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Application of mydriasis and eye steering in ultrawide field imaging for detecting peripheral retinal lesions in myopic patients

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ABSTRACT

Purpose To compare mydriatic and eye-steering ultrawide field imaging (UWFI) with standard non-mydriatic UWFI examination in detecting peripheral retinal lesions in myopic patients.

Methods Cross-sectional, observational study. 220 eyes of 110 myopic patients with known peripheral retinal lesions in at least one eye under Goldmann three mirror contact lens examination were recruited. Non-mydriatic standard and eye-steering UWFI images were taken centrally and with eye-steering technique in upper, lower, nasal and temporal gazes under Optomap UWFI (Daytona, Optos, UK). Mydriatic standard and eye-steering UWFI was captured in central gaze and four different peripheral gazes. Sensitivity of detecting peripheral retinal lesions under different UWFI settings was compared.

Results 141 (64.09%) eyes were with peripheral retinal lesions. The sensitivity for detecting peripheral lesions from low to high was 41.84% (95% CI 33.62% to 50.54%) under non-mydriatic standard UWFI setting, 52.48% (95% CI 44.08% to 60.75%) under mydriatic standard setting, 75.18% (95% CI 67.21% to 82.06%) under non-mydriatic eye-steering setting and 86.52% (95% CI 79.76% to 91.69%) under mydriatic eye-steering setting. Both mydriasis and eye-steering technique increased sensitivity of detecting peripheral lesions with statistical significance ($p<0.001$). By applying eye-steering technique, sensitivity of detecting lesions located in superior and inferior quadrants witnessed a greater increase compared with other two quadrants ($p<0.05$). Neither spherical equivalence ($p>0.05$) nor axial length ($p>0.05$) was an independent influence factor for detecting peripheral lesions.

Conclusions Eye-steering technique and mydriasis could both efficiently improve the sensitivity of detecting peripheral retinal lesions in myopic patients. Lesions of superior and inferior quadrants benefited more from eye-steering technique.

INTRODUCTION

The incidence of myopia has been increasing globally each year[1] and myopia-related maculopathy has been found to be one of most common causes for blindness.[2] Nowadays, more than 3 million myopic patients have been seeking for surgical treatment to correct myopia, with nearly half of them were high myopes.[3 4] Previous studies showed that high myopia itself, retinal holes or tears, peripheral degenerations like lattice degeneration and planned intraocular surgeries were all independent risk factors for retinal detachment.[5–8] The detection and photodocumentation of peripheral retinal pathologies, especially those predisposing retinal detachment, were in demand in clinical practice.[9]

Ultrawide field imaging (UWFI) uses ellipsoid mirror to obtain an unprecedented large-angle view of up to 200° without pupillary mydriasis and have achieved a wide application in diabetic retinopathy,[10] uveitis,[11] age-related macular degeneration[12] and myopia,[13] etc. It has a profound advantage over traditional retinal examinations like indirect binocular ophthalmoscope, Goldmann three mirror contact lens by providing image-based counselling for patients with peripheral retinal lesions.[14]

By manipulating eye-steering technique, there were reported cases that lesions that missed out in standard gaze could be detected.[15 16] Sensitivity of detecting peripheral retinal lesions in UWFI would theoretically be elevated under eye-steering setting.

In simulated mydriatic state, model eyes were found to obtain a wider angle view under UWFI.[17] Mydriasis would possibly benefit patients with small pupils or lesions that situated in far periphery.[15] However, there has been no reports of UWFI allied with mydriasis and eye-steering technique among patients with peripheral retinal lesions.

The current application of UWFI in clinical scenario was mostly in the non-mydriatic and standard settings without fully using the inherent imaging acquisition software of 'the eye-steering mode' to obtain the possibly maximum visualised retinal area.[10 18] This study aims to investigate the efficacy of UWFI allying mydriasis and eye-steering technique in detecting peripheral retinal lesions in myopic patients.

METHODS

Study design and participants

A cross-sectional, observational study: 110 myopic patients were enrolled from November 2019 to July 2020 in Eye and ENT Hospital of Fudan University. The eligibility criteria for this study were: aged ≥18 years, with known peripheral retinal lesions under Goldmann three-mirror contact lens examination in at least one eye. Patients with history of adverse reaction to pupil dilation, inability of eye fixation,

Table 1 Sensitivity and specificity of detecting peripheral retinal lesions in four UWFI settings

Eyes with and without peripheral retinal lesions		Non-mydriatic Optomap Standard (95% CI)	Mydriatic optomap standard (95% CI)	Non-mydriatic optomap eye-steering (95% CI)	Mydriatic optomap eye-steering (95% CI)	P value			
						Non-mydriatic optomap	Mydriatic optomap	Standard optomap	Eye-steering optomap
						Standard versus Eye-steering	Standard versus Eye-steering	Non-mydriatic versus mydriatic	Non-mydriatic versus mydriatic
Eyes with lesions		41.84% (33.62% to 50.54%)	52.48% (44.08% to 60.75%)	75.18% (67.21% to 82.06%)	86.52% (79.76% to 91.69%)	<0.001	<0.001	<0.001	<0.001
Eyes with lesions needed no treatment		39.44% (28.69% to 51.32%)	49.3% (38.06% to 60.60%)	74.65% (62.69% to 83.77%)	83.10% (72.25% to 90.28%)	<0.001	<0.001	<0.001	<0.001
	Lattice degeneration	36.67% (24.59% to 50.10%)	50% (37.22% to 62.78%)	73.33% (60.34% to 83.93%)	85.00% (72.52% to 92.41%)	<0.001	<0.001	<0.001	<0.05
	Pigmentary degeneration	60.00% (16.68% to 91.83%)	80% (28.66% to 97.55%)	100.00% (47.82% to 100.00%)	100.00% (47.82% to 100.00%)	NA	NA	NS	NA
	Snail track degeneration	42.86% (9.90% to 81.59%)	28.57% (3.67% to 70.96%)	71.43% (29.04% to 96.33%)	57.14% (18.41% to 90.10%)	NS	NS	NS	NS
Eyes with lesions needed treatment		36.21% (27.70% to 45.67%)	47.41% (38.35% to 56.65%)	76.72% (67.97% to 84.07%)	89.66% (82.63% to 94.54%)	<0.01	<0.001	<0.001	<0.001
	Round holes	37.68% (26.29% to 50.17%)	49.38% (37.02% to 61.59%)	73.91% (61.94% to 83.75%)	91.3% (82.03% to 96.74%)	<0.05	<0.001	<0.001	<0.01
	Atrophic holes	39.47% (24.04% to 56.61%)	50.00% (33.38% to 66.62%)	84.21% (68.75% to 93.98%)	84.21% (68.75% to 93.98%)	<0.001	<0.001	<0.05	NS
	Horseshoe tears	27.27% (6.02% to 60.97%)	36.36% (10.93% to 69.21%)	72.73% (39.03% to 93.98%)	100.00% (71.51% to 100.00%)	<0.05	NA	NS	NA
Eyes without lesions		98.73% (91.56% to 99.82%)	97.47% (90.44% to 99.37%)	100.00% (95.44% to 100.00%)	100.00% (95.44%, 100.00%)	NS	NS	NS	NS

P value could not be calculated since sensitivity reached 100.
NA, not applicable; NS, not significant; UWFI, ultrawide field imaging.

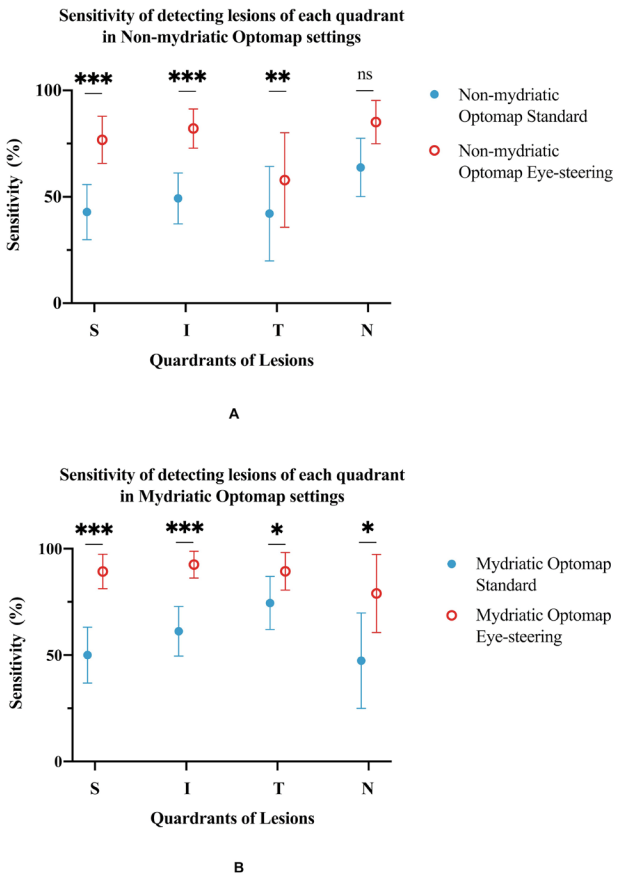

Figure 1 Sensitivity of detecting lesions of each quadrant under non-mydriatic (A) and mydriatic (B) eye-steering UWFI. I, inferior; N, nasal; S, superior; T, temporal; UWFI, ultrawide field imaging.ns:not significant; *P<0.05; **P<0.01; ***P<0.001.

systemic or ocular diseases other than myopia that interfering with image acquisition like cataract, vitreous haemorrhage, etc were excluded from this study.

Table 2 (A) Lesions needed treatment under different gazes of non-mydriatic UWFI

Location	Nasal	Temporal	Superior	Inferior	Whole periphery (detected proportion%)	Lesion no
(A) Lesions needed treatment	Gazes of non-mydriatic UWFI under eye-steering					
Nasal	6	0	4	3	9 (75.00)	12
Temporal	1	21	20	13	31 (86.11)	36
Superior	3	6	27	4	30 (76.92)	39
Inferior	5	14	4	35	39 (69.64)	56
Total	15	41	55	55	109 (76.22)	143
(B) All recorded lesions	Gazes of mydriatic UWFI under eye-steering					
Nasal	9	2	11	9	17 (80.95)	21
Temporal	4	45	43	24	60 (89.55)	67
Superior	10	19	61	12	66 (90.41)	73
Inferior	13	32	15	76	84 (90.32)	93
Total	36	98	130	121	227 (89.37)	254

(B) All recorded lesions under different gazes of mydriatic UWFI.
UNFI, ultrawide field imaging.

In this study, 220 eyes of 110 myopic patients (75 female, 35 male) with a mean age of 28.08±6.37 (ranging from 18 to 50) were included in this study. The spherical equivalence of study eyes averaged −8.76±4.24 dioptres, ranging from −28.88 to −1.25 dioptres. The axial length of study eyes averaged 27.28±1.75 mm, ranging from 24.52 to 34.85 mm.

Image acquisition

All the images were taken under Optomap Panoramic Daytona device (Daytona, Optos, UK) in pseudocoloured pattern obtained by dual lasers at 532 nm and 633 nm. A masked experienced ophthalmologist performed the UWFI in a dark room without knowing the location and type of retinal pathologies and other ophthalmic findings. Patients were guided to look inside the green dot to get non-mydriatic UWFI standard images with patients' eyes centred on the fovea. In the eye-steering settings, patients were guided to look at the red dot inside the UWFI device with a slight shifting of the gaze in the superior, inferior, temporal or nasal direction in turn to get the peripheral view of fundus.

Tropicamide Phenylephrine Eye-Drops (0.5% tropicamide and 0.5% epinephrine, Santen Pharmaceutical, Japan) were applied in subjects' eyes every 10 min for three times to dilate the pupils. Pupils were regarded fully dilated when they were completely unresponsive to pen light. Mydriatic UWFI standard and eye-steering images were taken the same as in the non-mydriatic state.

In four UWFI settings, any image with the macula and the optic disc obscured or peripheral lid artefacts covering more than 50% mid-peripheral area was defined insufficient image acquisition and would be retaken instantly to get a qualified one.

Grading protocol

Images were all reviewed under Optos V.2 Vantage Pro Review V.2.8.0 software (Optos, Dunfermline, UK). Grading of each image was based on the pseudocoloured imaging. All the images were graded independently by two ophthalmologists with types and locations of the all lesions recorded. Both reviewers were masked to other ophthalmic findings of enrolled patients. One of the ophthalmologists regraded the same images after 1-month wash-out interval for assessing interobserver agreement.

Images that the two graders had diverged opinions on were reassessed by another specialist using localised magnification, 3D stereo projection or combing red-free and green-free channels to determine the final results. The final assessment under UFWI was compared with dilated fundus examination with Goldmann three mirror contact lens.

The fundus was divided according to clock hours and four quadrants as following: superior quadrant (10:30–1:30 clock hours), inferior quadrant (from 4:30 to 7:30 clock hours), temporal quadrant (7:30–10:30 for right eye; 1:30–4:30 for left eye), nasal quadrant (1:30–4:30 for right eye; 7:30–10:30 for left eye).

Data collection and analysis

Categorical variables were summarised by frequencies and percentages. Continuous variables were summarised by mean±SD. A sample size at least 62 eyes with peripheral retinal lesions was calculated with an estimated sensitivity of 80% and precision of estimate of 0.1.[19 20] Sensitivity was defined as true positive/(true positive +false negative). Specificity was defined as true negative/(true negative +false positive). McNemar paired test was applied to compare sensitivity and specificity in different

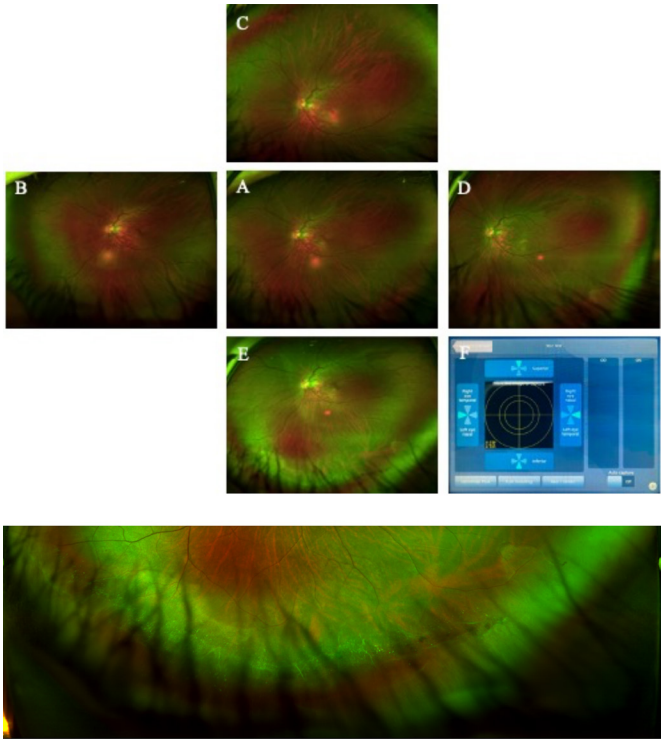

Figure 2 Example of peripheral retinal lesions detected in corresponding gaze under eye-steering UWFI. (A) Standard gaze, (B) nasal eye-steering, (C) superior eye-steering, (D) temporal eye-steering, (E) inferior eye-steering. lattice degeneration and an atrophic hole (white arrow) were only observed in inferior gaze and missed out in standard and all other three gazes. (F) Interface of the eye-steering software. UWFI, ultrawide field imaging.

UWFI settings. Cochran-Mantel-Haenszel test was used to further explore the difference of detecting peripheral lesions in low-to-moderate (SE ≥−6.00D), high (−10.00D<SE<−6.00D) and ultrahigh (SE <−10.00D) myopic subjects. To avoid the impact of the fellow eye in this study, generalised estimating equations were applied to avoid the influence of the contralateral eye with the fellow eye as covariate. Statistical analyses were performed with SAS V.9.4 (SAS Institute). A $p<0.05$ was considered statistically significant.

RESULTS

Frequency and distribution of peripheral retinal lesions

64.09% (141/220) eyes were with peripheral retinal lesions while 35.91% (79/220) were without peripheral pathologies. Of all eyes with peripheral lesions, 116 (52.73%) eyes had peripheral retinal holes or tears. Sixty-nine (31.36%) eyes were with round holes followed by 38 (17.27%) eyes with atrophic holes and 11 (5.00%) eyes with horseshoe tears. Of all eyes with peripheral retinal degenerations, 60 (27.27%) eyes were with lattice degeneration, followed by 7 (3.18%) eyes with snail track degeneration and 5 (2.27%) eyes with pigmentary degeneration. 25.91% (57/220) eyes had more than one type of peripheral pathology and 29.54% (65/220) eyes had peripheral lesions in more than one quadrant. The frequency of peripheral retinal lesions distributed in each semi meridian numbered according to clock hours was detailed in online supplemental figure 1.

Lesions detected by UWFI in four settings: non-mydriatic UWFI standard, non-mydriatic UWFI eye steering, mydriatic UWFI standard and mydriatic UWFI eye steering

All enrolled eyes completed UWFI under four settings. The interobserver kappa value was 0.84±0.03 for UWFI reading between the two graders. The interobserver kappa value was 0.91±0.01 before and after 1-month wash-out.

Sensitivity for detecting each specific lesion was summarised in table 1. Sensitivity was of no statistical significance between different subtypes of retinal holes or between peripheral retinal holes and degenerations ($p>0.05$).

By allying eye-steering technique, sensitivity of detecting peripheral retinal lesions increased by 33.33% (95% CI 25.31% to 41.26%) and 34.04% (95% CI 26.22% to 41.86%) in non-mydriatic and mydriatic state. Mydriasis increased the sensitivity of detecting peripheral retinal lesions by 10.64% (95% CI 4.21% to 17.07%) and 11.35% (95% CI 26.22% to 41.86%) in standard and eye-steering gazes. Both mydriasis and eye-steering technique increased sensitivity of detecting peripheral lesions with statistical significance($p<0.001$). The sensitivity of detecting peripheral degenerations were of no difference compared with that of detecting peripheral retinal holes under all four settings of UWFI ($p>0.05$). Specificity of detecting peripheral retinal lesions remained unchanged with either mydriasis or eye-steering technique ($p<0.001$).

Comparison of detecting lesions of each quadrant under UWFI

By applying eye-steering technique, sensitivity of detecting lesions located in superior quadrant underwent maximal increase compared with that of all other three quadrants($p<0.05$). Lesions of superior quadrant increased from 42.86% (95% CI 29.90% to 55.82%) to 76.79% (95% CI 65.73% to 87.84%) under non-mydriatic state($p<0.001$) and from 50.00% (95% CI 36.90% to 63.10%) to 89.29% (95% CI 81.18% to 97.39%) under mydriatic state($p<0.001$). Lesions of inferior quadrant also witnessed the increase of sensitivity under both non-mydriatic (from 49.25% to 82.09%) and mydriatic (from 61.19% to 92.54%) settings($p<0.001$). Detailed sensitivity of each quadrant was shown in figure 1.

Peripheral lesions detected with eye-steering technique in four gazes

Distribution of detected peripheral retinal lesions in four gazes conformed to a 'diagonal principle', namely lesions of one specific quadrant could be most likely detected in the corresponding gaze. Numbers of peripheral lesions and those in need of treatment detected in different gazes of non-mydriatic and mydriatic UWFI were available in table 2A,B, respectively. Lesions that could be detected in the corresponding gaze only accounted for 79.38% (154/194) and 84.14% (191/227) of all detectable lesions under non-mydriatic and mydriatic settings. With the help of images from other three gazes, the detection rate increased with statistical significance ($p<0.001$) in both non-mydriatic (increased by 15.75%) and mydriatic circumstances (increased by 14.17%). An example of peripheral retinal lesions that missed in the standard setting but detected in the corresponding gaze with eye steering was shown in figure 2.

Detection of peripheral retinal lesions of different myopia severity

The sensitivity of detecting peripheral retinal lesions in low-to-moderate, high and ultrahigh myopic subjects were 38.71% (95%

Table 3 The detection of peripheral retinal lesions of different myopia severity

Myopia severity		Non-mydriatic optomap standard (95% CI)	Mydriatic optomap standard (95% CI)	Non-mydriatic optomap eye-steering (95% CI)	Mydriatic optomap eye-steering (95% CI)	P value			
						Non-mydriatic optomap	Mydriatic optomap	Standard optomap	Eye-steering optomap
						Standard versus eye-steering	Standard versus eye-steering	Non-mydriatic versus mydriatic	Non-mydriatic versus mydriatic
Low-to-moderate myopia (SE >−6.00D)	Eyes with lesions	38.71% (21.85% to 57.81%)	48.39% (31.16% to 66.01%)	74.19% (55.39% to 88.14%)	90.32% (74.25% to 97.96%)	<0.001	<0.001	NS	NS
	Eyes with lesions needed treatment	33.33% (15.63% to 55.32%)	41.67% (23.25% to 62.74%)	79.17% (57.85% to 92.87%)	87.50% (67.64% to 97.34%)	<0.001	<0.001	NS	NS
	Eyes with lesions needed no treatment	27.78% (9.69% to 53.48%)	50.00% (26.02% to 73.98%)	66.67% (40.99% to 86.66%)	88.89% (65.29% to 98.62%)	<0.01	<0.01	NS	NS
High myopia (−10.00D≤SE≤−6.00D)	Eyes with lesions	41.18% (29.37% to 53.77%)	55.88% (43.32% to 67.92%)	76.47% (64.62% to 85.91%)	86.76% (76.36% to 93.77%)	<0.001	<0.001	<0.01	<0.05
	Eyes with lesions needed treatment	35.00% (24.00% to 47.86%)	48.33% (36.45% to 60.41%)	75.00% (62.14% to 85.28%)	91.67% (81.61% to 97.24%)	<0.001	<0.001	<0.01	<0.01
	Eyes with lesions needed no treatment	38.89% (23.85% to 56.39%)	47.22% (31.27% to 63.77%)	80.56% (64.10% to 90.58%)	83.33% (67.23% to 92.42%)	<0.001	<0.001	NS	NS
Ultra-high myopia (SE <−10.00D)	Eyes with lesions	42.11% (27.45% to 58.29%)	50.00% (34.24% to 65.76%)	76.32% (59.76% to 88.56%)	81.58% (65.67% to 92.26%)	<0.001	0.001	NS	NS
	Eyes with lesions needed treatment	39.29% (22.41% to 59.18%)	50.00% (31.18% to 68.82%)	82.14% (63.11% to 93.94%)	85.71% (67.33% to 95.97%)	<0.001	0.001	NS	NS
	Eyes with lesions needed no treatment	46.67% (21.27% to 73.41%)	46.67% (21.27% to 73.41%)	66.67% (38.38% to 88.18%)	73.33% (50.79% to 87.99%)	NS	<0.05	NS	NS

NS, not significant.

CI 21.85% to 57.81%), 41.18% (95% CI 29.37% to 53.77%) and 42.11% (95% CI 27.45% to 58.29%) under non-mydriatic standard UWFI and increased to 90.32% (95% CI 74.25% to 97.96%), 86.76% (95% CI 76.36% to 93.77%) and 81.58% (95% CI 65.67% to 92.26%) with mydriasis and eye-steering technique applied. No statistical difference was observed in each UWFI setting between the three groups. Detection of peripheral retinal lesions of different myopia severity was summarised in table 3. Since spherical equivalence and axial length were strongly correlated(R^2=0.71), the detection of peripheral retinal lesions of different axial length group was detailed in online supplemental table 1. Neither spherical equivalence(p>0.05) nor axial length(p>0.05) was an independent influence factor for detecting peripheral lesions after adjusting for age and sex in each UWFI setting.

DISCUSSION

UWFI has long been applied in clinic practice for assessing and photo-documenting vitreoretinal pathologies, with an advantage of visualising the peripheral area.[21–23] It was not yet clear that whether or not mydriasis or eye-steering technique could increase the sensitivity of detecting peripheral retinal lesions in clinical practice.

In this study, mydriasis helped increase the sensitivity in standard gaze position by around 10% for peripheral retinal lesions and also for retinal holes and degenerations. It is in consistency with the results from Oishi *et al* in model eyes which proved that eyes with an 8 mm pupil had a 10° increase in visualised retinal area in each direction compared with that of pupils with a diameter of 2 mm.[17]

Eye-steering technique hugely improved the sensitivity of detecting peripheral lesions by more than 30%, not only in the non-mydriatic condition but also in the mydriatic circumstance. Gupta *et al* found that by applying eye-steering technique in UWFI, 34.5% of retinal area could be revisualised.[24] Mydriatic UWFI combined with eye-steering technique could achieve the highest sensitivity up to 86.52% in this study. It could be comparable to the sensitivity of 5-gaze position (ahead, superior, inferior, right, left) in the latest version of UWFI Optos California (89.2%).[20] And it much exceeded the sensitivity of non-mydriatic standard UWFI reported by previous studies, ranging from 33% to 74%.[25–28]

Peripheral retinal lesions of superior and inferior quadrants were reported more susceptible to be missed out in clinic practice.[25 29] For UWFI, nasal and temporal quadrants exposed much more retina area than superior and inferior ones under simulated non-mydriatic and mydriatic pupils.[30 31] Chen *et al* also proved in patients' eyes the asymmetry of captured retinal area for horizontal and vertical directions.[32] Our study proved that lesions situated in superior and inferior quadrants benefited more from eye-steering technique, which implied an approach of overcoming the disadvantage of UWFI designing that using an elliptical mirror.[17]

In this study, a detectable lesion under UWFI could not be 100% detected in the corresponding gaze, even under the mydriatic condition. One reason is that the detected retinal area in four corresponding gazes was not strictly the same as the divided four quadrants. Another reason is, as stated above, the disparity of captured retinal area under UWFI.

A thorough and careful preoperative fundus examination was necessary for myopic patients, as 88.2% postoperative peripheral retinal breaks were adjacent to previous detected lesions.[33] Up to now, the effects of surgical interventions in eyes with asymptomatic retinal holes has not yet been verified.[34] The interventional strategy in this study was that all peripheral retinal holes, regardless of subtypes, were all treated with laser photocoagulation, peripheral retinal degenerations were suggested to be followed up.

Lesions that needed treatment were more prioritised by refractive surgeons. The results of this study showed that peripheral lesions that needed prophylactic treatment were of no difference in detection compared with that needed no treatment under all four settings of UWFI.

Neither axial length nor spherical equivalence influenced the sensitivity of detecting peripheral retinal lesions in each UWFI setting, which actually confirmed to the clinical experience. And previous studies have already proved that high myopia and long axial length had more impact on the sharpness of peripheral retina rather the visualised retinal area.[24 35]

Limitations of this study include, first, this was a cross-sectional study without follow-up image data. Second, limited number of specific peripheral retinal lesions reduced the power of analysing difference between the detection of different lesions. Third, the inherent distortion and loss of image sharpness of the peripheral retina could not be dismissed in the process of flattening of the three-dimensional image of the eyeball to generate a two-dimensional fundus photograph.

In summary, mydriasis and eye-steering technique could both efficiently improve the sensitivity of detecting peripheral retinal lesions in myopic patients. Lesions of superior and inferior quadrants benefited more from eye-steering technique.

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Competing interests None declared.

Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

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