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Article

Clinical Application of 25-MHz Ultrasound Biomicroscopy for Lens Opacity Degree Measurements in Phacoemulsification

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Purpose: To evaluate the correlation between lens opacity degrees and phacoemulsification cumulated dissipated energy (CDE) values in patients with age-related cataract by applying 25-MHz panoramic ultrasound biomicroscopy (UBM).

Methods: This observational study was conducted in 227 patients (294 eyes) with age-related cataract. Patient ages ranged from 45 to 91 years. According to the lens images acquired by 25-MHz UBM, the objective indexes of lens opacity degrees were determined by using the ImageJ software. The correlation between lens opacity degrees (pixel units) and CDE values of phacoemulsification were mainly analyzed.

Results: The means of measurements were as follows: preoperative LogMAR corrected distance visual acuity, anterior chamber depth, and central lens thickness was 1.10 ± 0.61, 2.52 ± 0.51, and 4.34 ± 0.60 mm, respectively. The mean 25-MHz UBM-measured lens opacity degree was 101.30 ± 19.70 pixel units, and the mean CDE value was 9.74 ± 9.10. There was a linear correlation between pixel units and the CDE value, as well as LogMAR corrected distance visual acuity ($r = 0.38$ and 0.50, respectively; both $P < 0.05$). Age correlated with anterior chamber depth and lens thickness ($r = -0.18$ and 0.16, respectively; both $P < 0.05$) but not with pixel units ($r = -0.08$, $P > 0.05$).

Conclusion: The 25-MHz UBM has significant advantages in displaying the opacity feature of age-related cataract. The 25-MHz UBM combined with ImageJ software can be used to evaluate the opacity degree of age-related cataract quantitatively and may help predict the phacoemulsification parameters in cataract surgery.

Translational Relevance: Combination of the lens ultrasonic image and image analysis software enables researchers to evaluate lens opacity degree quantitatively and predict the parameters of phacoemulsification surgery.

Introduction

The current standard for grading cataract is the Lens Opacification Classification System III (LOCS III). Because this assessment is based on a slit-lamp evaluation by ophthalmologists, the results are potentially subjective due to interpretation and a lack of consistency.[1] Concerns about the reproducibility within observers encourage the presence of objective methods based on anterior segment inspecting equipment, such as anterior segment optical coherence tomography (AS-OCT) and Scheimpflug imaging (Pentacam).[2,3] Most in vivo studies have shown validity and reliability of both methods and a correlation with the nuclear cataract lens density. However, these two modalities have limitations in displaying the complete morphology of the lens. Moreover, due to the imaging limitation, advanced cortical and posterior subcapsular (PSC) opacities may interfere with the quality of the objective measurements. Thus, previous researches did not incorporate all types of age-related cataract into observation.

In clinical practice, the assessment of lens opacity is helpful for assessing the type, severity, and progression of cataracts and predicting the dynamic process of phacoemulsification.[4] The mean cumulative dissipated energy (CDE) value represents the mean percentage of power spent during ultrasound. Previous studies have reported the correlation between nuclear density measurement and CDE in patients with nuclear opacity.[5,6] However, due to the limitation of the optical instruments, the correlation between cortical and PSC opacities and CDE value were not widely discussed.

The conventionally used ultrasound biomicroscopy (UBM) is 50 to 100 MHz. Due to the frequency and penetration power, it can display the anterior segments, the anterior capsule of the lens, and a small portion of posterior lens capsule, except for the whole morphology of lens. With the emergence of 25-MHz UBM, which possesses a relatively low frequency but high penetration compared with 50-MHz UBM, its ultrasonic focal point mainly locates in the lens. Thus, it is possible to fully display the condition of lens, from anterior to the posterior capsule, as well as the zonule, and study the morphologic characteristics of age-related cataract opacity.[7,8]

This study explored the ultrasonic image features of age-related cataract by using 25-MHz UBM, quantified the cataract opacity degree by ImageJ software, and analyzed the correlation between lens opacity degree and phacoemulsification parameters. To our knowledge, this is the first paper to show a linear relationship between objective lens density measured with 25-MHz UBM and phacodynamics during cataract surgery, with a view to evaluate merits and demerits of the 25-MHz UBM for the assessment of age-related cataract.

Patients and Methods

This observational study was performed at the Ophthalmology Department, The Fourth Affiliated Hospital of China Medical University (Shenyang, Liaoning, China). It comprised patients with age-related cataract who underwent phacoemulsification from February 2017 to November 2017. The study did not include other types of cataracts, such as traumatic, concurrency, and congenital cataract. Inclusion criteria were age-related cataracts without other ocular and systemic diseases affecting vision. All patients were fully informed of the details and possible risks of the examination. Written informed consent was obtained from all subjects before examination following the tenets of the Declaration of Helsinki. The study was approved by The Ethics Committee of the Fourth Affiliated Hospital of China Medical University (no. 2015-029) and registered at www.chictr.org.cn. (registration no. ChiCTR – DOD –15007603).

The preoperative ophthalmic examinations included logMAR corrected distance visual acuity (CDVA), routine slit lamp examinations after mydriasis, and 25-MHz UBM (MD-320; MEDA Co. Ltd., Tianjin, China) examination; a double blind method was used for slit lamp and UBM examination. The slit lamp images of lens were captured and the types of cataract were defined by an experienced cataract doctor (JZ) two days before surgery.

Due to the concern about the contact-checking feature of UBM, parameters of anterior segment including anterior chamber depth (ACD) and lens thickness (LT) were measured when these patients were taking examinations in an out-patient clinic. For homogenous comparison, all the parameters were measured three times and averaged. When these patients with cataract were admitted to hospital, UBM examinations were performed by a skilled operator (MS) with these in-hospital patients 1 day before cataract surgery. The scanner was equipped with a 25-MHz transducer allowing 4- to 5-mm and 9- to 10-mm tissue penetration and axial resolution of approximately 50 μm. An immersion technique was used: the patient was placed in the supine position, after superficial anesthesia, placing a sterile sclera cup into conjunctival sac, filled with distilled water as a coupling agent. Clear images of anterior segments were captured at vertical/horizontal directions and two oblique axes perpendicular to each other without mydriasis. Images obtained by the 25-MHz UBM were imported to ImageJ software for further analysis. The outline of the elliptical mask (including the lens capsule, cortex, and nucleus) was identified by software automatically, but some local positions need to be adjusted manually (Fig. 1). Lens density was measured in pixel units on a scale of 0 to 255 by using the ImageJ software.

All surgeries were performed using the Infiniti Vision System (Alcon, Fort Worth, TX), and the same US and fluidic settings were used by a single experienced surgeon (JZ). With a routine phaco-chop technique, the torsional mode and 100% amplitude were selected. The vacuum limit was 450 mm Hg, and the aspiration flow rate was 30 mL/min. Balanced salt solution (BSS plus; Alcon) was used as irrigation solution. At the end of each surgery, CDE values displayed on the screen were noted.

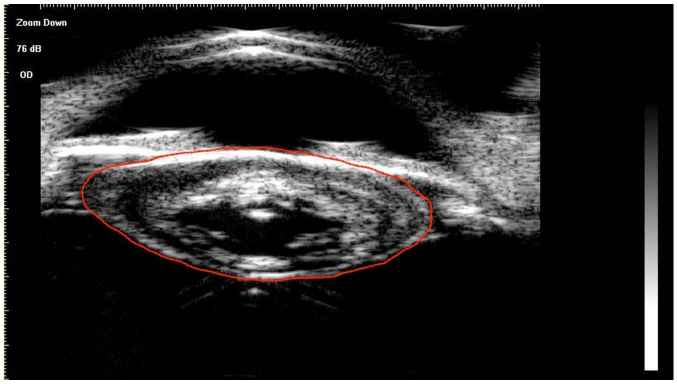

Figure 1. The lens image of 25-MHz UBM exported to ImageJ software for measuring lens opacity degree in the region of interest, indicated by the red elliptical mark.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 19, SPSS Inc., City, State, Country). The results were presented in terms of mean ± SD along with the 95% confidence intervals (CIs). The comparison of anterior segment parameters and pixel units among four axial sections was calculated using one-way ANOVA, and a $P < 0.05$ was considered a statistically significant difference. Correlation analysis of all variables was calculated using the Spearman correlation coefficients, and a $P < 0.05$ was considered a statistically significant correlation.

Results

In this study, 294 eyes of 277 patients (129 females, 148 males) were evaluated, and the mean age of the patients was 69.3 ± 11.2 years (range from 45 to 91 years). The means of measurements were as follows: preoperative LogMAR CDVA, ACD, and LT were 1.10 ± 0.61, 2.52 ± 0.51 mm, and 4.34 ± 0.60 mm, respectively. The mean 25-MHz UBM-measured lens opacity degree was 101.30 ± 19.70 pixel units, and the mean CDE value was 9.74 ± 9.10.

Among all the photos captured by slit lamp, 188 eyes were cortical cataract, 84 eyes were nuclear cataract, 14 eyes were PSC cataract, and 8 eyes were mixed cataract. Compared with slit lamp photos, age-related cataract had six types of ultrasonic morphological features on 25-MHz UBM images: 69 eyes were capsular/subcapsular lens opacity, 26 eyes were globular hyperechoic lens opacity, 93 eyes were concentric circular lens opacity, 84 eyes were thick lens, 14 eyes were PSC lens opacity and 8 eyes were mixed lens opacity (Fig. 2).The first three types of ultrasonic images (capsular/subcapsular, globular hyperechoic, and concentric circular lens) (Fig. 3, the first row) represented the slit lamp image of cortical cataract (Fig. 3, the second row); the ultrasonic image of the thick lens, the PSC lens, and the mixed lens (Fig. 3, the third row) were in accordance with the slit lamp image of pure nuclear

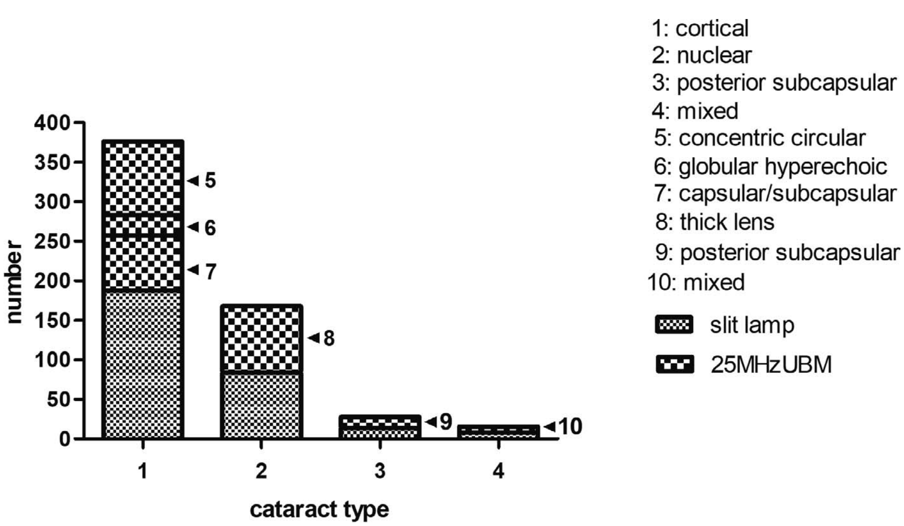

Figure 2. The eyes number distribution of different types of age-related cataract obtained with slit lamp and 25-MHz UBM. Numbers 1, 2, 3, and 4 represented the eyes number distribution of the cortical, nuclear, PSC, and mixed cataract defined by slit lamp, respectively. Numbers 5, 6, 7, 8, 9, and 10 represented the eyes number distribution of the capsular/subcapsular, globular hyperechoic, concentric circular, thick lens, PSC, and mixed lens opacity defined by the image of 25-MHz UBM, respectively.

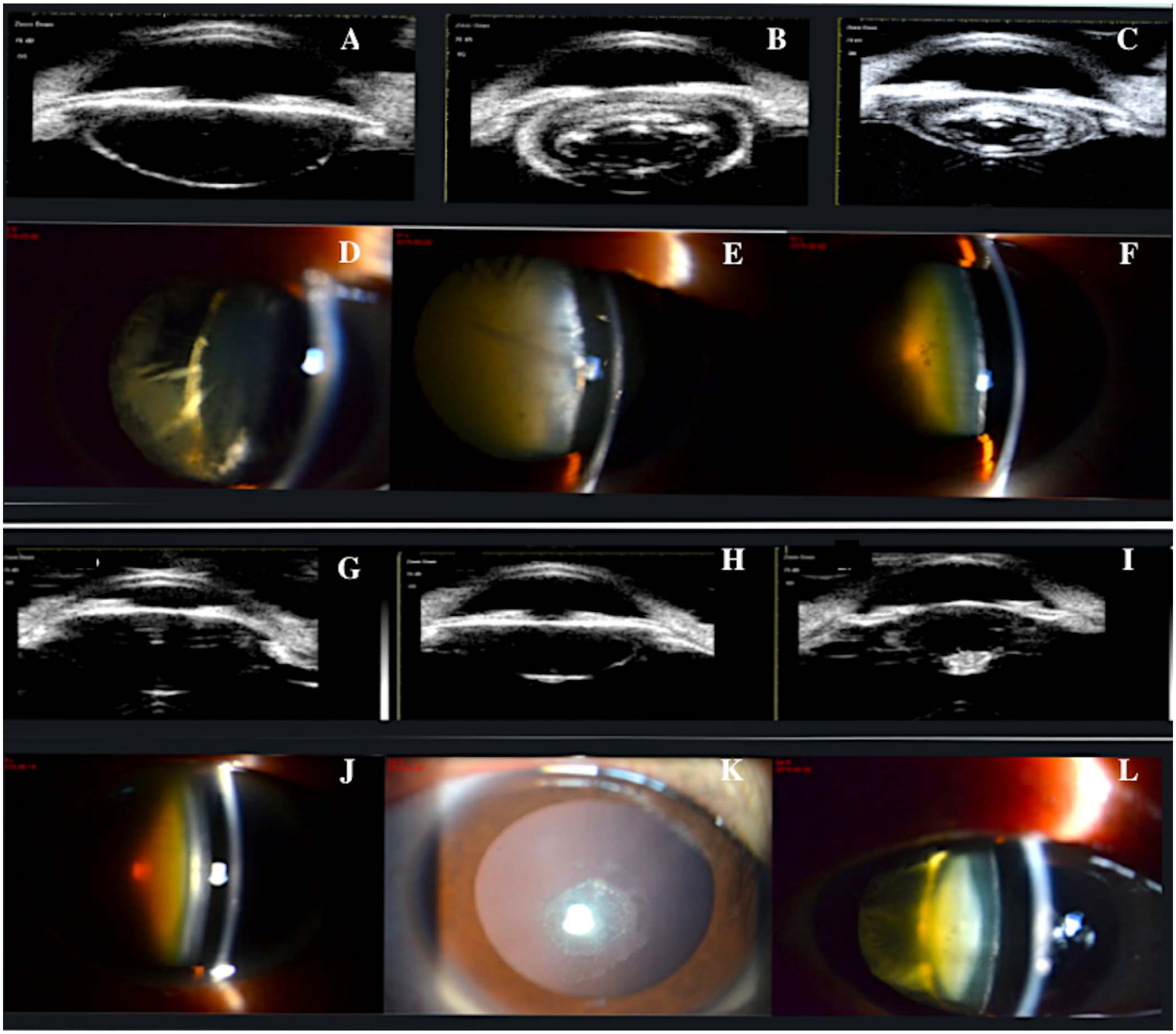

Figure 3. The images of age-related cataract obtained with 25-MHz UBM and slit lamp. The first and the third row showed the 25-MHz UBM images. From *left to right*, *top to bottom* were capsular/subcapsular, globular hyperechoic, concentric circular, thick lens, PSC, and mixed lens opacity. The second and the fourth row were the corresponding slit lamp images (D–F, J–L) matched with the 25-MHz UBM images (A–C, G–I).

cataract, PSC, and mixed cataract (Fig. 3, the fourth row), respectively.

In terms of phacodynamics, pixel units were positively correlated with the CDE value ($r = 0.38$, $P < 0.05$; Fig. 4A). The increased pixel units were associated with increased LogMAR CDVA ($r = 0.50$, $P < 0.05$; Fig. 4B). The correlation between age and ACD and LT were shown in Figure 5. Age had a negative correlation with ACD and a positive correlation with LT ($r = -0.18$ and 0.16, $P < 0.05$; Fig. 5A, 5B) but not with lens opacity degree (pixel units; $r = -0.08$, $P > 0.05$).

Discussion

UBM is a painless and noninvasive diagnostic technique that offers high-resolution anterior segment imaging.[9] Compared with conventional 50-MHz UBM, 25-MHz UBM maintains high resolution and possesses a higher penetrability that can reach to 9-mm tissue depth. Because the ultrasonic focus is

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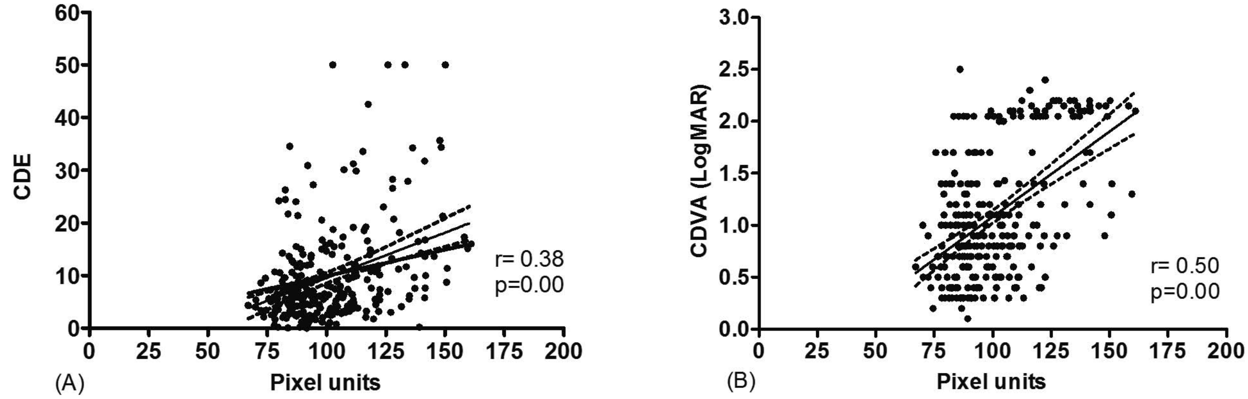

Figure 4. The correlation between pixel units and CDE values and LogMAR CDVA.

located in the lens, it is possible to observe complete morphology of lens and its lesions objectively in vivo. The lens fibers are the main components of the lens cortex and nucleus. The transparency of lens depends on the regular arrangement of lens fibers, and disordered lens fibers is the main cause of different types of cataract.[10] By observing the lens under slit lamp, the types of cataract are mainly subjectively determined by the opacity part after mydriasis rather than pathological change process. Unlike the images observed under slit lamp, ultrasonic images displayed by 25-MHz UBM can reflect the pathological lesions of different lens component and provide an objective-imaging basis for diagnosis and classification of age-related cataract. Furthermore, the objective lens opacity images can be analyzed and quantified by ImageJ software. ImageJ software is a Java-based public image analysis and processing software,[11] and the pixel units can be used to quantitatively evaluate the lens opacity degree. Objective lens opacity degree quantification can assist in predicting phacoemulsification dynamics in cataract surgery and evaluating risk factors for cataract development.[12]

The mean CDE values represent the mean percentage of power spent during phacoemulsification and is calculated in the torsional mode (torsional amplitude × torsional time × 0.4). The correlation between CDE value and the lens opacity degree is a comprehensive index in phacoemulsification. Hard nucleus requires more phacoemulsification energy, and the energy recorded as the CDE reflects the hardness of the nucleus.[13] Many previous researches used the optical anterior segment devices such as Scheimpflug system or AS-OCT to study the correlation between lens density and phacoemulsification parameters. Kim et al.[13] reported a positive linear correlation between the CDE value and the lens density measured by the Scheimpflug system in age-related nuclear cataract. Thus, the Scheimpflug system enables quantitative cataract grading and may help predict phacodynamics in cataract surgery. Although Scheimpflug system can provide accurate and objective measurement of lens density, it is

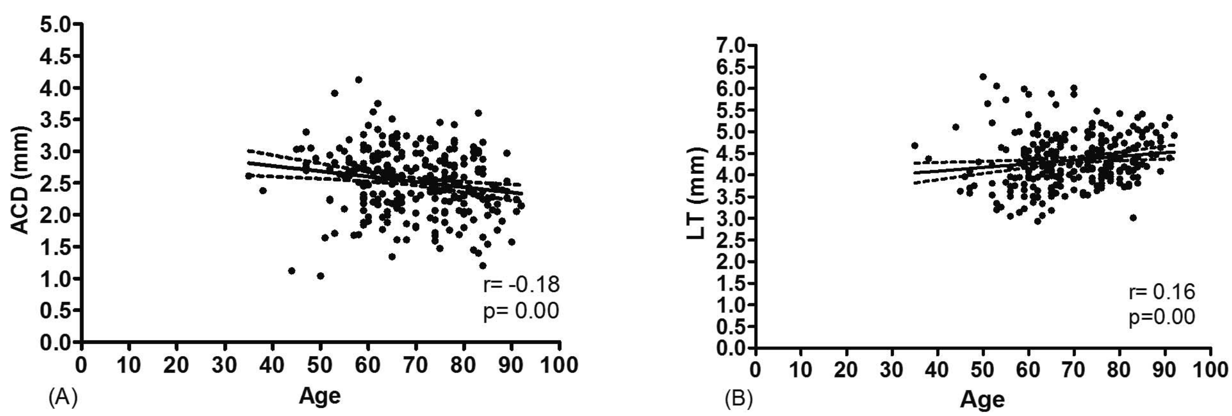

Figure 5. The correlation between age and ACD and LT.

affected by the corneal opacity, insufficient pupil dilatation and the clarity of the refractive media.[14] In clinical practice, it would be difficult to measure the cortical and PSC opacities by the Scheimpflug system, even if the pupil is fully dilated.[13] Besides, the Scheimpflug-measured lens density software displays a lower value for high-grade cataract because the density is too high to allow light to pass through the nucleus.[15] These limitations were particularly manifested in cataract with severe cortical opacity in our pretest. In the present study, we found that nearly 50% of globular hyperechoic lens opacity cannot be measured accurately by Scheimpflug system. AS-OCT is another imaging modality that has been developed for objective assessment of lens density. Wong et al.[2] pointed that AS-OCT is a reliable instrument for lens opacity measurement. Unlike the Scheimpflug system, AS-OCT possesses the ability for providing a clear visualization of the anterior and posterior cortical opacities, but the shadowing by the anterior cortical opacities reduces the visibility of the posterior cortex. Moreover, as the visibility of anterior cortex decays, the cortical opacities may be underestimated. With regard to PSC opacities, it is difficult to distinguish the opacities and the light reflex from the posterior capsule that may lead to overestimation of subcapsular cataract. Makhotkina et al. found there is a moderate correlation between CDE and lens nuclear density measurement using AS-OCT. Due to the technical limitation of AS-OCT, advanced cortical and PSC opacities may interfere with the quality of objective measurements. Meanwhile, no effect on the correlations between lens density measurements and phacoemulsification energy was observed in these types of cataract patients. As shown in Figure 4A, the positive liner relationship between lens opacity degree obtained by 25-MHz UBM and CDE value indicates that the ultrasonic image of lens is a novel and objective evaluating index of age-related cataract. Our results manifest that 25-MHz UBM can display the lens lesions integrally without being affected by refractive media opacity and pupil size. Therefore, it can be applied to evaluate the relationship between all types of age-related cataract opacity degree and phacoemulsification parameters without restriction of nuclear cataract. In addition, due to the advantage on showing lens morphology completely, 25-MHz UBM could be used for the observation of lens subluxation and the integrity of the posterior lens capsule, among others.[8]

LOCS III is based on the evaluation of three sets of photographs taken under the slit lamp and compared with the standard color photographic transparencies of cortical cataract, nuclear opalescence, nuclear color, and PSC.[17] The LOCS III cataract grading system enhances the ability to estimate ultrasonic energy expenditure during phacoemulsification. Preoperative LOCS III cataract classification can help to create a more formally organized, integrated, customized operative plan. Scheimpflug system and AS-OCT were applied to evaluate the relationship between objective measurement of lens nuclear density and subjective measurement of LOCS III grading score for nuclear opalescence and nuclear color.[2,13] In our study, the lens image obtained by 25-MHz UBM was imported to the ImageJ software to calculate the pixel units and evaluate the degree of lens opacity. As shown in Figure 3, the boundaries between lens cortex and nucleus displayed by two-dimensional section image of 25-MHz UBM are ambiguous. Meanwhile, echoes are rather rare inside the lens especially in the types of capsular/subcapsular, thick lens, and PSC lens opacity. We speculate that the ultrastructural features of the above three types of cataract may have a relationship with the growth characteristic of lens fibers. Lens fibers continue to generate lifelong with new fibers pressing the original ones to the center and then form the nucleus. With aging, insoluble crystalline aggregates in the lens nucleus lead to the formation of a brown nuclear cataract. Because the process is homogeneous, there is no definite boundary between the lens cortex and nucleus.[17] Thus, it is inaccurate and unobjective to classify the opacities of the lens cortex and nucleus like the classical LOCS III system by the 25-MHz UBM.

There are three important issues in estimating the need for cataract surgery, including the lens opacity degree, visual acuity, and patient concern.[12] As shown in Figure 4B, the pixel units had a significant correlation with visual impairment, and the increased pixel units of lens opacity degree is associated with increased preoperative LogMAR CDVA. As a quantitative and objective parameter, the ImageJ-measured indexes according to 25-MHz UBM image can present the degree of lens opacity and associated visual impairment from all types of age-related cataract. This result is in good agreement with the findings of Pei et al.,[12] who reported a correlation between lens density and visual acuity by the Scheimpflug system.

Choosing the representative index of peak or mean value in lens density measurement is controversial in the application of Scheimpflug system.[15] Vertical and horizontal axes are the most commonly used scan directions. To fully display the lens structure, we added two mutual perpendicular oblique axes as well. The parameters were determined by the average data obtained in these four directions. In the present study, four axial images of anterior segment were captured by 25-MHz UBM to observe the entire lens lesions, and no statistically significant differences were observed in ACD, LT, and pixel units in these four axial sections. Thus, it is reasonable to take the average value of four axial sections for relevant analysis and comparison. With a view to evaluate the relative factors in age-related cataract formation, no correlation was observed between age and the pixel units, which suggests that age is not a necessary factor for lens opacity degree. As for the correlation between age and morphology of anterior segment observed by 25-MHz UBM (Fig. 5), the results are consistent with Jonas et al.[18] who report that that the ACD becomes shallower and the LT becomes thickened with the aging process. Because ultrasound does not develop in homogeneous media without acoustic impedance,[19] the central part of thick lens is almost hollow in the 25-MHz UBM image. The main pathological changes of thick lens cataract are nuclear sclerosis, and its histological appearance is homogeneous mass.[20] As a result, the obtained pixel units according to the 25-MHz UBM image are low, and the CDE value may be underestimated. This demerit is similar to the lower Scheimpflug-measured lens density for high-grade cataract.[13] Therefore, we suppose 25 MHz maybe not suitable for observing severe thick lens cases.

In conclusion, as a novel and objective anterior segment imaging technique, 25-MHz UBM has an obvious advantage in showing the opacity features of different types of age-related cataract. This study focused on the combination of 25-MHz UBM ultrasonic imaging and ImageJ software, which would also be a quantitative tool for evaluating the lens opacity degree and phacoemulsification parameters. Nevertheless, imaging with UBM has several limitations. Due to the contact nature of examination, there is a risk for infection or corneal abrasion. Meanwhile, the procedure is more time consuming and requires a skilled operator to obtain high-quality images. According to the imaging characteristics of ultrasonic and optical methods, we predict the possible usefulness of 25-MHz UBM in planning parameters relating to femtosecond laser cataract surgery and helping the surgeon preplanning the cataract surgery. Although UBM may be a promising tool for lens density evaluation, further studies to elucidate the potential of this imaging modality are required in the future.

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