· Clinical Research ·

Comparison of three fundus inspection methods during phacoemulsification in diabetic white cataract

Shu Su, Jian Wu, Min Ji, Yu Guan, Yao Shen, Huai–Jin Guan

Eye Institute, Affiliated Hospital of Nantong University, Nantong 226001, Jiangsu Province, China

Correspondence to: Huai-Jin Guan. Eye Institute, Affiliated Hospital of Nantong University, 20 Xisi Road, Nantong 226001, Jiangsu Province, China. guanhjeye@163.com

Received: 2023-04-14 Accepted: 2023-08-08

Abstract

● **AIM:** To investigate whether Wild Field Imaging System (WFIS SW-8000), 25G endoilluminator, and intraoperative optical coherence tomography (iOCT) can perform real-time screening and diagnosing in patients with suspicious diabetic retinopathy (DR) during phacoemulsification, especially in cases of white cataract.

● **METHODS:** A cross-sectional study was carried out. A total of 204 dense diabetic cataractous eyes of 204 patients with suspected DR treated from April 2020 to March 2021 were included. Phacoemulsification combined with intraocular lens implantation was performed. Following the removal of the lens opacity, the 25G endo-illuminator, fundus photography, and iOCT were performed successively. Optical coherence tomography (OCT) and/or fundus fluorescein angiography (FFA) were used to verify the fundus findings postoperatively. Intraoperative and postoperative results were compared to verify the accuracy of intraoperative diagnosis in each group.

● **RESULTS:** Intraoperative and postoperative examinations revealed 58 and 62 eyes with DR, respectively (positive rate, 28.43% and 30.39%, respectively). During the phacoemulsification, WFIS SW-8000 detected 44 eyes with DR (the detection rate, 70.97%); 25G endo-illuminator found 56 eyes with DR (the detection rate, 90.32%); iOCT found 46 eyes with DR (the detection rate, 74.19%); and 58 eyes with DR were found by combining the three methods (the detection rate, 93.55%). There were statistically significant differences in the diagnostic sensitivity for DR among the methods (χ^2=16.36, *P*=0.001).

● **CONCLUSION:** WFIS SW-8000, 25G endo-illuminator, iOCT, and especially their combination can be used to inspect the fundus and detect DR intraoperatively; they are helpful for the timely diagnosis and treatment of DR in patients with dense cataract.

● **KEYWORDS:** diabetic white cataract; fundus inspection; phacoemulsification; diabetic retinopathy

DOI:10.18240/ijo.2023.11.07

Citation: Su S, Wu J, Ji M, Guan Y, Shen Y, Guan HJ. Comparison of three fundus inspection methods during phacoemulsification in diabetic white cataract. *Int J Ophthalmol* 2023;16(11):1782-1788

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease resulting from inadequate insulin production or ineffective insulin utilization. It is one of the most common systemic diseases worldwide with increasing prevalence[1-2]. Type 2 diabetes (T2D) is a risk factor for cataract development. With T2D prevalence increasing, the burden of cataract-associated vision loss will also increase[3-4]. The risk of cataract development in DM is fivefold higher than that in the general population, and cataract is diagnosed twice as frequently in diabetic subjects. Diabetic cataract (DC) is one of the main ocular complications that may lead to significant visual impairment[5]. To recover sight, these patients need to receive cataract surgery. However, one study reported that intraocular inflammatory factors may increase significantly within 24h after phacoemulsification due to mechanical injury, anterior chamber instability, vitreous disturbance, and destruction of the blood-eye barrier[6]. In clinical practice, we observed that ocular trauma and inflammatory reaction of cataract surgery maybe aggravated the existing diabetic retinopathy (DR) and diabetic macular edema (DME)[7-8], and these complications could lead to poor visual acuity recovery. In patients with DC, especially dense cataract that obscures the preoperative view of the retina, on-table fundus examination after cataract removal for macular or retinal pathologies allows for prognostication.

Traditionally, fundus visualization during ophthalmic surgery is achieved by contact or noncontact vitrectomy viewing systems. Alternatively, surgeons can use a binocular indirect ophthalmoscope intraoperatively. However, traditional binocular indirect ophthalmoscopy is time-consuming, and the results cannot be saved. There is currently no effective fundus detection technique during phacoemulsification.

We used the Wild Field Imaging System (WFIS SW-8000), 25G endoilluminator, and intraoperative optical coherence tomography (iOCT) to examine the fundus intraoperatively with satisfactory results. Herein, we demonstrated the results of these techniques for evaluation without violating the vitreous body or making any additional incisions.

SUBJECTS AND METHODS

Ethical Approval This cross-sectional intraoperative observational study was performed at the Affiliated Hospital of Nantong University from April 2020 to March 2021. The procedures used in this study conformed to the tenets of the Declaration of Helsinki, and the Institutional Review Committee of the Affiliated Hospital of Nantong University approved the study (No.2019-K068). All patients provided a signed written informed consent for surgery and examination.

Patients with DC planned for phacoemulsification were prospectively enrolled in the study. In particular, cataracts with total opacification of the lens cortex leading to a white-colored total cataract appearance on the slit lamp were included. We excluded patients with systemic comorbidities that would make imaging difficult, such as Alzheimer's disease, involuntary tremor, abnormal blood transfusion series, or obvious opacity in the refractive interstitium of the cornea and vitreous body.

Surgical and Examinational Procedure Preoperative comprehensive examination was performed, including uncorrected and corrected distance visual acuity, intraocular pressure, biometry for intraocular lens (IOL) power calculation, and B-scan ultrasonography for posterior segment evaluation. All the surgeries received intraoperative fundus photography and iOCT examinations.

All the surgeries were performed by a single surgeon experienced in phacoemulsification. The media were rendered clear by standard phacoemulsification and removal of the cataract. After removal of the lens matter, prior to IOL implantation, the anterior chamber and capsular bag were filled with a viscoelastic substance. After turning off the light of the microscope, the 25G endoilluminator was inserted into the capsular bag through the corneal incision, and a handheld irrigating planoconcave contact lens (11 D) was then placed over the cornea. The operating microscope was focused (brought nearer to the eye) to get a clear view of the fundus. Some reflections had to be avoided by manipulation of the contact lens (Figure 1).

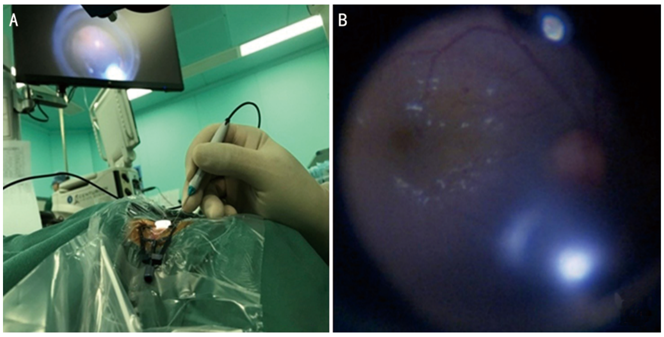

Figure 1 25G endoilluminator was used to examine the fundus intraoperatively A: Using the illumination of 25G endoilluminator, the posterior pole was focused with the help of a handheld irrigating contact lens; B: Star-like exudation and microaneurysm were detected with 25G endoilluminator.

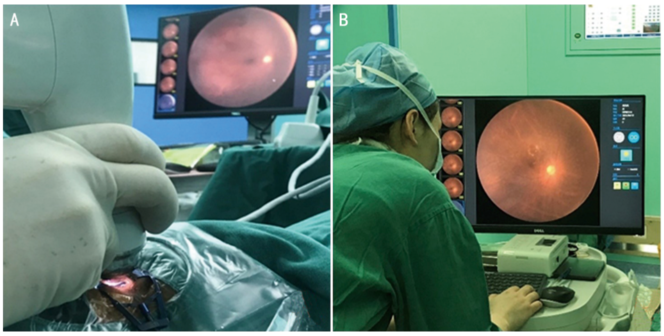

Figure 2 WFIS SW-8000 was used to examine the fundus intraoperatively WFIS: Wild Field Imaging System.

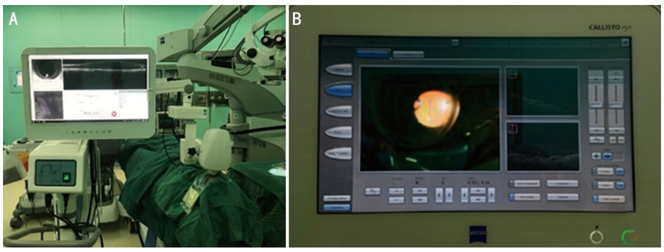

Figure 3 iOCT was used to examine the macular region intraoperatively A: The working interface of the Optovue iVue OCT System; B: The working interface of the ZEISS RESCAN 700 OCT System. iOCT: Intraoperative optical coherence tomography.

To see the whole fundus and peripheral retina intraoperatively, we attempted to use the WFIS SW-8000, similar to Retcam, which is routinely applied in screening for retinopathy of prematurity. The sterile SW-8000 probe was placed vertically in front of the operative eye and on the surface of the cornea. Observing the display screen, we took retinal photographs of the posterior optic disc, macula, temporal side, upper part, nasal side, and lower part to record the results of fundus examination (Figure 2).

To improve the diagnostic rate of macular disease, iOCT examination was performed after IOL implantation. iOCT scans were obtained using the Optovue iVue OCT System (Optovue Inc., Fremont, CA, USA) mounted on a stand, and imaging was performed by a single highly experienced operator. The system obtained 26 000 A-scans per second, with an axial resolution of about 5 μm inside the retinal tissue. The laser wavelength was 830 nm, and the best achievable lateral resolution was 11.4 μm. Scan patterns included cross-line and three-dimensional modes. The iOCT was centered and focused on the macula. Good quality macular scans were obtained by such a technique (Figure 3).

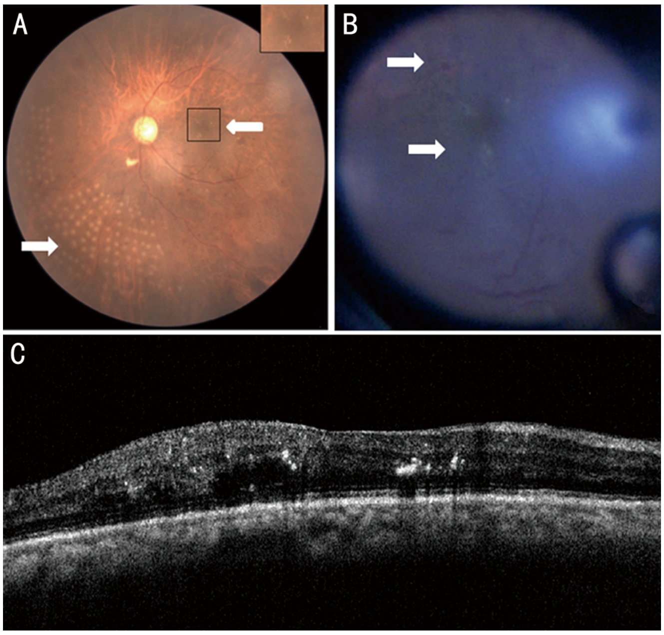

Figure 4 Intraoperative manifestations of diabetic cataract complicated with DME and PDR A: Hard exudates and laser spots were detected with SW-8000; B: Hard exudates and hemorrhage were detected with 25G endoilluminator; C: iOCT confirmed the diagnosis of DME. DME: Diabetic macular edema; PDR: Proliferative diabetic retinopathy; iOCT: Intraoperative optical coherence tomography.

Recently, for intraoperative imaging, we also used the ZEISS RESCAN 700 (Carl Zeiss Meditec, Oberkochen, Germany), a real-time intraoperative spectral domain optical coherence tomography (SD-OCT) integrated with an operating microscope. The iOCT was centered and focused at the macula. Cube scans were taken for all of the cases. For adequate centration, the cube position was independently changed by the surgeon using the foot pedal or by the observer from the integrated touch-screen liquid crystal display (LCD) monitor. A single observer did all the scans with enhanced image quality. A typical output can be seen in Figure 4, with the horizontal and vertical optical coherence tomography (OCT) images shown on the top right and bottom right of the screen, respectively.

Postoperatively, the visual acuity, intraocular pressure, and the inflammation of anterior chamber of the operative eye were recorded. Another ophthalmologist performed super field lens and OCT examination after pupil dilation in all the surgeries and also conducted fluorescein angiography (FFA) examination when necessary. The OCT characteristics for the diagnosis of DR are as follows: macular edema, intraretinal cysts, disorganized retinal inner layers (DRIL). The doctor was blinded to the patients' condition and intraoperative examination results. The intraoperative and postoperative results were compared to verify the accuracy of intraoperative diagnosis.

Table 1 Intraoperative DR detection of patients with diabetes and dense cataract (number of eyes)

Diagnosis	Interoperative	Postoperative	Detection rate (%)
No DR/DME	146	142	-
With DR/DME	58	62	93.55
Mild NPDR			
With DME	3	3	100.00
Without DME	14	18	77.78
Moderate NPDR			
With DME	10	11	90.91
Without DME	8	6	-
Severe NPDR			
With DME	4	3	-
Without DME	2	4	50.00
PDR			
With DME	14	14	100.00
Without DME	3	3	100.00
Total	204	204	-

DR: Diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; DME: Diabetic macular edema.

Statistical Methods IBM SPSS version 23.0 software (IBM SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Counting data were expressed as frequencies and percentages. The Chi-square test was used to compare the detection rate of fundus lesions between intraoperative and postoperative methods. The value of $P<0.05$ was set for statistical significance.

RESULTS

Detection Rate of DR by Three Methods None of the patients had operative complications. The diagnosis of DR was based on the International Clinical Diabetic Retinopathy Disease Severity Scale. The diagnosis of DME was based on the retinal thickening within one disk diameter of the center of the macula or definite hard exudates in this region.

A total of 58 eyes with DR were found by three examination methods (intraoperative positive rate, 28.43%). A total of 62 eyes with DR were found by postoperative OCT and/or FFA examination (postoperative positive rate, 30.39%). The postoperative positive rate was higher than the intraoperative positive rate, but the difference was not statistically significant (χ^2=0.19, P=0.66; Table 1).

1) WFIS SW-8000 group: DR was found in 44 eyes intraoperatively, while postoperative FFA detected DR in 62 eyes [13 eyes with mild non-proliferative diabetic retinopathy (NPDR) and five eyes with moderate NPDR], with the detection rate of 70.97%.

2) 25G endoilluminator group: DR was detected in 56 eyes intraoperatively, while postoperative FFA results showed DR in 62 eyes (six eyes with mild NPDR), with the detection rate of 90.32%.

Table 2 The detection of diabetic retinopathy in each group (number of eyes)

Examination methods	Intraoperative detection	Postoperative detection	Detection rate (%)	*vs* 1		*vs* 2		*vs* 3	
				χ^2	*P*	χ^2	*P*	χ^2	*P*
WFIS SW-8000[1]	44	62	70.97	-	-	-	-	-	-
25G endoilluminator[2]	56	62	90.32	7.44	0.01[a]	-	-	-	-
iOCT[3]	46	62	74.19	0.16	0.69	5.53	0.02[a]	-	-
Combination[4]	58	62	93.55	10.83	0.001[a]	0.44	0.51	8.58	0.003[a]

[1]WFIS SW-8000 group; [2]25G endoilluminator group; [3]iOCT group; [4]The combination of the three methods group; [a]$P<0.05$, the Chi-square test. iOCT: Intraoperative optical coherence tomography;

Table 3 The detection of different lesions in each group (number of eyes)

Examination methods	Microaneurysm			DME		
	Intraoperative	Postoperative	Detection rate (%)	Intraoperative	Postoperative	Detection rate (%)
WFIS SW-8000	40	62	64.52	19	31	61.29
25G endoilluminator	56	62	90.32	24	31	77.42
iOCT	37	62	59.68	31	31	100.00
Combination	58	62	93.55	31	31	100.00

DME: Diabetic macular edema; iOCT: Intraoperative optical coherence tomography.

3) iOCT group: DR was found in 46 eyes intraoperatively, whereas postoperative FFA results showed DR in 62 eyes (13 eyes with mild NPDR and three eyes with moderate NPDR), with the detection rate of 74.19%.

4) The combination of the three methods group: A total of 58 eyes with DR were found intraoperatively, while postoperative FFA results showed DR in 62 eyes (four eyes with mild NPDR), with the detection rate of 93.55%.

The fundus examination results of each group are presented in Table 2. Compared with the results of postoperative examination, there was a statistically significant difference in the intraoperative detection rate of DR among the various methods (χ^2=16.36, P=0.001). The results of pairwise comparisons between the detection rates of each group are presented in Table 2. Correlation analysis also suggested that there were differences in the similarity of detection rates among the groups (Figure 5). The combination group had the highest intraoperative detection rate of DR, and this method was more sensitive than any of the single methods.

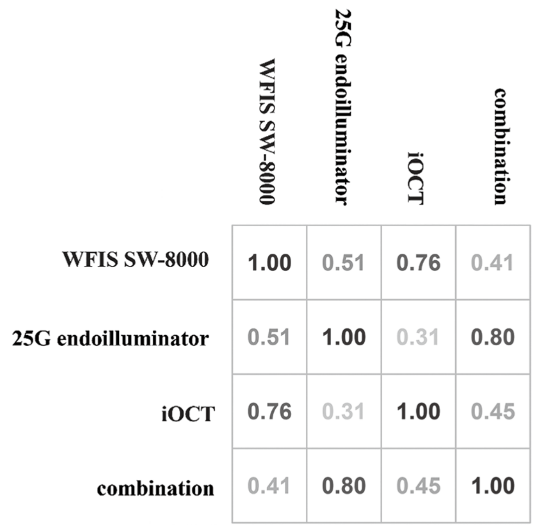

Figure 5 Correlation analysis of diabetic retinopathy detection rate among each group WFIS: Wild Field Imaging System; iOCT: Intraoperative optical coherence tomography.

Detection Rate of Common Lesions of DR by the Three Methods Based on the diagnosis of FFA and OCT postoperatively, the results of the three intraoperative fundus examination methods for microaneurysms and DME were as follows: 1) Microaneurysms: the combination of the three methods had the highest detection rate of microaneurysms, and 22 eyes were missed by fundus photography. The 25G endoilluminator method missed microaneurysms in six eyes, and the iOCT method missed it in 25 eyes (no DME, the microaneurysms was not in the macular region; Table 3). 2) Macular edema: the detection rate of the iOCT method was the highest, whereas the 25G endoilluminator method missed seven eyes (no hard exudates), and 12 eyes were missed by fundus photography (Table 3).

As shown in Figure 4, both fundus photography and 25G endoilluminator methods showed hard exudates in the macular region, suggesting the possibility of macular edema, and then iOCT confirmed the diagnosis of DME. As shown in Figure 6, fundus photography showed no obvious abnormalities. However, hemorrhage and cotton-wool spots were seen above the macula by the 25G endoilluminator method, and no hard exudates were detected in the macular region. Furthermore, iOCT showed the presence of DME. As shown in Figure 7, fundus photography showed yellow-white exudates above the optic disc without any hemorrhage, whereas hemorrhage and cotton-wool spots were seen by the 25G endoilluminator method; in contrast, iOCT showed no significant abnormality in the macular region. To sum up, there were a few omissions in the diagnosis of DR, especially mild and minor lesions by single examination methods.

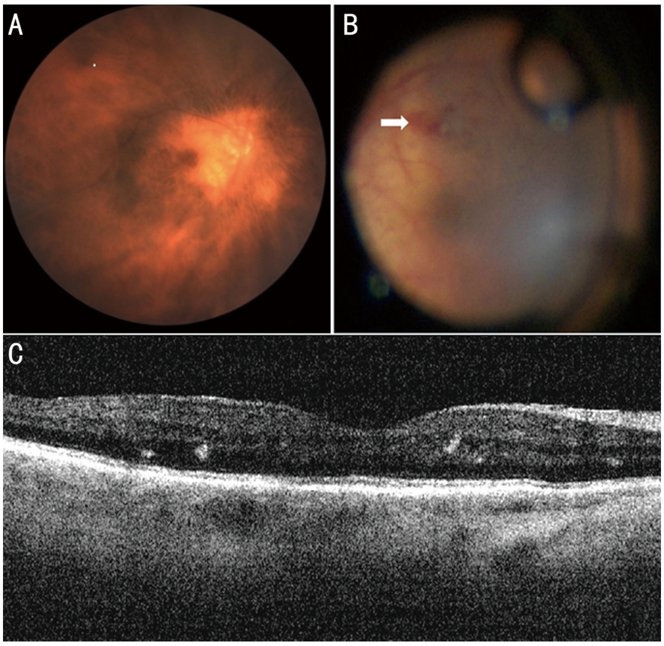

Figure 6 Intraoperative manifestations of diabetic cataract complicated with DME and moderate NPDR A: No obvious abnormality was detected with SW-8000; B: Hemorrhage and cotton-wool spots were detected with 25G endoilluminator; C: iOCT confirmed the diagnosis of DME. DME: Diabetic macular edema; NPDR: Non-proliferative diabetic retinopathy; iOCT: Intraoperative optical coherence tomography.

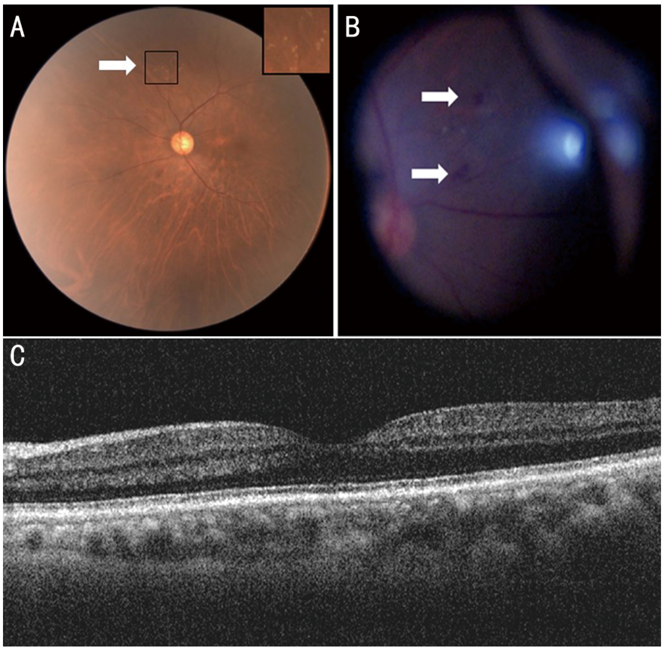

Figure 7 Intraoperative manifestations of diabetic cataract complicated with moderate NPDR A: Hard exudates were detected with SW-8000; B: Hemorrhage and exudates were detected with 25G endoilluminator; C: No obvious abnormality was detected by iOCT. NPDR: Non-proliferative diabetic retinopathy; iOCT: Intraoperative optical coherence tomography

Intervention and treatment of DR/DME For patients with DME, intraoperative vitreous injections were given in 20 eyes after obtaining informed consent before and during surgery to reduce macular oedema and improve postoperative visual acuity, and to avoid secondary vitreous injections in some patients in the short term, reduce treatment costs and relieve patient stress, and improve patient satisfaction and compliance. Patients with immediate intraoperative treatment are being closely followed up.

DISCUSSION

With recent advances in surgical techniques and technology, cataract surgery yields excellent visual acuity outcomes and is regarded as a very safe procedure for most patients. However, recently, this was partly contested by a large study from the United Kingdom on 81 984 eyes that underwent cataract extraction; that is, the study reported that in a sample of 4485 eyes of diabetic patients, even eyes with no retinopathy had an increased risk ratio (RR) of postoperative macular edema of 1.80 compared with the reference cohort. The RR increased to a maximum of 10.34 with escalating severity of DR and did not resolve even in eyes with panretinal photocoagulation[9-10]. In the presence of preoperative DME, the risk of worsening became particularly marked, potentially diminishing or even vanishing the benefits of cataract removal on visual acuity[11-13]. In dense DCs or white cataracts, preoperative visualization of the retina and macular region may not be possible[14]. Evaluation of the posterior segment in such cases is limited by ultrasonography, which cannot provide finer details of the macula and retina.

It has been reported that cytokines change significantly during phacoemulsification, reaching the peak 24h after surgery[6]. In addition, it is often difficult to see the fundus of the operative eye within 24h after surgery because of varying degrees of corneal edema or aqueous humor and vitreous opacity. Thus, it would be crucial to identify patients with diabetes and their grade of retinopathy and maculopathy after opacity lens removal during cataract surgery so that they can benefit from adequate intraoperative therapeutic preventive measures to reduce the risk of postoperative complications. Moreover, it is important to inform patients about the risk of a poor visual result after cataract extraction. However, real-time fundus examination in cataract surgery has not been reported. Over the past two years, we explored the fundus inspection equipment commonly used in vitrectomy, such as contact lens, but it was impossible to see the fundus clearly due to the lack of intravitreal illumination. Traditional direct or indirect ophthalmoscopy is time-consuming, and the results cannot be saved. Handheld non-dilating fundus camera is not only hard to focus but also prone to contamination. By trial and error, we have successfully used WFIS SW-8000—which was originally used to detect retinopathy of prematurity—to record the fundus intraoperatively. Using the WFIS SW-8000 system, 130° digital fundus photographs were obtained[15]. The images were clear and intuitive. The digital fundus photographs can not only be diagnosed in real time during operation but can also be saved digitally for follow-up observation. Although this technique has a wide field of vision, it mainly focuses on the surface and superficial layers of the retina, and it is difficult to detect tiny lesions, especially macular edema and deep retinal lesions. In fact, in our study, the detection rate of DR using WFIS SW-8000 was only 70.97%. The detection rate of microaneurysms was 64.52% and that of DME was 61.29%.

In order to improve the positive rate and accuracy of diagnosis and facilitate clinical application, 25G endoilluminator used in vitrectomy surgery was inserted into the capsule; then, a contact lens was placed on the surface of the cornea. The fundus of the eye was examined under an operating microscope, and 90.32% detection rate was obtained. The detection rate of microaneurysms was 90.32% and that of DME was 77.42%. With high magnification, small lesions, such as small hemorrhages, microaneurysms, and small exudative foci, were observed more clearly using 25G endoilluminator. While using the endoilluminator, one should be careful not to damage the posterior capsule. In addition, this method can mainly observe the fundus of the posterior pole, and the scope is relatively limited. The combination of endoilluminator and fundus photography can benefit from their individual strengths to offset their own weaknesses and improve the accuracy of diagnosis. However, these two methods mainly observe the superficial retinal layer and are less sensitive to detect the deep lesions of the retina. These two methods allow the detection of lipid exudates but lack stereopsis. Although the presence of lipid exudates indicates associated macular thickening[16], the two findings are not synonymous; the presence of lipid alone is an unreliable surrogate for DME[17-20]. Therefore, these two methods are not sensitive for the diagnosis of DME[21].

In order to observe DME or deep retinal lesions, our group used iOCT to detect maculopathy, and we achieved a detection rate of 74.19%. The detection rate of microaneurysms was 51.61% and that of DME was 100%. This technology enables us to detect cystic spaces and subretinal fluid at the fovea on the operating table immediately after cataract extraction[22-23]. The importance of OCT in diagnosing DME cannot be overemphasized[24]. Optovue iVue OCT System and ZEISS RESCAN 700 were the two devices used for iOCT in our study. Optovue iVue OCT System not only provided a qualitative analysis of the macula but also allowed quantification of the central macular thickness. Nevertheless, this device requires the surgical procedure to be paused to capture the images, thus prolonging the duration of surgery. ZEISS RESCAN 700, a kind of microscope-integrated iOCT[25-26], seamlessly integrates image acquisition while performing surgery and allows for a real-time assessment of the various surgical steps. One limitation of this technology is the lack of an integrated caliper.

Our technique can be used for the benefit of patients with dense cataracts, as a good preoperative evaluation of the posterior segment is difficult in such cases. Combining all three methods, almost all severe and blinding retinopathy can be detected, and an accurate and real-time diagnosis of fundus disease can be realized intraoperatively. These three methods can be used for qualitative and quantitative, horizontal and longitudinal, and superficial and deep comprehensive examinations, significantly improving the accuracy of intraoperative diagnosis. These techniques enable the surgeon to intraoperatively analyze and document the macular morphology and retinal condition. Potential uses of this technique include intraoperative decision-making regarding the concurrent use of anti-vascular endothelial growth factor agents or steroids in cases with dense cataracts where preoperative fundus examination is difficult. This approach reduces the number of interventions and hospital visits for the patient, helps to calculate IOL degrees, and improves the satisfaction of patients[27-30]. If the medical condition is limited, we suggest the use of 25G endoilluminator for fundus examination, which has a higher detection rate than the other two methods and may be easier to popularize in primary hospitals.

To the best of our knowledge, this is the first comprehensive report on the uses and applications of WFIS SW-8000, 25G endoilluminator, and iOCT for real-time visualization of the fundus. However, these three examination methods also have some disadvantages. Intraoperative fundus examination may miss some small and deep lesions, and postoperative FFA is still the gold standard. In addition, the intraoperative examination is time-consuming, which may increase the operative time and the possibility of infection. In future studies, we will actively seek out the optimal combination and strive to identify efficient and accurate intraoperative examination and treatment methods.

ACKNOWLEDGEMENTS

Foundations: Supported by National Natural Science Foundation of China (No.81974129); the Technology and Science Foundation of Jiangsu Province (No.2016699); the Technology and Science Foundation of Nantong (No.22019012; No.2019078).

Conflicts of Interest: **Su S,** None; **Wu J,** None; **Ji M,** None; **Guan Y,** None; **Shen Y,** None; **Guan HJ,** None.

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