Clinical Study

The Predictability of Preoperative Pilocarpine-Induced Lens Shift on the Outcomes of Accommodating Intraocular Lenses Implanted in Senile Cataract Patients

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Purpose. To evaluate the predictability of lens shift induced by pilocarpine (LS Pilo) on the outcomes of accommodating intraocular lens (Acc-IOL) implantation. Methods. Twenty-four eyes of 24 senile cataract patients who underwent phacoemulsification and Acc-IOL implantation were enrolled. LS Pilo was evaluated with anterior segment optical coherence tomography (AS-OCT). At 3 months postoperatively, the best corrected distance visual acuity (BCDVA), distance-corrected near visual acuity (DCNVA), and subjective and objective accommodations were measured. IOL shifts under accommodation stimulus (IOLS Acc) were evaluated with AS-OCT. Results. The mean LS Pilo was 112.29 ± 30.72 μm. LS Pilo was not associated with any preoperative parameters. The mean IOLS Acc was 130.46 ± 42.71 μm. The mean subjective and objective accommodation were 1.54 ± 0.39 D and 1.27 ± 0.41 D, respectively. The mean postoperative BCDVA and DCNVA (log MAR value) were 0.22 ± 0.11 and 0.24 ± 0.12, respectively. LS Pilo positively correlated with IOLS Acc (r = 0.541; P = 0.006), subjective accommodation (r = 0.412; P = 0.022), and objective accommodation (r = 0.466; P = 0.045), respectively. Conclusion. LS Pilo is an independent preoperative parameter associated with the postoperative Acc-IOL mobility and pseudophakic accommodation. It may offer valuable information for ophthalmologists in determining the suitable candidates for Acc-IOL implantation.

1. Introduction

Restoration of accommodation in pseudophakic patients is a major goal of modern cataract surgery. So far a variety of devices and surgical techniques have been introduced to solve the problem of presbyopia correction and to provide satisfactory distance and near vision without spectacles after cataract surgery. An example is implantation of multifocal intraocular lenses (MF-IOLs) with diffractive or refractive optic designs that improve uncorrected near vision at the expense of reduced contrast sensitivity, halos around lights, and night glare [1–3]. To overcome these visual side effects induced by MF-IOLs, the so-called accommodating intraocular lenses (Acc-IOLs) were developed [4].

The mechanism of the current available Acc-IOLs is based on the Helmholtz theory of accommodation [5], which assumes that the force is transmitted from the ciliary muscle to the lens via the zonular apparatus. These IOLs are designed to transform such forces of the ciliary muscle into a forward shift of the IOL optic through the incorporates hinges, therefore increasing the effective refraction power for near vision [6]. However, the outcomes vary dramatically among patients implanted with Acc-IOLs [6–10]. Most patients achieved both satisfactory distance and near vision without spectacles, while some patients gained very limited accommodation and near vision. Multiple factors may contribute to the variation in the outcomes of Acc-IOLs among individuals [11–14]. On the basis of the optic-shift concept, the postoperative accommodation of an Acc-IOL is dependent on ciliary muscle contraction. We hypothesize that the individual differences in the function of ciliary muscle may play a key role in the variation of Acc-IOLs implanting outcomes.

Unfortunately, there is no established method to assess the potential of ciliary muscle contraction before cataract surgery. It is well known that there is an increase of curvature and anterior movement of the crystalline lens during...
accommodation [15]. In senile cataract patients, the lens loses its deformability, while the axial movement of cataractous lens driven by ciliary muscle contraction may still exist [16, 17], which may work as a function of contractile ability of the ciliary muscle. So we hypothesize that the preoperative evaluation of the lens mobility may indicate the potential contraction power of ciliary muscle related to the postoperative accommodation of an Acc-IOL. Pilocarpine induced lens shifts have been used to assess accommodation in phakia and pseudophakia in previous studies [8, 18], and it might be applicable to senile cataract patients.

The aim of this study was to evaluate the preoperative pilocarpine-induced lens shift, and its predictability on the outcomes of Acc-IOL implantation in senile cataract patients. To the best of our knowledge, for the first time, the accommodation potential assessment is incorporated into the preoperative evaluations of cataract surgery and is considered as a possible indication for Acc-IOL implantation.

2. Patients and Methods

This study is a prospective case series. Eligible patients were enrolled at Cataract Department of the Eye Hospital of Wenzhou Medical University from December 2013 to November 2014. Inclusion criteria were age-related cataract and good overall physical constitution. Exclusion criteria were corneal astigmatism of 1.50 diopters (D) or more, a history of ocular trauma or intraocular surgery, laser treatment, diabetes mellitus requiring medical control, pseudoxefoliation syndrome, glaucoma, uveitis, and retinal pathology that would limit postoperative restoration of vision. Patients who did not return for prescribed follow-ups or had any intraoperative complications were removed from the study.

The study was approved by the Ethics Committee and the Institutional Review Boards of Wenzhou Medical University. All researches and measurements followed the tenets of the Declaration of Helsinki, and informed consents were obtained from all patients.

2.1. Preoperative Evaluation. Each patient underwent a complete eye examination including visual acuity, manifest refraction, keratometry, slit lamp microscope, intraocular pressure (IOP), and dilated retinal examination. Pupil diameter was measured using a template rule (Matheson Optometrists, UK) under standard room light before any eye drop was administered. The LOCS III [19] nuclear opacity was graded on a scale of 0.1 to 6.9 by comparing a digital photograph of each lens with standard color photographic transparencies of nuclear opalescence (NO) and nuclear color (NC) using a slit lamp after dilation by the same ophthalmologist. Biometry including corneal curvature, corneal diameter (white-to-white, WTW), and axial length were obtained with the IOLMaster device (Carl Zeiss Meditec AG, Jena, Germany). The required IOL power was calculated using the SRK/T formula with a postoperative refractive target between plano and −0.50 D.

The central corneal thickness (CCT) and lens shift induced by pilocarpine (LS_{Pilo}) were evaluated with an anterior segment optical coherence tomography (AS-OCT, Visante-1000, Carl Zeiss Meditec., Dublin, Germany). The device was calibrated with an artificial eye before each measurement. The anterior chamber depths (ACDs, distance from the anterior surface of the lens to the corneal vert) both in the baseline unaccommodated state and after induced accommodation with 2% pilocarpine drops (one drop placed every 5 minutes, 6 times in total prior to testing) were measured. The washout time between application of pilocarpine and dilation eye drops should be at least 12 hours. Examination of the intraocular distances was made with the device's software by manually set calipers. LS_{Pilo} was defined as the Δ-values of these two ACDs, LS_{Pilo} = ACD_{Baseline} − ACD_{Pilo}. The measurement was repeated 3 times.

2.2. Surgical Procedure. All surgeries were performed by a single surgeon (DC) under topical anesthesia. A 2.75 mm watertight clear corneal incision was made and 5.0 to 6.0 mm continuous curvilinear capsulorhexis was performed. The nucleus was removed by phacoemulsification in the capsular bag and the residual cortex was aspirated with the I/A handpiece. Viscoelasticity was then used to inflate the capsular bag, and a piece of monooptic Acc-IOL TetraFlexHD® (Lenstec Inc., St. Petersburg, FL, USA) was slowly injected into the bag. The lens was then moved back and forth along the long axis of the lens with a lens hook to verify that the leading and trailing haptics were properly positioned in the capsular bag. Viscoelasticity was then removed and the wound was verified for stability. All patients received the same postoperative regimen of antibiotic and corticoid eye drops (tobramycin + dexamethasone) (Tobradex® Ophthalmic Suspension, Alcon Laboratories Inc., Fort Worth, Texas) for 4 weeks at a dose of 4 times daily initially and then in tapered doses.

2.3. Postoperative Evaluation. At 3 months after surgery, each eye underwent postoperative examinations including visual acuities, manifest refraction, slit lamp, IOP, pupil diameter, CCT, corneal curvature, corneal diameter (WTW), and axial length. Visual acuities were measured using Early Treatment Diabetic Retinopathy Study (ETDRS) charts for distance and near vision at 6 m and 40 cm. Uncorrected distance visual acuities (UCDVA), best corrected distance visual acuities (BCDVA), uncorrected near visual acuities (UCNVA), and distance-corrected near visual acuities (DCNVA) were documented in logarithm of the minimum angle of resolution (log MAR) units.

The amplitudes of subjective and objective accommodation under the maximum near stimulus were measured. Subjective near-point accommodation (NPA) was measured with the defocus method. This method involved placing a lens in front of the eye that created a +3.00 D add over the best distance refraction. The reading target was placed 0.33 m away from the eye. The patient was asked to focus on the line just above the lowest discernable line, and −0.25 D spherical lenses were sequentially placed in front of the eye until the visual target blurred. The NPA power was the sum of the dipters of all minus lenses added until the target blurred. The objective accommodation was measured with the Optical Quality Analysis System (OQAS®, Visiometrics, Terrassa,
to the preoperative baseline, there was no significant change (15/24) and 79.2% (19/24) of eyes, respectively. Comparing vision, UCNVA and DCNVA were 20/40 or better in 62.5% the preoperative baseline (improvement in the BCDVA (logMAR value) comparing to patients at 3 months after surgery. There was a significant

ters listed in Table 1.

ACDs, IOLS

induced lens shift (LS

305.50 \mu m, and the mean ACD after application of pilocarpine was 2452.71±297.74 \mu m. The mean pilocarpine-induced lens shift (LS\textsubscript{pilo}) was 112.29±30.72 \mu m (P < 0.05, Figure 1). Multiple linear regression analysis indicated that LS\textsubscript{pilo} was not associated with any of the preoperative parameters listed in Table 1.

Table 2 shows the main postoperative results of all patients at 3 months after surgery. There was a significant improvement in the BCDVA (logMAR value) comparing to the preoperative baseline (P < 0.001). For postoperative near vision, UCNVA and DCNVA were 20/40 or better in 62.5% (15/24) and 79.2% (19/24) of eyes, respectively. Comparing to the preoperative baseline, there was no significant change in WTW diameter, CCT, pupil size, and axial length after surgery (all P > 0.05). No significant intraoperative or postoperative complications were recorded. Mild posterior capsular fibrosis was noted in 9 eyes (37.50%) at the 3-month follow-up.

### Table 1: Preoperative clinical characteristics in eyes enrolled in this study (n = 24).

| Factors                  | Data                          |
|--------------------------|-------------------------------|
| Age, y                   | 63.50 ± 6.86 (48–75)         |
| Sex (% women)            | 58.33%                        |
| Laterality (% right eye) | 45.8%                         |
| Spherical equivalent (D) | −0.72 ± 1.15 (−2.75 ± 1.88)  |
| BCVA (log MAR)           | 1.24 ± 0.72 (0.4–2.0)        |
| Axial length (mm)        | 24.35 ± 2.32 (21.5–27.3)     |
| WTW diameter (mm)        | 11.56 ± 0.45 (10.7–12.2)     |
| CCT (\mu m)              | 513.43 ± 37.48 (450–565)     |
| Mean keratometric value  | 44.38 ± 1.27 (42.14–46.86)   |
| Pupil size (mm)          | 4.32 ± 0.55 (3.3–5.4)        |
| Nuclear opalescence      | 2.98 ± 1.12 (1–5)            |
| Nuclear color            | 2.92 ± 1.11 (1–5)            |
| IOP (mmHg)               | 15.14 ± 2.96 (11–20)         |
| ACD (\mu m)              | 2565.60 ± 305.50 (2136–3018) |
| LS\textsubscript{pilo} (\mu m) | 112.29 ± 30.72 (50–185)     |
| IOL power (D)            | 19.92 ± 2.16 (14–25)         |

### Table 2: Results of ocular factors at 3 months postoperatively.

| Factors                  | Data                          |
|--------------------------|-------------------------------|
| Spherical equivalent (D) | −0.40 ± 0.74 (−1.02 ± 0.63)  |
| UCDVA (log MAR)          | 0.26 ± 0.14 (0.1–0.52)       |
| BCMDVA (log MAR)         | 0.22 ± 0.11 (0–0.40)         |
| UCNVA (log MAR)          | 0.27 ± 0.15 (0.1–0.60)       |
| DCNVA (log MAR)          | 0.24 ± 0.12 (0.05–0.52)      |
| WTW diameter (mm)        | 11.60 ± 0.53 (10.8–12.1)     |
| CCT (\mu m)              | 521.16 ± 36.55 (458–573)     |
| Pupil size (mm)          | 4.29 ± 0.59 (3.1–5.5)        |
| Axial length (mm)        | 24.38 ± 2.29 (21.7–27.2)     |
| Postoperative ACD (\mu m)| 3197.92 ± 349.71 (2785–3961) |
| Subjective accommodation (D) | 1.54 ± 0.39 (0.95–2.22)     |
| Objective accommodation (D) | 1.27 ± 0.41 (0.75–2.25)     |
| IOLS\textsubscript{Acc} (\mu m) | 130.46 ± 42.71 (73–215)   |
| IOP (mmHg)               | 12.63 ± 2.44 (8.7–18.2)      |

D: diopters; UCDVA: uncorrected distance visual acuity; logMAR: logarithm of the minimum angle of resolution; WTW: white-to-white; CCT: central corneal thickness; IOP: intraocular pressure; ACD: anterior chamber depth; LS\textsubscript{pilo}: lens shift induced by pilocarpine; IOL: intraocular lenses. Results are expressed as means ± standard deviation (range).
The mean postoperative ACD was 3197.92 ± 349.71 μm at baseline and was 3067.46 ± 341.26 μm at the maximum accommodation stimulus. The mean IOL shift under the accommodation stimulus (IOLS\textsubscript{Acc}) was 130.46 ± 42.71 μm \( (P < 0.05, \text{Figure 1}) \). IOLS\textsubscript{Acc} was positively correlated with LS\textsubscript{Pilo} \( (r = 0.541; P = 0.066) \) (Figure 2). The mean postoperative subjective accommodation measured with NPA was 1.54 ± 0.39 D, the mean objective accommodation measured with OQAS was 1.27 ± 0.41 D, and there was a strong correlation between subjective and objective accommodations \( (r = 0.715; P < 0.001) \). There was positive correlation between LS\textsubscript{Pilo} and subjective and objective accommodation \( (r = 0.412; P = 0.022) \) (Figure 2). The postoperative DCNVA was correlated with objective accommodation \( (r = 0.381; P = 0.067) \) (Figure 2), but not directly with LS\textsubscript{Pilo} \( (r = 0.381; P = 0.067) \) (Figure 2).

Postoperative objective accommodation and DCNVA were selected as indicators of the efficacy of Acc-IOL implantation. The potential preoperative predictive factors for these two indicators were revealed by multiple linear regression analysis. Objective accommodation was associated with LS\textsubscript{Pilo} \( (\beta = 0.380; P = 0.016) \) and AL \( (\beta = -0.353; P = 0.032) \); the postoperative DCNVA (logMAR value) was associated with pupil diameter \( (\beta = 0.311; P = 0.049) \) and age \( (\beta = 0.368; P = 0.038) \).

4. Discussion

The great development of cataract surgery has led to an increase in the number of intraocular lenses (IOLs) that attempt to achieve the best uncorrected visual acuity possible at all distances. The multifocal intraocular lenses (MF-IOLs) seem to be dominant in the market in recent years. However, this type of IOL has intrinsic drawbacks of reduced contrast sensitivity, halos around lights, and night glare [1–3], due to its basic principle of redistribution of the light energy with no single focus receiving all the energy as it happens in normal physiological accommodation. The single-optic accommodating intraocular lens (Acc-IOL) is another option for restoration of accommodation in pseudophakic patients after cataract surgery [4]. Current Acc-IOL designs are based on the “focus shift” principle: contraction of the ciliary muscles causes the optic to move anteriorly through various mechanisms, thereby increasing the dioptric power of the eye. However, according to different reports, there was a big variation in the outcomes among individuals after uncomplicated cataract surgery and Acc-IOL implantation [6–10]. The underlying causes remain unknown. Currently there is no effective method to predict the postoperative accommodation based on the preoperative evaluations or established criteria to determine the proper candidate for Acc-IOL implantation.

It is well known that the most accepted model of accommodation is based on the theory of Helmholtz in terms of the interactions between the ciliary muscle, zonule, and lens. There is an increase of curvature and to some extent an anterior movement of in the crystalline lens during accommodation [15]. The prime cause of the development of presbyopia has been interpreted to be lenticular growth and the associated changes in its viscoelastic properties as a function of age [23]. Meanwhile the ciliary muscle maintains most of its contraction power in presbyopic eyes and just declines slightly over age [24]. In senile or age-related cataract patients, the lens loses its properties of deformation due to increased density and rigidity; however, the axial movement driven by ciliary contraction may still exist. In our study, there was a significant translational forward lens shift of about 112 μm under pilocarpine. The amount of pilocarpine-induced lens shift (LS\textsubscript{Pilo}) may indirectly reflect the potential contraction power of ciliary muscles. In addition, we found that LS\textsubscript{Pilo} was independent of other preoperative parameters including age, which confirms that the contraction power of ciliary muscles may not change as a function of age.

The measurement of the IOL shift under accommodation stimulation has been used to evaluate the accommodation efficiency of Acc-IOLs [8, 18, 25, 26]. Marchini et al. [25] measured the forward shift of the Crystalen® AT-45 Acc-IOL.
Figure 2: Correlation of preoperative lens shifts induced by pilocarpine ($L_{Pilo}$) and different postoperative parameters. (a) The preoperative $L_{Pilo}$ positively correlated with the postoperative intraocular lens shift under an accommodation stimulus ($IOLS_{Acc}$) ($r = 0.541; P = 0.006$). (b) The preoperative $L_{Pilo}$ positively correlated with the postoperative subjective accommodation of Acc-IOLs ($r = 0.435; P = 0.033$). (c) The preoperative $L_{Pilo}$ positively correlated with the postoperative objective accommodation of Acc-IOLs ($r = 0.485; P = 0.016$). (d) The preoperative $L_{Pilo}$ did not correlate with the postoperative distance-corrected near visual acuities (DCNVA) (logMAR value) ($r = 0.381; P = 0.067$).

with accommodative effort using ultrasonic biological microscope (UBM) and found that the forward shift could reach 330 μm 6 months after their implantation. Dong et al. [8] observed that the forward mobility of TetraFlex® Acc-IOL under stimulated accommodation with pilocarpine was 337 μm measured with AS-OCT 3 months after surgery. Koepll et al. [18] indicated that IOL movement may be overestimated when using pilocarpine to stimulate accommodation in aged subjects. Therefore, we measured the IOL shift under physiological accommodation stimulation with AS-OCT. The forward mobility of TetraFlexHD under stimulated accommodation was around 130 μm, which is less than the previous reports listed above. The discrepancy may be attributed to the different designs of Acc-IOLs, accommodative stimulations, as well as the assessment methods adopted. The postoperative $IOLS_{Acc}$ correlated positively with the preoperative $L_{Pilo}$. The underlying link between these two parameters is that both the cataractous crystalline lens and Acc-IOL are dependent on the ability of ciliary muscle contraction. Therefore, the preoperative $L_{Pilo}$ might be considered as an indicator of the mobility of the Acc-IOL to be implanted.

In this study, we utilized OQAS to measure objective accommodation to make up for the weakness within the subjective NPA method. The subjective accommodation and objective accommodation were significantly correlated, while the former was slightly higher than the latter. The difference between the subjective and objective measurements of accommodation may be attributed to the inclusion of depth-of-focus effects [27]. Both subjective and objective accommodation correlated positively with the preoperative $L_{Pilo}$ and postoperative $IOLS_{Acc}$. In addition, the objective accommodation was also associated with the preoperative axial length. This can be explained by the “focus shift” principle of Acc-IOL design. The degree of accommodative effect is related not only to the degree of IOL movement but also to the
power of IOL, which largely depends on the axial length [28]. Nawa et al. [29] demonstrated that a 1 mm displacement equates to a 0.8 D change in power in an eye with an axial length of 27 mm, keratometry 7.7 mm, and IOL power 11 D, whereas a 1 mm displacement equates to 2.3 D of change in power in an eye with an axial length of 21 mm, IOL power 30, and the same keratometry. However, in the current study, the Acc-IOL shifts were inadequate to produce the amount of accommodation according to the mathematical calculations. In fact, the accommodation of pseudophakic eye (pseudophakic accommodation) is different from the true accommodation of natural crystal lens in phakia. Sergienko et al. [30] suggested that the accommodative ability of pseudophakic eye was composed of two components: artificial accommodation resulting from axial optic movement and pseudoaccommodation as a consequence of a particular depth of focus, and the proportion between artificial accommodation and pseudoaccommodation of Acc-IOL was nearly 1:2. Beside the depth of focus, myopic astigmatism [11], corneal multifocality [31], and aberrations [13] may also contribute to the pseudophakic accommodation. All these factors may account for the difference between the mathematical calculation and clinical measurement of accommodation in pseudophakia.

Most subjects in our study achieved fairly good near vision despite the relatively limited accommodation of Acc-IOLs as measured. This is not surprising to us since patients with monofocal IOL implantation having good uncorrected visual acuity for distance and near vision are occasionally noted from clinical experience. Depth of focus, an intrinsic characteristic of all optical systems that is attributed to aberrations and pupil size, is considered to be one of the most significant contributing factors to near vision in pseudophakic eyes [30]. This was confirmed with the association between DCNVA and pupil diameter in our study. Obviously, all these factors affecting pseudophakic accommodation are responsible for the near vision [11–13]. In addition, decreased near vision ability of pseudophakic patients proportional with age was found by Hayashi et al. [14]. Similar inverse association between the postoperative near vision and age was demonstrated in our study. The aging decay of visual perception is the main causative factor for this phenomenon [14].

This study has some limitations. We did not rule out the possibility of other factors that may affect the postoperative pseudophakic accommodation and near vision, such as dynamic change in pupil size during accommodation, corneal astigmatism, aberrations, and posterior capsular fibrosis. The small sample size and short duration of follow-up also limit the power of this study. Future studies based on a larger population and longer follow-up will be performed to investigate the multiple factors that are associated with the accommodation and visual outcomes of Acc-IOLs.

In conclusion, LS_pilo is an independent preoperative parameter associated with the postoperative Acc-IOL mobility and pseudophakic accommodation. As an indicator of the potential of ciliary muscle contraction, LS_pilo may give valuable information for ophthalmologists in determining the suitable candidates for Acc-IOL implantation.

Competing Interests
The authors have no proprietary or commercial interests in any materials discussed in this paper.

Authors’ Contributions
Jin Li and Qi Chen contribute equally to this work.

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