodative optical response in prepresbyopic and young subjects (Figure 2, *C*). The per-diopter accommodative decrease in pupil diameter in prepresbyopic subjects and young subjects was −0.677 mm/D and −0.480 mm/D, respectively.

Accommodative changes in each UBM measured biometric parameter as a function of autorefractor-measured accommodative optical response for each subject were fitted with linear regressions and tested for statistical significance. Only data from individual subjects with statistically significant linear relationships were included in the population plots. The number of subjects with statistically significant linear relationships between accommodative optical response and each biometry parameter were as follows: ACD (n = 20), lens thickness (n = 24), anterior lens radii of curvature (n = 24), posterior lens radii of curvature (n = 12), and anterior segment length (n = 9). With accommodation, there was a decrease in ACD, an increase in lens thickness, a decrease in the radii of curvature of the lens surfaces (anterior and posterior), and an increase in anterior segment length in both the prepresbyopic subjects and the young subjects (Figure 3, *A* to *E*). All 5 biometry parameters (ACD, lens thickness, anterior and posterior lens radii of curvature, and anterior segment length) had statistically significant linear correlations with accommodative optical response ($P < .0001$). The per-diopter accommodative response changes in biometry (indicated by the slope of the linear regression equations) for prepresbyopic subjects were ACD, −0.053 mm/D; lens thickness, +0.073 mm/D; anterior lens radii of curvature, −0.938 mm/D; posterior lens radii of curvature, −0.170 mm/D; and anterior segment length, +0.035 mm/D. The per-diopter changes were similar and not significantly different between the prepresbyopic subjects and the young subjects for all accommodative biometry parameters except posterior lens radii of curvature ($t = -2.667$ and $P = .011$, independent-sample *t* test).

With accommodation, the anterior lens surface moved anteriorly linearly and the posterior lens surface moved posteriorly linearly in the younger subjects and older subjects ($P < .0001$) (Figure 3, *F*). The lens geometric center moved anteriorly during accommodation. In this prepresbyopic population, the anterior and posterior lens surface movement



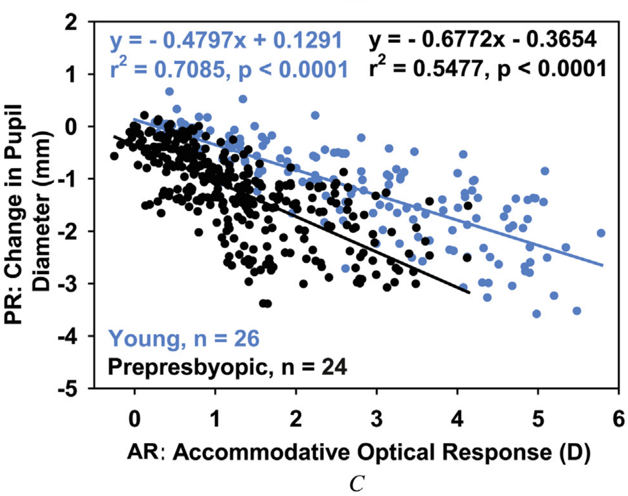




**Figure 2.** *A*: Comparison of the accommodative optical responses (AOR) measured with the autorefractor (AR) and photorefraction (PR) from 24 subjects. *B*: Bland-Altman comparison between autorefractor-measured and photorefraction-measured accommodative optical response. Blue lines represent 95% limits of agreement. C: Comparison of photorefraction-measured accommodative change in pupil diameter as a function of autorefractor-measured accommodative optical response. Data from young subjects are plotted for comparison.

contributed to a 63% and 37% change in lens thickness, respectively. The percentage contribution to change in lens thickness was similar between prepresbyopic subjects and young subjects. The UBM-measured biometry parameters were statistically significantly linearly correlated with each other, and 4 of the correlations are shown in Figure 4. Table 1 shows all the correlations.

The SDs of the UBM-measured biometry parameters were calculated from 50 UBM images for each subject for each stimulus demand from all trials. None of the measured parameter SDs showed significant relationships with the stimulus demand in any individual subject; therefore, the mean SD was calculated by taking the average SD of each measured biometry parameter for all stimulus demands for all trials from all subjects (Table 2).

Repeatability analysis showed that the UBM parameters had better intrasession than intersession repeatability (Table 3) and the repeatability estimates were comparable between the prepresbyopic subjects and young subjects.

Figure 5, *A*, shows the accommodative optical response predicted from each measured anterior segment biometry parameter for individual subjects and Figure 5, *B*, for the prepresbyopic subjects using 3 methods: (1) directly from the linear regression lines, (2) using the 95% confidence intervals (CIs), and (3) using the 95% prediction intervals. Briefly, the axes of each graph in Figure 3 were flipped so that biometry became the independent variable on the horizontal axis and accommodative optical response the dependent or predicted variable on the vertical axis. To predict the accommodative optical response from the 95% CI, the equations of the upper and lower CIs were computed. Because the 95% CI lines separate toward the extremes, the range of accommodative optical response was calculated as the mean difference between the *y*-values from the upper and lower 95% CI equations for all corresponding *x*-values. Matlab code was written to run a loop from the minimum to the maximum *x*-value in fixed steps (ACD, lens thickness, anterior segment length: 0.0001 mm; anterior and posterior

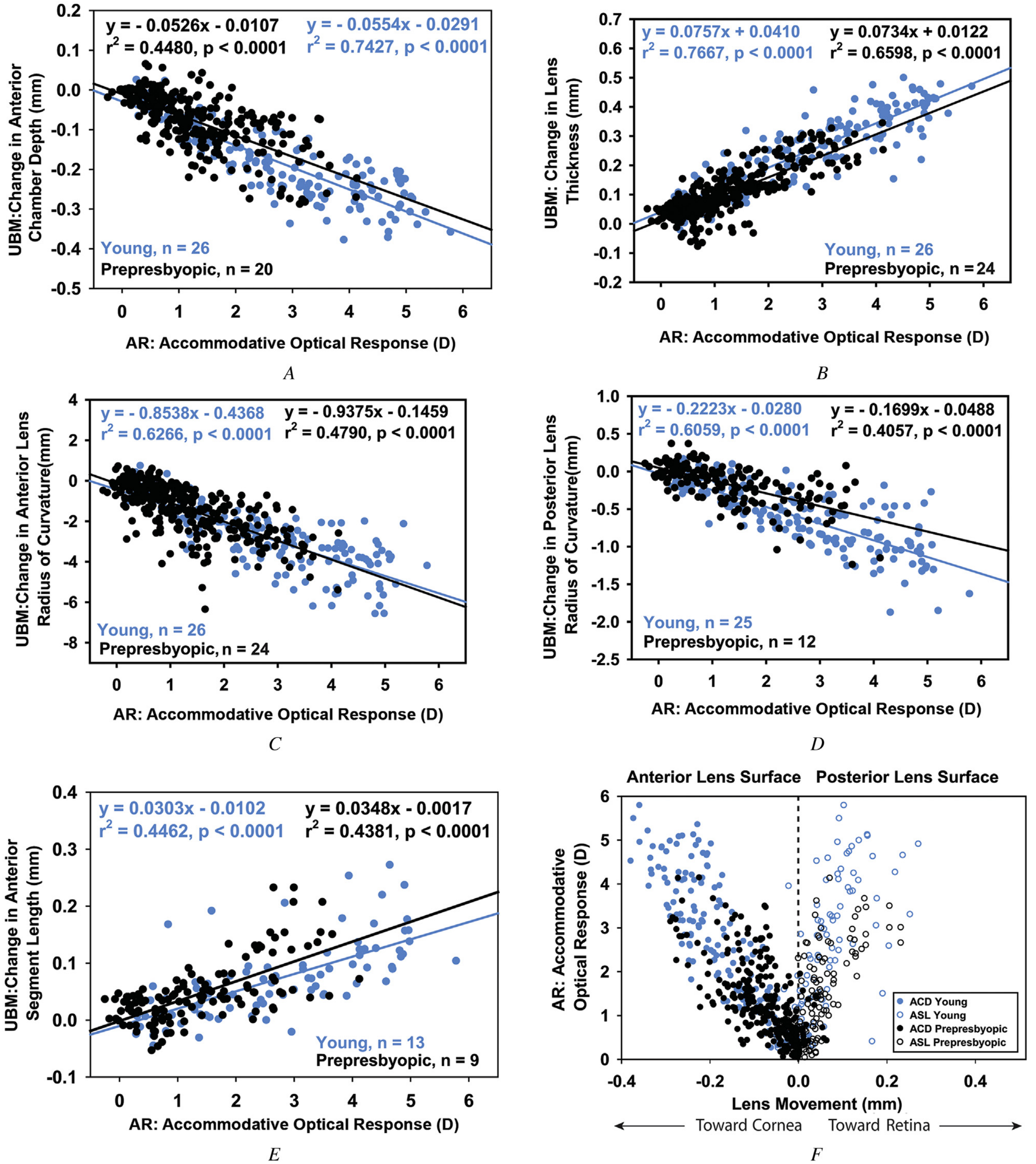



**Figure 3.** Ultrasound biomicroscopy-measured (UBM) ocular accommodative biometric changes as a function of the autorefractor-measured (AR) accommodative optical response showing data from prepresbyopic and young subjects. With accommodation, anterior chamber depth decreases (*A*), lens thickness increases (*B*), anterior lens radius of curvature decreases (*C*), posterior lens radius of curvature decreases (*D*), and anterior segment length increases (*E*). *F*: Accommodative movements of the anterior and posterior lens surfaces as a function of accommodative optical response in young subjects and prepresbyopic subjects. Each data point represents an average of all trials from each subject (ACD = anterior chamber depth; ASL = anterior segment length).

lens radii of curvature: 0.001 mm) to calculate the range of accommodative optical response for each *x*-value. The mean, SD, maximum, minimum, and median of the range was calculated for each biometry parameter. A similar calculation of the range of accommodative optical response was performed

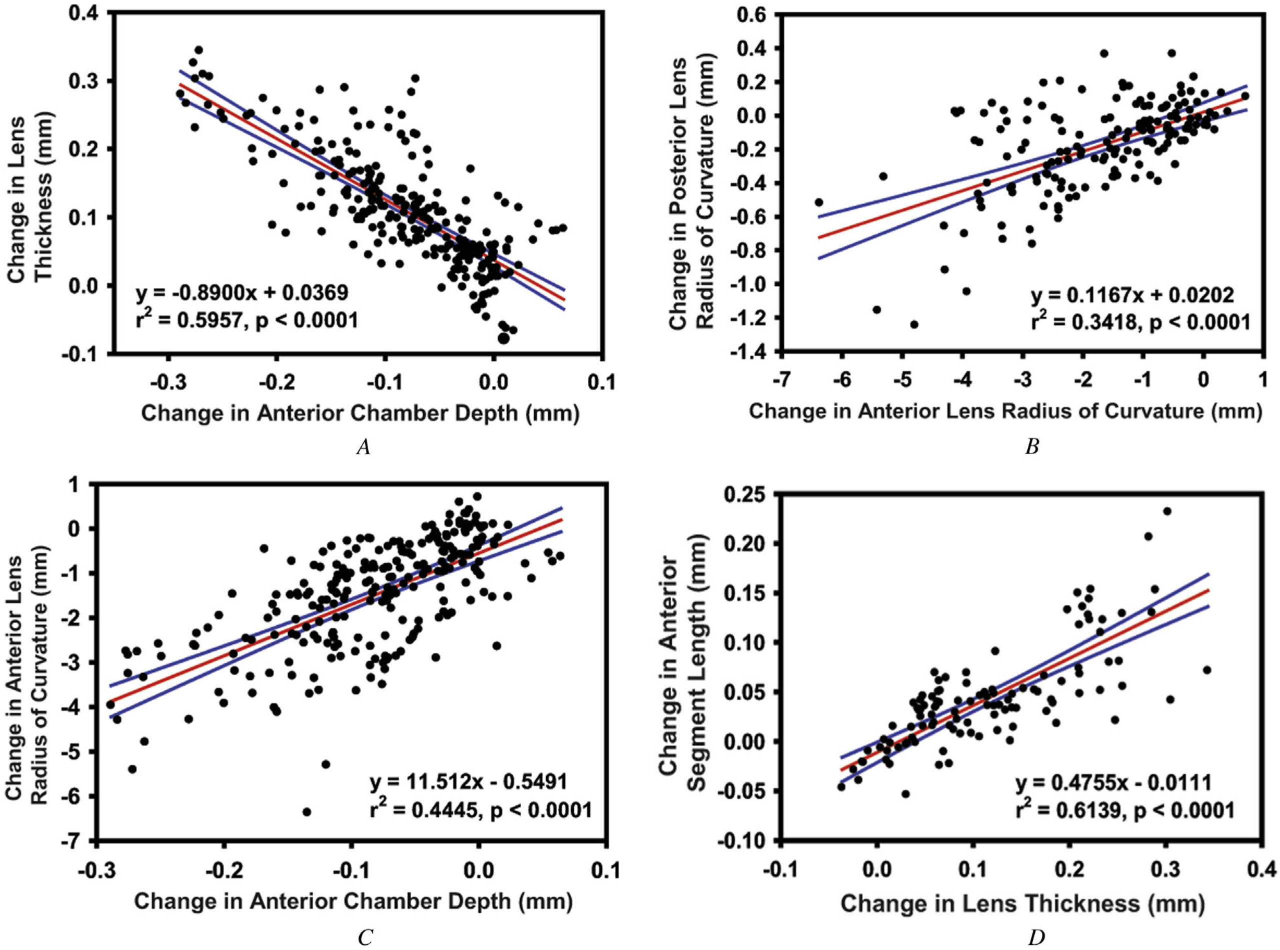



**Figure 4.** Linear relationships of change in ACD versus lens thickness (n = 20) (*A*), anterior lens radius of curvature versus posterior lens radius of curvature (n = 12) (*B*), ACD versus anterior lens radius of curvature (n = 20) (*C*), and lens thickness versus anterior segment length (n = 9) (*D*) in prepresbyopic subjects. Linear regression parameters for other statistically significant biometry relationships are shown in Table 1.

using the equations for the 95% prediction intervals. Statistically, the 95% CI will contain the true population mean of a parameter 95% of the time. The 95% prediction intervals will include the location of future data points that are sampled. Because of the uncertainty of the population mean and the scatter of the data points, prediction intervals are wider than CIs.

Standard deviations of predicted accommodative optical response were consistently smaller in the

**Table 1.** Linear regression parameters for UBM-measured anterior segment biometry parameters during accommodation (change in biometry). All regressions shown had statistically significant linear correlations ($P < .0001$) except ACD versus anterior segment length ($P = .006$) and posterior lens radius of curvature versus anterior segment length ($P = .032$).

| | Horizontal Axis | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ACD | | | PLRC | | | ALRC | | | LT | | |
| Vertical Axis | Slope | Intercept | $r^2$ Value | Slope | Intercept | $r^2$ Value | Slope | Intercept | $r^2$ Value | Slope | Intercept | $r^2$ Value |
| LT | −0.890 | 0.036 | 0.596* | — | — | — | — | — | — | — | — | — |
| ALRC | 11.512 | −0.549 | 0.444* | −11.30 | −0.101 | 0.510 | — | — | — | — | — | — |
| PLRC | 2.740 | 0.117 | 0.534 | −2.074 | 0.091 | 0.435 | 0.117 | 0.020 | 0.342* | — | — | — |
| ASL | −0.2653 | 0.024 | 0.088 | 0.475 | −0.011 | 0.614* | −0.022 | 0.019 | 0.267 | −0.055 | 0.039 | 0.065 |

ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; ASL = anterior segment length; LT = lens thickness; PLRC = posterior lens radius of curvature

*Data plotted in Figure 4

**Table 2.** Mean SD of UBM biometry measurements for the prepresbyopic subjects (current study) and young subjects.[15] Data from prior anterior segment biometry studies are shown for comparison.

| Biometry | Mean SD ± SD | | |
|---|---|---|---|
| | Prepresbyopic Subjects (n = 25) | Young Subjects (n = 26) | Mean SD from Prior AS Biometry Studies |
| ACD (mm) | 0.018 ± 0.004 | 0.017 ± 0.003 | 0.148[13] |
| LT (mm) | 0.028 ± 0.009 | 0.029 ± 0.008 | 0.224[13] |
| ALRC (mm) | 0.351 ± 0.194 | 0.335 ± 0.138 | 1.100[17] |
| PLRC (mm) | 0.154 ± 0.031 | 0.158 ± 0.038 | 0.550[30] |
| ASL (mm) | 0.034 ± 0.011 | 0.034 ± 0.009 | 0.239[13] |

ACD = anterior chamber depth; AS = anterior segment; LT = lens thickness; ALRC = anterior lens radius of curvature; ASL = anterior segment length; LT = lens thickness; PLRC = posterior lens radius of curvature

prepresbyopic subjects than in young subjects for predictions using the respective subject populations as a whole (Table 4) and from individual subjects (Table 5). The root-mean-square (RMS) error of accommodative optical response was calculated from linear regressions for each prepresbyopic subject for all UBM-measured biometry parameters. The mean RMS error of the predicted accommodative optical response from each UBM-measured biometry parameter was ACD, 0.33 ± 0.22 D; lens thickness, 0.28 ± 0.07 D; anterior lens radii of curvature, 0.30 ± 0.14 D; posterior lens radii of curvature, 0.53 ± 0.21 D; and anterior segment length, 0.56 ± 0.20 D.

Accommodative optical response was calculated independently from each of the UBM-measured biometry parameters for each prepresbyopic subject using linear regression equations (Table 6). The mean difference between the predicted and measured accommodative optical response from all the individual subjects from all stimulus demands was smaller in prepresbyopic subjects than in young subjects for all biometry parameters, with lens thickness providing the best prediction of accommodative optical response in both age groups (Table 6).

In the prepresbyopic subjects, there was a statistically significant linear correlation between A-scan-measured and UBM-measured ACD and lens thickness measurements (Figure 6, *A* and *B*). Data from subjects who individually had statistically significant linear regressions are plotted. Data circled in red are from a single subject whose measured A-scan values differed markedly from the rest of the population. The A-scan-measured ACD values were smaller than those measured with UBM by on average 63 μm and A-scan-measured lens thickness values were larger than those measured with UBM by on average 193 μm as shown in the Bland-Altman plots (Figure 6, *C* and *D*).

There was no statistically significant relationship between the SD of the A-scan measurements and stimulus demand in any individual prepresbyopic subject. Therefore, the mean SD of A-scan measurements of ACD and lens thickness were calculated as the average SD of 5 measurements for all stimulus demands for all trials from all subjects. The mean SD of the A-scan-measured ACD and lens thickness in the prepresbyopic subjects was similar to the data from young subjects (Table 7). The mean SD of the UBM measurements was consistently smaller than the

**Table 3.** Intrasession and intersession repeatability for various UBM-measured parameters.

| Repeatability Parameter | Intrasession Repeatability (n = 25) | | | | | | Intersession Repeatability (n = 3) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ACD | LT | ALRC | PLRC | ASL | CT | ACD | LT | ALRC | PLRC | ASL | CT |
| CoV | 0.006 | 0.008 | 0.030 | 0.030 | 0.005 | 0.022 | 0.006 | 0.008 | 0.031 | 0.025 | 0.005 | 0.024 |
| Mean SD of differences (mm) | 0.014 | 0.080 | 0.199 | 0.122 | 0.024 | 0.004 | 0.011 | 0.102 | 0.688 | 0.093 | 0.342 | 0.018 |
| CoR | 0.028 | 0.037 | 0.397 | 0.243 | 0.049 | 0.007 | 0.022 | 0.204 | 1.376 | 0.186 | 0.685 | 0.036 |
| CoR (%) | 0.890 | 0.953 | 3.585 | 4.585 | 0.641 | 1.304 | 0.674 | 5.385 | 11.227 | 3.174 | 9.079 | 6.966 |
| ICC | 0.999 | 0.998 | 0.989 | 0.982 | 0.996 | 0.995 | 0.989 | 0.900 | 0.833 | 0.992 | 0.856 | 0.954 |

ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; ASL = anterior segment length; CoR = coefficient of repeatability; CoV = coefficient of variation; CT = central corneal thickness; ICC = intraclass correlation coefficient; LT = lens thickness; PLRC = posterior lens radius of curvature

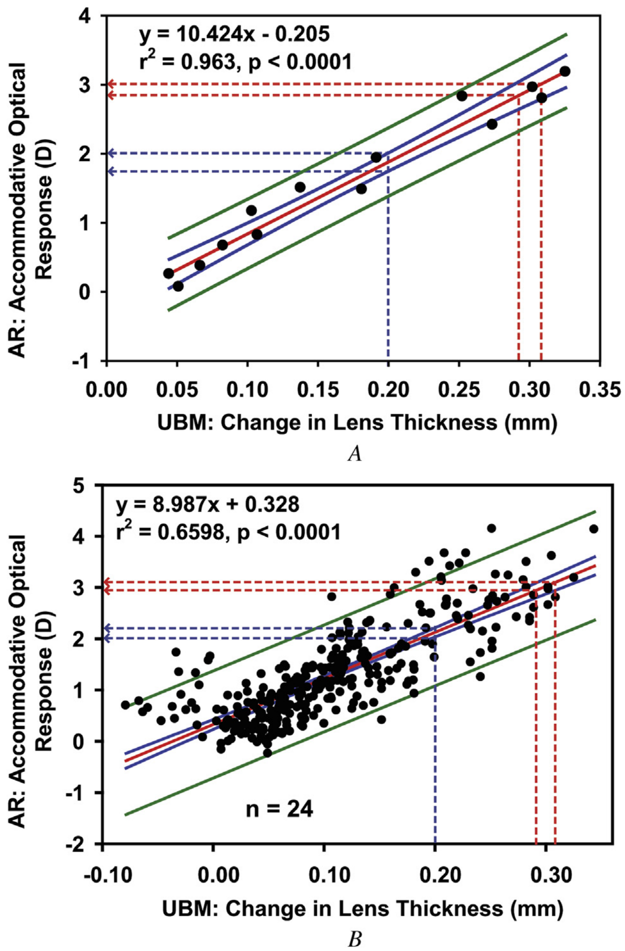



**Figure 5.** The range of accommodative optical response predicted for a single individual subject (*A*) and for the study population as a whole (*B*). Accommodative optical response was predicted from the linear regression lines (*red solid line*) and from the 95% confidence and prediction intervals (*solid blue* and *green lines*) from the biometry measurements. For each value on the horizontal axis, the range of accommodative optical response was calculated using the linear regression line with the mean SD of the UBM measurements (*red dashed line*), equations for the upper and lower 95% CIs (*blue dashed line*), and prediction intervals (not shown) (AR = autorefractor; UBM = ultrasound biomicroscopy).

mean SD from the A-scan measurements in both age groups.

The amplitudes of accommodation determined objectively from the young subjects and the prepresbyopic subjects as a function of age were fitted with a linear regression and when extrapolated to zero showed a complete loss of accommodation at age 54 years at the rate of −0.19 D a year (Figure 7, *A*). The mean accommodative amplitude was statistically significantly different between the 2 age groups ($t$ = 13.476, $P < .0001$, independent-sample $t$ test). With age, ACD decreased, lens thickness increased, posterior lens radii of curvature decreased, and the posterior lens surface occupied a more posterior position (Figure 7, *B* to *F*). There were statistically significant differences in mean lens thickness ($t$ = −4.834, $P < .0001$), mean anterior segment length ($t$ = −3.019, $P = .004$), mean posterior lens radii of curvature ($t$ = −2.509, $P = .016$), and mean A-scan lens thickness ($t$ = −4.339, $P < .0001$) between the 2 age groups based on the independent-sample $t$ test (Table 8).

## DISCUSSION

As described and discussed previously for young subjects,[15] infrared photorefraction overestimated the accommodative optical response measured by the WR-5100K autorefractor in prepresbyopic subjects. The per-diopter accommodative change in pupil diameter was larger in the prepresbyopic subjects than in the young subjects as reported previously, suggesting a greater accommodative effort in older subjects than in young subjects.[16,17] The absolute pupil diameter at the baseline stimulus demand was smaller in the prepresbyopic group as a result of age-related pupillary miosis; however, when absolute pupil diameters were plotted as a function of age, there was no statistically significant age-related trend ($r^2$ = 0.013, $P = .421$) (data not shown). The autorefractor did not measure pupil diameter; hence, comparisons could not be made with photorefraction-measured pupil diameters.

The per-diopter accommodative changes in the anterior segment biometry parameters in older subjects were similar to the values in young subjects. Previous studies[18,19] have similarly shown that per-diopter accommodative biometry changes do not change with age. In the current study, posterior movement of the posterior lens surface with accommodation was observed in 9 eyes (36% of the subjects). This is fewer than the 52% of subjects in which this was observed previously in young phakic eyes.[15] In the remaining eyes, the posterior lens surface did not move significantly during accommodation. This might suggest age-related changes in accommodation in which there is a forward translation of the anterior lens surface with less movement of the posterior lens surface in older eyes. This finding also suggests that gravity does not influence lens accommodative movements in most prepresbyopic subjects because the lens does not sag posteriorly during accommodation while subjects are supine.

The age-related decline in the accommodative ability in the present study is comparable to rates in prior studies.[20–22] Small differences between the

**Table 4.** Standard deviations of predicted accommodative optical response from UBM-measured biometry parameters using linear regressions, the 95% CIs, and 95% prediction intervals in prepresbyopic subjects and young subjects[15] as a whole.

| | Standard Deviations of Predicted Accommodative Optical Response (D) | | | | | |
|---|---|---|---|---|---|---|
| | Prepresbyopic Subjects | | | Young Subjects | | |
| Biometry | Linear Regression | 95% CI | 95% Prediction Interval | Linear Regression | 95% CI | 95% Prediction Interval |
| ACD | 0.15 | 0.28 | 2.68 | 0.24 | 0.37 | 3.05 |
| LT | 0.25 | 0.20 | 2.09 | 0.30 | 0.34 | 2.89 |
| ALRC | 0.09 | 0.30 | 2.60 | 0.24 | 0.46 | 3.66 |
| PLRC | 0.37 | 0.50 | 3.14 | 0.43 | 0.52 | 3.77 |
| ASL | 0.42 | 0.51 | 3.14 | 0.50 | 0.82 | 4.55 |

ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; ASL = anterior segment length; CI = confidence interval; LT = lens thickness; PLRC = posterior lens radius of curvature

studies might be due to differences in accommodation stimulation, noise, variability of the measurement technique, and variability in the subject population. Age-related changes (millimeters/year) in the UBM-measured biometry parameters in the current study are comparable to values in previous studies[18,19,23–29] (Table 9[22,24–29]). Age-related changes in the UBM-measured biometry parameters were observed except for anterior lens radii of curvature. When anterior lens radii of curvature were plotted with age, no statistically significant age-related trend was observed ($r^2 = 0.045$, $P = .131$) (data not shown). This is likely because of the limited number of lens surface pixels in the UBM images that can be used to fit a circle, which is limited by the pupil diameter and indistinct edges of the anterior lens surface.[12]

Smaller SDs and good repeatability of the UBM-measured anterior segment biometry parameters in the prepresbyopic subjects compared with the young subjects show that UBM, despite having low axial resolution, can provide accurate measurements in prepresbyopic subjects with lower accommodative amplitudes. Standard deviations of UBM-measured parameters were smaller than SDs reported in previous studies.[13,30] Differences observed between A-scan–measured and UBM-measured ACD and lens thickness in the current study were also observed in young subjects and have been discussed previously.[12] Ratios of A-scan measurements and UBM measurements of ACD and lens thickness were calculated from subjects with a statistically significant linear relationship for all stimulus demands to yield 244 UBM correction factors. The mean ± SD of all these ratios was 0.984 ± 0.02 and 1.049 ± 0.03, respectively, for ACD and lens thickness. The correction factors for ACD and lens thickness from prepresbyopic subjects are similar to values reported previously in young subjects.[12] Multiplying the UBM measurements by the correction factors would, on average, place the UBM measurements in agreement with the A-scan measurements.

In the current study, the SDs of the predicted accommodative optical response from the population as a whole was worse than predictions from

**Table 5.** Mean ± standard deviation (SD) of the standard deviations of predicted accommodative optical response from individual subjects in the presbyopic and young populations.[15]

| | Standard Deviations of Predicted Accommodative Optical Response (D) | | | | | |
|---|---|---|---|---|---|---|
| | Prepresbyopic Subjects | | | Young Subjects | | |
| Biometry | Linear Regression | 95% CI | 95% Prediction Interval | Linear Regression | 95% CI | 95% Prediction Interval |
| ACD | 0.25 ± 0.08 | 0.58 ± 0.38 | 1.69 ± 1.12 | 0.29 ± 0.05 | 1.51 ± 0.75 | 3.20 ± 1.54 |
| LT | 0.32 ± 0.06 | 0.50 ± 0.13 | 1.43 ± 0.36 | 0.36 ± 0.10 | 1.06 ± 0.46 | 2.25 ± 0.94 |
| ALRC | 0.29 ± 0.15 | 0.53 ± 0.25 | 1.53 ± 0.69 | 0.37 ± 0.11 | 1.34 ± 0.58 | 2.85 ± 1.19 |
| PLRC | 0.49 ± 0.19 | 0.94 ± 0.34 | 2.71 ± 1.04 | 0.79 ± 0.49 | 1.45 ± 0.74 | 3.12 ± 1.57 |
| ASL | 0.64 ± 0.30 | 0.98 ± 0.43 | 2.77 ± 1.08 | 1.04 ± 0.43 | 2.15 ± 0.95 | 4.40 ± 1.77 |

ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; ASL = anterior segment length; CI = confidence interval; LT = lens thickness; PLRC = posterior lens radius of curvature

**Table 6.** Comparison of accommodative optical response predictions using linear regression equations from biometry for prepresbyopic subjects and young subjects. Absolute differences between measured and predicted AOR were calculated from all individual subjects for all stimulus demands.

| Subjects/Biometry | Population Linear Regression Equations To Predict AOR from Biometry | Absolute Difference Between Measured AOR and Predicted AOR (D) | | | |
|---|---|---|---|---|---|
| | | Mean | SD | Minimum | Maximum |
| Prepresbyopic | | | | | |
| ACD | $AOR = -8.524 \times \Delta ACD + 0.627$ | 0.53 | 0.42 | 0.01 | 2.22 |
| LT | $AOR = +8.987 \times \Delta LT + 0.328$ | 0.41 | 0.33 | 0.00 | 1.70 |
| ALRC | $AOR = -0.511 \times \Delta ALRC + 0.586$ | 0.50 | 0.42 | 0.00 | 2.22 |
| PLRC | $AOR = -2.388 \times \Delta PLRC + 0.917$ | 0.62 | 0.47 | 0.01 | 2.75 |
| ASL | $AOR = +12.571 \times \Delta ASL + 0.807$ | 0.60 | 0.49 | 0.00 | 2.42 |
| Young | | | | | |
| ACD | $AOR = -13.405 \times \Delta ACD + 0.309$ | 0.62 | 0.44 | 0.02 | 1.87 |
| LT | $AOR = +10.121 \times \Delta LT + 0.219$ | 0.56 | 0.46 | 0.00 | 2.57 |
| ALRC | $AOR = -0.734 \times \Delta ALRC + 0.695$ | 0.74 | 0.54 | 0.00 | 3.08 |
| PLRC | $AOR = -2.726 \times \Delta PLRC + 0.991$ | 0.75 | 0.56 | 0.01 | 3.33 |
| ASL | $AOR = +14.678 \times \Delta ASL + 1.675$ | 0.91 | 0.65 | 0.00 | 3.29 |

Δ = accommodative change in; ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; AOR = accommodative optical response; ASL = anterior segment length; CI = confidence interval; LT = lens thickness; PLRC = posterior lens radius of curvature

individual subjects, as previously reported in young subjects.[15] The SDs of the predicted accommodative optical response from biometry using linear regression, 95% CIs, and prediction intervals were smaller in older subjects than in younger subjects. This might be due to the smaller slope of the linear regression equations and larger number of data points from the prepresbyopic subjects resulting from using more stimulus demands. The accommodative increase in lens thickness is primarily (approximately 63%) the result of the forward movement of the anterior lens surface, which results in a decrease in ACD. Therefore, change in ACD is dependent on forward movement of the anterior lens surface (change in lens thickness). A smaller proportion (approximately 37%) of the accommodative increase in lens thickness is due to the posterior movement of the posterior lens surface. As mentioned, all accommodative anterior segment biometry parameters were strongly linearly correlated. When the biometry parameters were put in a multiple linear regression model, it resulted in multicollinearity. When this occurs, the coefficient estimates become unstable and can vary widely from small changes in the data. The presence of multicollinearity did not provide improvement in accuracy to predict the dependent variable and resulted in inaccurate regression coefficients. Hence, the use of a multiple linear regression model was unsuitable.

One limitation of the current study is that the accommodative optical and biometric changes were not measured simultaneously; hence, linear correlations between accommodative optical response and biometry might not be as strong as they actually are. Refraction measurements recorded simultaneously with UBM biometry measurements in the contralateral eye could potentially be made using photorefraction. However, the refraction measurements from the autorefractor were considered more reliable than those from photorefraction because of the small pupil diameters. This meant the correlations were derived from sequential measurements of refraction and biometry in the same eye. Simultaneous measurements could provide better prediction of the accommodative optical response. Based on the current study, if accommodative changes in anterior segment biometry are measured, the linear regression equations provided (Table 6) can be used to calculate the accommodative optical response in the prepresbyopic subject population. On average, the prediction errors from the linear regressions were less than 0.65 D for all biometry parameters, with lens thickness being the best predictor for both age groups. Although only data from subjects who had statistically significant linear relationship between optical and biometric changes were used for accommodative optical response prediction, almost all subjects had a statistically significant linear relationship for lens thickness and anterior lens radii of curvature. Hence, it would be better to use lens thickness and anterior lens radii of curvature to estimate the accommodative optical response.

It might be of interest to see how the anterior segment parameters could collectively be used to predict the refraction and the accommodative

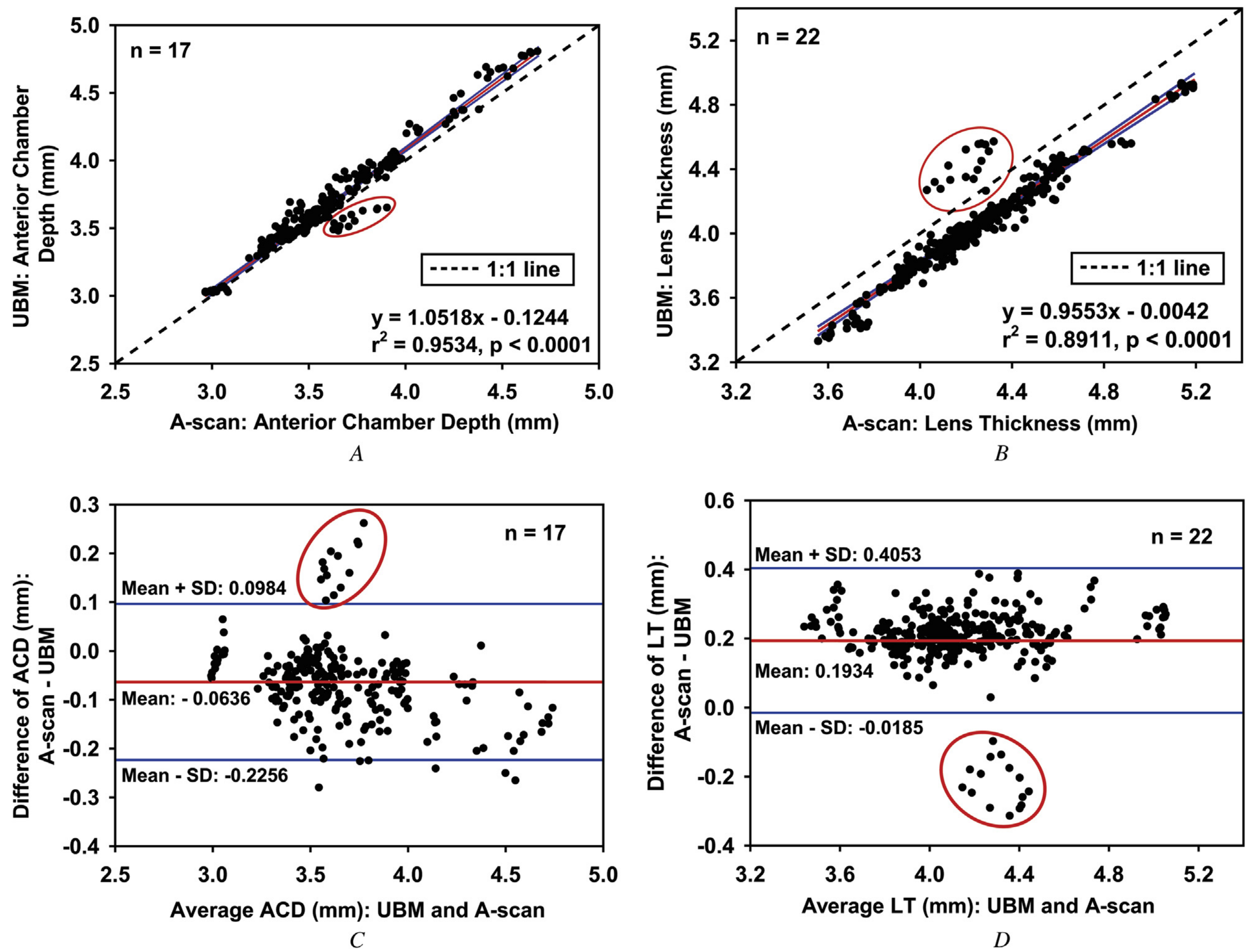



**Figure 6.** *A* and *B*: Linear correlation between A-scan ultrasound–measured and UBM-measured ACD and lens thickness, respectively. *C* and *D*: Bland-Altman comparison between A-scan ultrasound–measured and UBM-measured ACD and lens thickness, respectively. Data points circled in red are from a single subject who showed an unusual response. The data from this 1 subject is not included in the regression calculations/equations. The number of subjects with statistically significant linear fits is denoted by n (ACD = anterior chamber depth; LT = lens thickness; UBM = ultrasound biomicroscopy).

optical response of the eye. One approach would be to put all the measured anterior segment biometry parameters into a schematic eye model to calculate the refractive state of the eye and the accommodative optical response. This might be useful to understand if a better prediction could be obtained from a schematic eye model than from the individual linear correlations; however, schematic eye calculations also require measurements of the corneal curvature and AL of the eye.

From the current study and the previous study of young subjects,[15] it can be seen that individual

**Table 7.** Mean SDs of ACD and lens thickness during accommodation from UBM and A-scan ultrasound in prepresbyopic subjects and young subjects.[12]

| | Measured Biometry: Mean SD ± SD (mm) | | | |
|---|---|---|---|---|
| | Prepresbyopic Subjects (n = 24) | | Young Subjects (n = 24) | |
| Biometry | UBM | A-Scan | UBM | A-Scan |
| ACD | 0.018 ± 0.004 | 0.047 ± 0.026 | 0.017 ± 0.003 | 0.041 ± 0.024 |
| LT | 0.028 ± 0.009 | 0.041 ± 0.027 | 0.029 ± 0.008 | 0.039 ± 0.022 |

ACD = anterior chamber depth; LT = lens thickness; UBM = ultrasound biomicroscopy

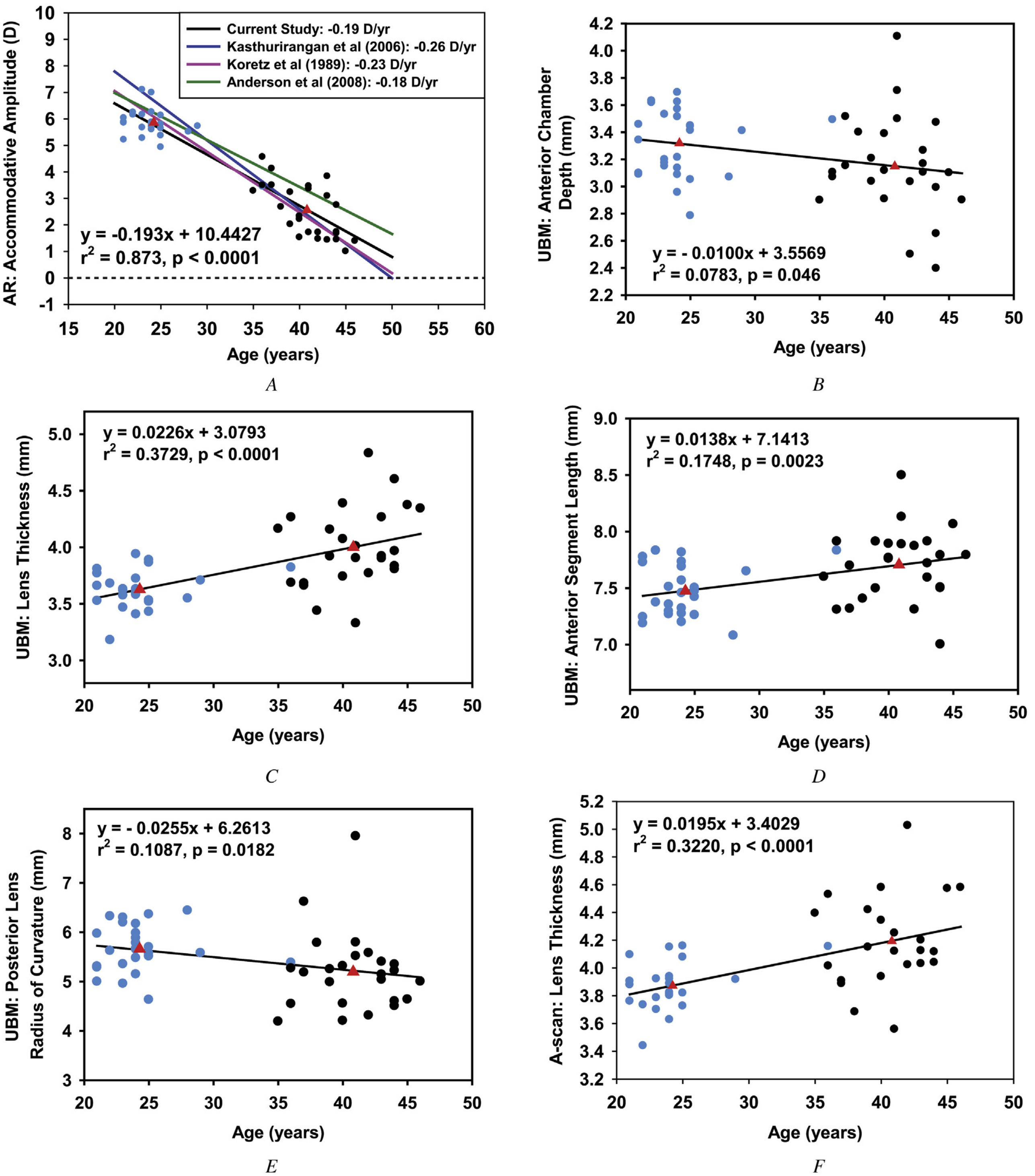



**Figure 7.** *A*: Age-related decline in the autorefractor-measured accommodative amplitude in young subjects (*blue symbols*) and prepresbyopic subjects (*black symbols*). Linear regression lines in previous studies are plotted for comparison. With age, ACD decreased (*B*), lens thickness increased (*C* and *F*), anterior segment length increased (*D*), and posterior lens surface radius decreased (*E*). Red triangles represent the mean values in both the age groups (AR = autorefractor; UBM = ultrasound biomicroscopy).

UBM-measured anterior segment parameters are robust enough to predict the accommodative optical response in young subjects with ample accommodation and in prepresbyopic eyes with lower accommodative amplitudes. This method of predicting the accommodative optical response could be applied in clinical accommodation studies in young and prepresbyopic phakic eyes. In addition,

**Table 8.** Comparison of demographics, optical, and anterior segment biometric measurements between young and prepresbyopic subjects. Except for accommodative amplitudes, all parameters are for the unaccommodated state.

| | Mean ± SD | | | |
|---|---|---|---|---|
| Parameters at Baseline | Young Subjects | Prepresbyopic Subjects | *t* Value | *P* Value |
| Sample size | 26 | 25 | — | — |
| Age (y) | 24.15 ± 3.03* | 40.80 ± 3.08* | −19.444 | <.0001 |
| Sex | | | | |
| Male | 8 | 8 | — | — |
| Female | 18 | 17 | — | — |
| Refractive error (D) | −1.31 ± 2.03 | −1.40 ± 1.98 | — | — |
| Autorefractor | | | | |
| Accommodative amplitude (D) | 5.86 ± 0.42* | 2.56 ± 1.01* | 13.476 | <.0001 |
| Infrared photorefraction | | | | |
| Accommodative amplitude (D) | 5.62 ± 1.29* | 2.67 ± 1.33* | 7.964 | <.0001 |
| Pupil diameter (mm) | 6.28 ± 0.84 | 6.14 ± 0.72 | — | — |
| Ultrasound biomicroscopy | | | | |
| Corneal thickness (mm) | 0.53 ± 0.03 | 0.54 ± 0.04 | — | — |
| ACD (mm) | 3.32 ± 0.24 | 3.15 ± 0.37 | — | — |
| ACD + corneal thickness (mm) | 3.85 ± 0.24 | 3.69 ± 0.37 | — | — |
| Lens thickness (mm) | 3.63 ± 0.17*,† | 4.00 ± 0.35* | −4.834 | .0001 |
| Anterior segment length (mm) | 7.47 ± 0.22*,‡ | 7.71 ± 0.31* | −3.019 | .004 |
| Anterior lens radius of curvature (mm) | 11.68 ± 1.44 | 11.00 ± 1.77 | — | |
| Posterior lens radius of curvature (mm) | 5.66 ± 0.47* | 5.20 ± 0.80* | 2.509 | .016 |
| Angle-to-angle distance (mm) | 10.81 ± 0.48 | 10.57 ± 0.39 | — | — |
| Left anterior chamber angle (deg) | 38.83 ± 7.02 | 36.37 ± 9.02 | — | — |
| Right anterior chamber angle (deg) | 40.59 ± 6.95 | 37.43 ± 9.62 | — | — |
| A-scan ultrasound | | | | |
| ACD + corneal thickness (mm) | 3.75 ± 0.23 | 3.66 ± 0.35 | — | — |
| Lens thickness (mm) | 3.87 ± 0.18*,† | 4.19 ± 0.32* | −4.339 | <.0001 |
| Anterior segment length (mm) | 7.62 ± 0.20*,‡ | 7.85 ± 0.32* | −3.041 | .004 |
| Vitreous chamber depth (mm) | 16.28 ± 1.30 | 16.37 ± 1.07 | — | — |
| Axial length (mm) | 23.90 ± 1.35 | 24.22 ± 1.12 | — | — |

ACD = anterior chamber depth
*Statistically significant differences between young and prepresbyopic subjects
†Statistically significant differences between UBM and A-scan measurements of lens thickness ($t = -4.965$, $P < .0001$)
‡Statistically significant differences between UBM and A-scan measurements of and anterior segment length ($t = -2.389$, $P < .021$)

**Table 9.** Comparison of age-related changes in the ocular anterior segment biometry parameters from previous human studies.

| | | Age-Related Changes in Anterior Segment Biometry (mm/Year) | | | | |
|---|---|---|---|---|---|---|
| Study | Instrument | ACD | LT | ASL | ALRC | PLRC |
| Current | UBM | −0.010 | +0.022 | +0.014 | NC | −0.026 |
| Koretz*[22] | Ultrasonography | −0.011 | +0.021 | +0.009 | NA | NA |
| Atchison*[24] | MRI | −0.011 | +0.024 | +0.013 | −0.044 | NC |
| Koretz*[25] | Scheimpflug | NA | NA | NA | −0.020 | −0.020 |
| Richdale*[26] | US/phakometry | −0.031 | +0.031 | NC | −0.110 | NC |
| Dubbelman*[27,28] | Scheimpflug | −0.010 | +0.024 | +0.015 | −0.057 | −0.012 |
| Koretz*[29] | Scheimpflug | −0.0215 | +0.0194 | NC | −0.0759 | NC |
| Koretz*[29] | MRI | −0.0215 | +0.0193 | NC | −0.0828 | NC |

ACD = anterior chamber depth; ALRC = anterior lens radius of curvature; ASL = anterior segment length; LT = lens thickness; MRI = magnetic resonance imaging; NA = not available; NC = no change; PLRC = posterior lens radius of curvature; US = ultrasound
*First author

prediction of the accommodative optical response as shown here might be useful to observe and evaluate the accommodative ability of accommodation restoration concepts. However, for the purpose of evaluating pseudophakic eyes, the relationships between biometric movements and accommodative optical response in eyes with specific types of IOLs would have to be established before predictions could be made.

In conclusion, this study has shown the ability to predict the accommodative optical response from UBM-measured anterior segment parameters in prepresbyopic eyes with SDs of less than 0.55 D using the linear regressions and 95% CIs. In general, the accommodative optical response predictions in prepresbyopic subjects were better than in young subjects. The SD and repeatability of UBM-measured biometry parameters were similar in prepresbyopic subjects and young subjects. Further study would be required of eyes with accommodation restoration concepts to determine whether an accommodative optical response could be predicted as described here.

## WHAT WAS KNOWN

- A previous study found that UBM-measured anterior segment biometry can be used to predict the accommodative optical response in young phakic eyes. It was not known whether UBM could predict the accommodative optical response in prepresbyopic eyes with low accommodative amplitudes.

## WHAT THIS PAPER ADDS

- Ultrasound biomicroscopy could be used to predict the accommodative optical response in prepresbyopic eyes, and the prediction errors were generally smaller than in young phakic eyes. Despite the low axial resolution, UBM is a useful clinical instrument for accommodation studies.

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