Clinical Research Protocol

The Clinical trial of myopia control for children using the Multi-segment (MS) lens

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1. List of abbreviations

AL	axial length
MD	myopic defocus
MI	masked investigator
MS	multi-segment
IOP	intra-ocular pressure
PD	Pupillary distance
Rx	refractive error
SER	spherical equivalent refraction
SFCT	subfoveal choroidal thickness
SD	standard deviation
SD-OCT	spectral Domain Optical Coherence Tomography
SV	single vision
UMI	unmasked investigator

2. Protocol Summary

Title	The Clinical trial of myopia control for children using the Multi-segment (MS) lens
Venue of data collection	Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University
Application of device	Myopia (shortsightedness) myopia in children and youngsters
Study design	2-year prospective, randomized and double-masked clinical study
Primary outcome	Changes in cycloplegic autorefraction (diopters, D)
Secondary outcome	Changes in axial length (mm)
Rationale for Number of Subjects	Treatment group: 90 Control group: 90
Subject criteria	Inclusion criteria: • Hong Kong Chinese • Age at enrolment: 8-13 year. • Spherical equivalent refraction (SER): -1.00 to -5.00D • Astigmatism and anisometropia: 1.50 D or less • Spectacle corrected monocular VA: 0.0 logMAR or better • No strabismus: checked by cover test at far and near. • No prior treatment of myopic control, e.g. orthokeratology, progressive addition lenses, bifocal lenses, drugs (e.g. atropine), etc. • Willingness to wear spectacle lenses regularly • Parents' understanding and acceptance of random allocation of grouping Exclusion criteria • Any ocular and systemic diseases and abnormalities might affect visual functions or refractive development Any eye pathology and conditions
Intervention device / Treatment	Multi-Segment (MS) lens (re-named as Defocus Incorporated Multiple Segments (DIMS) spectacle lens later)
Control	Control: single vision (SV) spectacle lens
Wearing module	Full-day wear
Visits of the study /main data collection	Baseline visit, follow-up visits every 6 months for 2 years Total: 5 data taking visits

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3. STUDY RATIONALE AND OBJECTIVES

3.1 Background

Myopia (also called 'shortsightedness) is a common refractive eye disorder. The prevalence of myopia is alarmingly high in many Asian countries such as Hong Kong and Singapore, as many as 80% of young adults is myopic. [1-3] There is a trend of increasing prevalence of myopia and increasing severity of myopia in the last decade. Myopic eyes are prone to a number of ocular diseases, such as retinal degeneration and glaucoma, which can lead to severe visual impairment.[4,5]

We have invented a contact lens, 'Defocus Incorporated Soft Contact (DISC) lens', for slowing progression of myopia in children. The DISC lens is a bifocal soft contact lens and is designed by the principle of simultaneous defocus. It provides clear vision and constant myopic defocus simultaneously for wearers in all viewing distances. The recent study has shown that DISC lens slowed myopia progression up to 50% in Hong Kong schoolchildren.[6]

The Hong Kong Polytechnic University and Sponsor (a lens company) have jointly invented a spectacle lens design using simultaneous defocus principle -Multi-Segment (MS) lens. The sponsor is able to manufacture the technical design which aims at correcting distance vision and at the same time producing MD images on the retina for all distances in the form of a spectacle lens. The MD aims at slowing down myopia progression. The purpose of this study is to investigate if the MS lens can slow myopia progression in schoolchildren.

3.2 Aims of the study

- To determine if wearing the MS lenses slows the progression of myopia and axial elongation in myopic schoolchildren over 2 years.

- To compare the changes in refractive error (Rx) and axial length (AL) in children wearing MS lens with those children wearing single vision (SV) spectacle lens (control).

4. METHODS AND STUDY DESIGN

4.1 Subjects: inclusion and exclusion criteria

Hong Kong Chinese myopic children aged from 8-13 years will be recruited in this study. This age range is selected because myopia progression rate has been found to be fastest compared with other ages and the mean progression rate in myopic children is about 1D annually.[3]

Inclusion criteria

Specific inclusion criteria are as follows:

- Ethnicity: Hong Kong Chinese
- Age at enrolment: 8-13 years
- Spherical equivalent refraction (SER): -1.00 to -5.00 Dioptres (D)
- Astigmatism and anisometropia of 1.50 D or less
- Spectacle corrected monocular VA: 0.0 logMAR or better
- Free of ocular and systemic abnormalities might affect visual functions or refractive development
- Willingness to wear spectacle lenses regularly
- Parents' understanding and acceptance of random allocation of grouping

Exclusion criteria

- Any ocular and systemic diseases and abnormalities might affect visual functions or refractive development

Any history of prior myopia control treatment, e.g. orthokeratology, progressive addition lenses, bifocal lenses, drugs (e.g. atropine), etc.

4.2 Study Design

This is a 2-year prospective, randomized and double-masked clinical trial. After visual screening, the children are fulfilled the inclusion criteria will be enrolled in the study. The children will be randomly allocated to wear either MS lenses or regular SV spectacle lenses. Allocation will be determined by a random software sequence in Excel.

Their refraction and AL will be followed up every 6 months over 2 years: baseline, 6-, 12-, 18- and 24-month visits. The changes in cycloplegic refraction and AL between two groups of children will be compared. Data collection will be performed in Centre for Myopia Research, the Hong Kong Polytechnic University (PolyU). Written assent and informed consent will be obtained from children and their parents before participation respectively.

4.3 Sample size estimation

The number of subjects required for the clinical trial is based on the power calculation for subject numbers. We use 90% power to detect 0.50D difference (with 0.6D of standard deviation (SD))[6] in myopia progression between two groups with a significance alpha level of 0.01 (2-tailed); the minimum subject number required to complete the study in each group is 43. Assuming a conservative dropout rate of about 40%, 72-75 children are required in each group.

The project will recruit altogether 180 subjects: 90 for control group and 90 for experimental group.

4.4 Spectacle lenses

MS lenses and spectacle prescription

The MS lens is a custom-made plastic spectacle lens. The lens power matches distant prescription. There are multi small defocusing zones of relatively positive embedded in the lens. Such design allows to introduce MD and to maintain clear vision simultaneously. The controls are the ordinary SV spectacle lenses are made of 1.6CR39HMC.

The final distance prescription of spectacles is determined on cycloplegic subjective refraction. The children will be instructed to wear lenses all the time.

Treatment group*: MS spectacle lenses*

Control group*: SV spectacle lenses*

4.5 Randomization process

A simple randomization will be adopted in this study. Group allocation will be determined by the random sequence generated by Excel.

4.6 Masking

In order to minimize observation bias, this study is designed as double-masked trial. Therefore, both the participated children (including their parents) and the masked investigator(s) responsible for assessing study outcomes will be aware of the treatment (DISC lenses) assignment. All children will be identified on all study documents by an identifying number that is not related to treatment assignment.

The study design is same as that in our previous study. Masked investigator (MI) is masked from grouping and not allow to see and handle contact lenses throughout the study. MI is responsible for refracting and conducting relevant ocular data measurement. The other is unmasked investigator (UMI) and responsible for group allocation, lens fitting and aftercare, measuring lens performance, record keeping and compliance checking, answering queries from subjects. The children and their parents will be not told which lens design was prescribed.

The masking procedures will follow the ‘Consolidated Standards of Reporting Trials ‘requirements for a double-masked trial.

4.7 Study outcomes and its measurement

Primary outcomes

- Changes in auto-refraction (SER in diopters) with cylcoplegia

Secondary outcomes

- Changes in axial length (mm) with cycloplegia

Refraction and AL under cycloplegia will be measured at baseline and at six-month intervals for 2 years. One drop of proparacine 0.5% and then 1-2 drops of cyclopentolate HCL 1 % will be instilled to induce cycloplegia. Cycloplegic refraction will be measured by the open-field autorefractor (Shin-Nippon NVision-K 5001 autorefractor). Five measurement are obtained for each eye. The SER of the representative value from these 5 readings was used for statistical analysis. AL will be measured by IOL Master (Carl Zeiss) Five measurements will be taken and then averaged.

Myopia progression (change in refraction) over 2 years will be determined by the difference between SER (from cycloplegic autorefraction) at the fifth and the first (baseline) visits.

4.8 Study visits, eye examination procedures

Figure 4.1 illustrates the overall plan of visits throughout the study. The participating children and their parents (or guardians) go through screening phone call, vision screening, baseline examination, lens delivery visit, contact lens follow-up visits and 4 comprehensive eye examinations (main data collection) at study months 6, 12, 18 and 24 months.

4.8.1 Subject recruitment and phone screening

The subjects are recruited through placing posters, public media and the study website. The screening phone call are carried out for recruit potentially eligible subjects, to exclude children who are not eligible, such as asking for age of the child, history of recent eye exam, spectacle prescription, etc. Then, a vision screening will be schedule vision screening for the potential children to confirm if they really fit for our study criteria (depend the schedule of the subject).

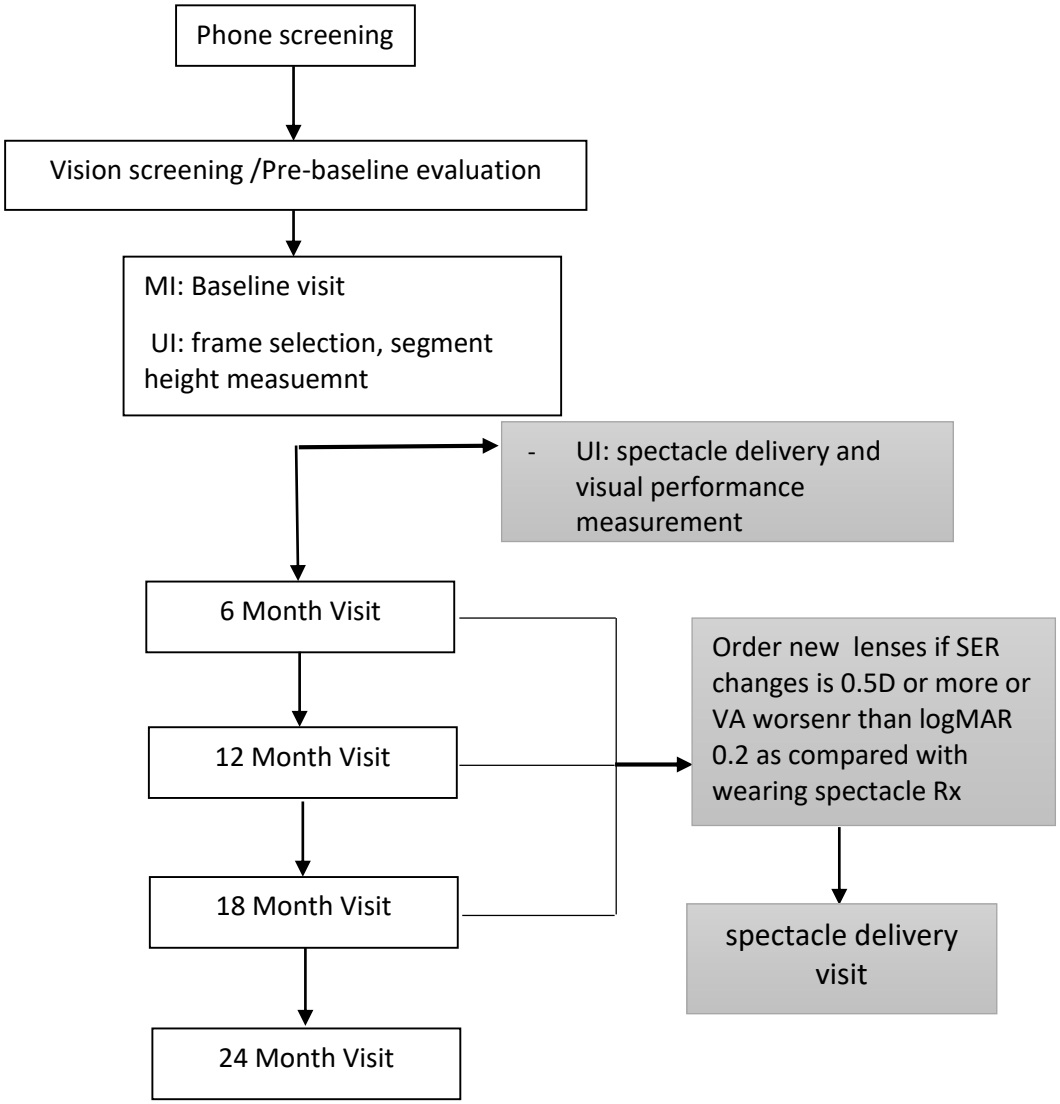

Figure 4.1 Overall plan of different visits in the study

4.8.2 Pre-baseline visual screening, baseline and main follow-up visits

Some screening tests are performed to determine if the children fit for our study criteria. The pre-baseline screening tests include: autorefraction, cover tests, non-contact IOP, subjective refraction, best corrected VA and external ocular health exam by slit-lamp.

If the subjects pass the screening tests, they and their guardians will be asked to sign the consent if they agree to join the clinical trial after explaining the nature and details of the study by UMI. Then the participated children will have a comprehensive eye examination and baseline data measurement without and with cycloplegia. These procedures will be repeated every 6-month over 2 years. Key baseline measurements included refraction, axial length (AL), keratometry and phoria biometry will be undertaken either at the same time as the vision screening session or in a follow-up session.

The lists of the study procedures and measurements to be performed at different visits and is summarized in **Table 4.1**. All the data collection will be conducted at our Optometry Research Clinic, School of Optometry, the Hong Kong Polytechnic University.

The following measurement and eye tests will be performed by MI at baseline, 6, 12, 18 and 24M visits (5 visits over 2 years).

<u>Without cycloplegia</u>

- Determination of dominant eye
- Subjective and objective refraction
- Best corrected visual acuity
- Corneal curvature/ topography
- Binocular vision tests: phoria tests, stereopsis
- Accommodative tests: amplitude of accommodation, lag of accommodation with 3D stimulus
- Pupil diameters under different illumination, during distance and near viewing
- Non-contact IOP
- Subfoveal choroidal thickness (SFCT) by Spectral Domain Optical Coherence Tomography (SD-OCT)

<u>With cycloplegia</u>

- Subjective refraction (as reference for the prescription of contact lenses)
- **Objective refraction**: measured by using Shin-Nippon NVision-K 5001 (open-field) autorefractor. Five measurement are obtained for each eye and the average of SER of was used for statistical analysis.
- **AL measurement**: measured by IOL Master (Carl Zeiss). Five measurements were taken and averaged.
- Peripheral refraction: measured by using a Shin-Nippon NVision-K 5001 autorefractor at center, 10, 20 and 30 degrees at the nasal and temporal visual field across the horizontal meridian.
- Dilated fundus examination

Table 4.1 Examination procedures/ items for each visit.

Procedures /measurements	*Screening	Baseline	2 wk	1M	3M	6M	12M	18M	24M
Consent form signed		x							
History-initial	x	x							
History-Update			x	x	x	x	x	x	x
Non-cycloplegic autorefraction	x	x				x	x	x	x
Habitual spec VA	x	x				x	x	x	x
Subjective refraction	x	x				x	x	x	x
Best-corrected VA	x	x				x	x	x	x
Cover test (distance, near)	x								
Phoria (distance and near)		x				x	x	x	x
Lag of accommodation		x				x	x	x	x
Amplitude of accommodation		x				x	x	x	x
Stereopsis		x				x	x	x	x
Pupil size		x				x	x	x	x
Keratometry		x				x	x	x	x
Slit-lamp exam, external ocular health check	x	x				x	x	x	x
IOP measurement	x	x				x	x	x	x
Choroidal thickness measurement		x	x	x	x	x	x	x	x
Eye drops: Anesthetic, Cycloplegics		x				x	x	x	x
Cycloplegic subjective refraction		x				x	x	x	x
Cycloplegic autorefraction		x				x	x	x	x
Axial length measurement		x				x	x	x	x
Peripheral refraction		x				x	x	x	x
Dilated fundus exam		x				x	x	x	x

VA with habitual spectacle			x	x	x	x	x	x	x
Questionnaire of visual habits and spectacle lens performance									x

* Screening day may be at the same day of baseline measurement.

4.8.3 Spectacle prescription and visual performance of lenses

The final distance prescription of spectacles is determined on cycloplegic subjective refraction performed by the masked optometrist. UI do frame adjustment, mark and measure PD and fitting heights for all subjects whatever they are wearing MS lenses or SV lenses because the subjects are masked from the grouping.

Visual performance, including visual acuity at distance and near under high and low contrast, with spectacle lenses will be assessed at the first delivery visit. Subject will wear lenses on a daily

The lens will be replaced and upgraded if the equivalent sphere of refraction (SER) is changed by 0.5D or more (or habitual aided LogMAR VA worsen than 0.2) in either eye as compared with wearing spectacle refraction. The children will be instructed to wear lenses all the time throughout the study. Aided VA at both distance and near will be measured in delivery of new spectacles.

4.9 Questionnaire

Parents or guardians will be complete a questionnaire regarding the child's vision habits and parents' Rx, and the number of years that the child has been myopic before they enroll in this trial. Questions regarding how much time the children spend reading and outdoor activities will be included. In addition, patient-reported measures on lens performance are also assessed using questionnaire.

4.10 Visual performance of lenses

Visual performance tests of the lenses will be carried out in the visit of contact lens delivery. The items include:

- Objective Visual Assessment
- Distance and near visual acuity in low and high contrast:
- Binocular vision tests:
- Horizontal phoria at distance and near
- Stereoacuity (minute of arc)
- Amplitude of accommodation (D)
- Lag of accommodation

- Patient-Reported Measures of Lens Performance using questionnaire.

4.11 Statistical analysis

Data of two groups will be presented as the mean ± SD. Only data of the right eyes will be used for data analysis if there are high correlation of data between two eyes. Baseline data between two groups between males and female will be analyzed by unpaired t-tests. Welch correction is applied if the difference of SD between the groups is statistically significant.

Primary outcomes

- Changes in auto-refraction (SER in diopters) with cylcoplegia

Secondary outcomes

- Changes in axial length (mm) with cycloplegia

1. Repeated measures ANOVAs were used to compare the changes from the baseline visit in SER, and AL over time and between the two study groups in study. Interactions between time and groups were also assessed. If repeated measures ANOVA showed significant results between groups and significant interaction between time and groups, unpaired *t* tests were used to test for differences in SER, AL, between the two groups after the 24-month follow up period, and plots of the change will be plotted for showing trends. Bonferroni corrections were used to take account of *post-hoc* comparisons. The efficacy of myopic control will be determined by dividing the difference in mean SER changes of two groups with the mean SER change in the SV group times 100%.

2. The correlations between changes in Rx, biometric parameters and related factors (e.g. lens wear time, time spent on outdoor activities) are analyzed using Pearson correlations. Multivariate analyses of variance are used to examine the effect on treatment outcomes of various factors, including age, gender, initial refraction, etc.

3. To examine the choroidal response to MD in MS lens, changes in choroidal thickness over time and between two groups will be compared by the same statistically methods used for SER and AL mentioned above (*point 1*). Besides, the correlation between changes in choroidal thickness and axial length will be calculated using Pearson's correlation coefficient. Correlation between the pupil sizes, peripheral refraction and the effect in myopic control in terms of axial length elongation will be calculated using Pearson's correlation coefficient.

5 CLINICAL EXAMINATION PROCEDURES BY MI

5.1 Introduction

In order to maintain the integrity of double masked study, clinical examination will comprise two sessions: Clinical Examination by masked MI (or masked optometrist) and UMI (unmasked optometrist). The MI will be responsible for obtaining the required key data.

Objectives:

i. to collect required data
ii. to provide Rx for contact lens prescription
iii. to maintain integrity of double masked design

Summary of eye examination procedures and data collection

Without cycloplegia

- Determination of dominant eye
- Pupillary distance (PD)
- Subjective refraction
- Autorefraction and kerometry
- Best corrected visual acuity
- Binocular vision tests: phoria tests, stereopsis
- Accommodative tests: amplitude of accommodation, lag of accommodation
- Pupil diameters under different illumination, during distance and near viewing
- Non-contact IOP
- Subfoveal choroidal thickness (SFCT) by Spectral Domain Optical Coherence Tomography (SD-OCT)
-

With cycloplegia

- Subjective refraction (as reference for the prescription of contact lenses)
- **Objective refraction**: autorefraction
- **AL measurement**: measured by IOL Master (Carl Zeiss). Five measurements were taken and averaged.
- Peripheral refraction: measured by using a Shin-Nippon NVision-K 5001 autorefractor at center and 10, 20 and 30 degrees at the nasal and temporal visual field across the horizontal meridian.[3]
- Dilated fundus examination

One drop of proparacine 0.5% and then 1-2 drops of cyclopentolate HCL 1 % will be instilled to induce cycloplegia. Cycloplegic refraction will be measured by the open-field autorefractor (Shin-Nippon NVision-K 5001 autorefractor). Five measurement are obtained for each eye. The SER of the representative value from these 5 readings was used for statistical analysis. AL will be measured by IOL Master (Carl Zeiss) Five measurements will be taken and then averaged.

5.2 Determination of dominant eye

Procedures:

i. Ask subject to make a circle with thumbs and first fingers
ii. Hold arms straight in front and view the spot light
iii. Researcher to occlude each eye in turn to determine which eye is seeing the letter with habitual glasses

5.3 PD measurement

Shin-nippon PD-82 will be used to measure monocular and binocular PDs.

Procedures:

i. Turn the target distance lever to infinity.
ii. Press the main switch.
iii. Apply the instrument to the subject's forehead and nose, using the forehead rest and the nose rest.
iv. Instruct the subject to look at the fixation target inside the instrument
v. Slide either of the PD levers for right and or left, and match the PD pointer with the bright point reflecting on the subject's pupil.
vi. Read the digital values (in mm) shown on the display window on the instrument top. The value in the center shows the interpupillary distance. The values R and L indicate the distances from the nose center to the right and left pupils respectively. Record PD, RPD and LPD.
vii. Measure near PD. Set the target distance lever to 40cm and repeat step iv. – vi

5.4 Non-cycloplegic Autorefraction and keratometry

The Shin-Nippon NVision-K 5001 autorefractor will be used to measure Rx objectively.

Procedures:

i. Set the measurement mode into 'R' and 'K' that allows to measure the autorefraction and corneal curvature/ power at the same time.
ii. Place the fixation target (Figure 5.1) 6 m from the machine.
iii. Vertex distance is set to 12 mm.
iv. The subject's chin is set on the chin rest and his/her forehead against the forehead rest.
v. The subject should be able to see the fixation target in front of him/her through the "wide view" window.

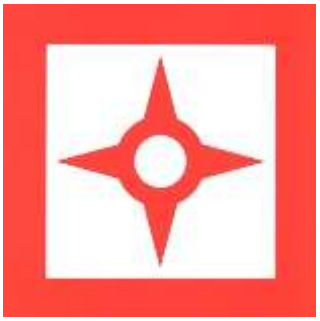

Figure 5.1 Fixation target

vi. Ask the subject to look at the white circle in the middle of the fixation target (Figure 5.1).

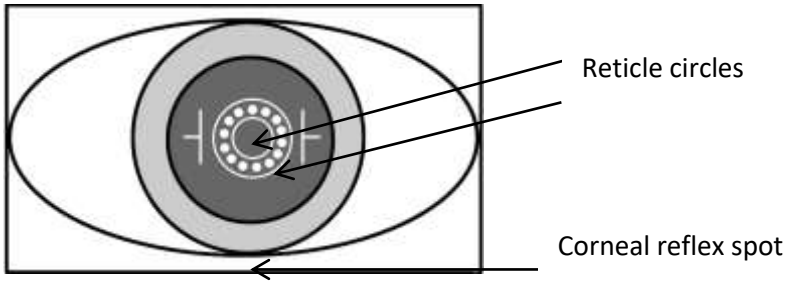

Figure 5.2 Reticle circles and corneal reflex spot

vii. While viewing the right eye on the CRT screen, carry out alignment: position the reticle circles so that they are both completely located inside the boundary of the pupil. (Figure 5.2)
viii. The subject will see a faint red on the "wide view" window once the start button is pressed, and the subject will be requested to report the target position relative to the red ring.
ix. The target will be adjusted as necessary until it is judged to be located at the centre of the red ring. The non-tested eye is then uncovered.
x. Carefully maneuver the joystick to reduce corneal reflex spots to their smallest size. Press the button on the joystick to start measurements.
xi. **Five measurements** will be taken.
xii. Repeat the step vi. – xi. for the left eye.
xiii. Press PRINT key and attach the printout to the record sheet.
xiv. Record the **representative value** as the result of auto-refraction which is under the dashed line in the printout, for both eyes.

5.5 Subjective Refraction

Procedures:

i. Starting with autorefraction obtained above, refine subjectively.
ii. Occlude the left eye.
iii. Determine best sphere first.
Add +0.25D and ask if "worse or the same". If "the same" add +0.25D and repeat until the answer "worse" is given. If "worse" add -0.25D and ask if "better or the same". If "better" add -0.25D and check for improvement in VA; repeat until the answer given is "the same". Do not add the -0.25 D at this stage.

iv. Determine cylindrical error.
Add -0.25D to best sphere and carry out cross-cylinder. Check axis and then power. Using a non-directional letter as a target.

v. Refine sphere using +1.00D blur back test monocularly and finish by offering a binocular +0.25D add. Give this if "no difference". Stop if "worse". Repeat until "worse".
vi. Binocular balance (prism dissociation): with the monocular subjective result in the phoropter, add +1.00D to each eye, then add 3Δ base-down OD and 3Δbase-up OS. Use the 0.3 logMAR line as the target. If the upper line letter appears clearer than the lower line letters, add +0.25D to right eye. If the lower line letters appear clearer than the upper line, add +0.25D to left eye. Stop when no difference between the upper and lower line.

5.6 Visual acuity

- Distance VA, including BCVA of both eyes will be assessed using Logarithmic 2000 series ETDRS Chart and Low Contrast ETDRS Charts at 4 m (Precision Vision Inc.) with the illuminator cabinet (450 cd/m^2).
- Near VA (40cm) will be measured by the Near Vision Test Card from the Hong Kong Polytechnic University.

5.7 Phoria measurement

Procedures:

i. Howell phoria card will be used to measure phoria
ii. Insert 6Δ base down right eye into the trial frame with the best subjective refraction
iii. Phoria at distance is measured by asking the subject to indicate the number on the bottom line that is nearest to the top arrow, when viewing the large phoria chart at 3 m. Always ask the subject to keep the letters clear.
iv. The blue even numbers indicate exophoria and the yellow odd numbers indicate esophoria
v. Phoria at near is measured by asking the subject to indicate the number on the bottom line that is nearest to the top arrow, when viewing the small phoria chart at 33 cm. Always ask the subject to keep the letters clear.
vi. Record the distance and near phoria (-ve: exo; +ve: eso)

5.8 Stereopsis

Stereoacuity (minute of arc) will be measured with Randot Stereotest (refer to user guide) at 40 cm with Polaroid goggles.

5.9 Amplitude of accommodation

Amplitude of accommodation (D) will be measured with RAF ruler for monocluarly and binocularly. Average of 3 measurements will be used for data analysis.

5.10 Lag of Accommodation

Procedures:

i. Place the subject's best subjective refraction in the trial frame and position the subject in the Shin-Nippon NVision-K 5001 autorefractor.
ii. Place the distance target (0 logMAR letters) at 6 m. While encouraging the subject to look clear the letters, take 5 readings on the subject's right eye, followed by 5 readings on the left eye. The eye not being measured will be occluded.
iii. Place the near target (0 logMAR letters) at 33 cm (3D near stimulus). While encouraging the subject to look clear the letters, take 5 readings on the subject's right eye, followed by 5 readings on the left eye. The eye not being measured will be occluded.
iv. The lag of accommodation will be calculated for each eye by summating the difference in the mean spherical equivalents between the 5 distance readings and the 5 near reading s and 3D (matrix is also used in calculation).

5.11 Choroidal thickness measurement

Choroidal thickness measurement will be measured at the following schedule (please refer to Table 4.1):

- Baseline visit
- Delivery of 1st pair of CL, 2 week of CL wear, 1 month of CL wear, 3 month of CL wear
- 6-month FU, 12-month FU, 18-month FU and 24-month FU.

Choroidal thickness will be obtained by a modified dual wavelength Spectral Domain Ocular Coherence Tomograper (SD-OCT) by Heidelberg Engineering (Spectralis HRA+OCT, Heidelberg Engineering, Germany) using enhanced depth imaging mode and with the help of 1060nm. This OCT uses a dual light source of 870nm and 1060nm at scanning speed of 40000A-scan/second. Cross sectional images with axial resolution of 3.9μm and transverse resolution of 14μm will be obtained. Choroid in an OCT image is defined as the boundary between the highest reflected interfaces from retinal pigmented epithelium to the chorio-scleral junction. The choroidal thickness is determined using the built-in software of SD-OCT (Heidelberg Eye Explorer) automatically. Subfoveal and parafoveal choroidal thickness at 1mm and 3mm away from the fovea in temporal, nasal, superior and inferior quadrants will be measured. The changes in choroidal thickness are compared between the MS lens and the SV groups.

To avoid diurnal variation of CT, we will arrange data collection for subject at similar time in each follow-up visit if possible.

5.12 IOP and cycloplegia

i. Measure non-contact IOP using Nidek NT-4000. Excluded if IOP > 22 mm Hg and CD ratio >0.6.
ii. Explain purpose of eyedrops to parent. Handout sheet stating normal reaction will be given to the parent with telephone numbers. Ask to contact if any different reaction occurs.
iii. Cycloplegia is induced by instilling 1 drop proparacaine (0.4%) then 2 drops cyclopentolate HCL (1%) into each eye at 5-minute intervals. Subject is asked to hold puncta.

5.13 Cycloplegic Autorefraction

Procedures:

iv. 30 minutes later check pupils. If dilated, measure amplitude of accommodation using push-up method. If not dilated add one further drop of cyclopentolate to each eye.
v. Autorefract when **accommodation <2.00D**.

vi. Carry out autorefraction using Shin-Nippon NVision-K 5001 (open-field) autorefractor as in **Non-cycloplegic Autorefraction section.** Five **measurements** are obtained for each eye.
vii. The SER of the representative value of will be used for statistical analysis.

5.14 Axial Length Measurement with will be used

The Zeiss IOL Master will be used to measure axial length.

Procedures:

i. Press 🗁bottom to input new subject data or select old subject data.
ii. Finished entering then press <NEW> button. This will automatically activate the "Overview"mode.
iii. The fixation light and the illumination LEDs are on
iv. Align the eyes with the red marks on the side rails of the headrest.
v. Ask the subject to look at the yellow fixation light in the middle
vi. Adjust the instrument until the 6 light spots appear focused on the screen.
vii. The circle of lights should be approximately centered to the pupil and cross hairs
viii. Then push button on the joystick
ix. Make sure "phakic" mode is on. It can be checked in the AL Setting in the screen
x. The instrument now automatically changes the magnification: a smaller section of the eye becomes visible with the reflection of the alignment light and vertical line.
xi. Ask the subject to look at the red fixation light. On the display, a crosshair with a circle in the middle appears.
xii. Fine-align the instrument so that the reflection of the alignment light appears within the circle
xiii. Push the button on the joystick to start the measurement
xiv. By pressing the button on the joystick continuously, next measurements will be started.
xv. If the result of one measurement differs by more than 0.2mm from the others, an "Evaluation" message will be displayed in place of the average.
xvi. If the signal received by the instrument was poor, an exclamation mark will be shown besides the value of that measurement.
xvii. All the value marked with special marking as stated above will be deleted.
xviii. Five consecutive readings were made for each measurement; each reading showing signal-to-noise ratio above 2.0 and differing by less than 0.20 mm from the others. Any reading which not fit the criterion was deleted and re-measured. (Not more than 20 measurements can be taken on each eye per day).
xix. Record the mean axial length in mm.

5.15 Final Prescription

The final distance prescription of spectacles will be determined on cycloplegic subjective refraction. Masked Optometrist to write final prescription on the clinical examination record (Masked) and take subject, parent and Rx to the unmasked investigator (UI) for lens ordering. The lens will be replaced and upgraded if the equivalent sphere of refraction (SER) is changed by 0.5D or more (or habitual aided LogMAR VA worsen than 0.2) in either eye as

compared with wearing spectacle refraction. The children will be instructed to wear lenses all the time.

If dispensing and frame adjustment are necessary, proceed to spectacle lens dispensing and delivery visit. All dispensing works are performed by UI.

6. CLINICAL EXAMINATION BY UMI

The UMI will be responsible for measuring the aided VA, to check contact lens fitting and related measurement.

Objectives:

i. to measure aided VA
ii. to check contact lens fitting
iii. to modify contact lens fitting and prescription when necessary
iv. to educate the parents and the subjects how to insert and remove contact lens safety, about lens cleaning and disinfection procedures, etc.
v. to perform the tests for assessing visual performance of contact lenses
vi. to ask history, ask the child and parent to sign consent form, fill in questionnaire, etc.
vii. to maintain integrity of double mask design

Starting from the first 6-month intervals Clinical Examination visit, UMI will be responsible for:

i. the entry of subject details,
ii. measurement of aided logMAR VA at distance and near
iii. checking the contact lens fitting
iv. checking the contact lenses
v. re-adjustment of the CL fitting and prescription when necessary
vi. external ocular health checking
vii. checking compliance of CL
viii. collect and check the logsheet about lens wear time and lens compliance
ix. collect contact lens (to maintain masking) and take the child and parent to masked optometrist

Child and parent will be informed not to raise any questions about contact lenses with the masked optometrist or MI. Those questions should be addressed to the unmasked optometrist or UMI.

6.1 Visual performance of spectacle lenses

Objective Visual Assessment

1. Visual acuity in low and high contrast:

- Distance Log MAR VA High contrast (100%) and low contrast (10%) LogMAR VA will be assessed under both low and low illumination using Logarithmic 2000 series ETDRS Chart and Low Contrast ETDRS Charts at 4 m (Precision Vision Inc.) with

the illuminator cabinet (450 cd/m^2) respectively. The high and low near VA (40cm) will be measured by the Near Vision Test Card from the Hong Kong Polytechnic University under both high and low illumination.

2. Binocularity:

- Horizontal phoria at distance and near will be measured with Howell-Phoria cards.
- Stereoacuity (minute of arc) will be measured with Randot Stereotest at 40 cm with Polaroid goggles.
- Amplitude of accommodation (D) will be measured with RAF ruler.
- Accommodative Response- Refractive state will be measured by the open-field auto-refractor binocularly with a target 33cm away.

Patient-Reported Measures of Lens Performance

Vision performance and vision comfort with lenses will be graded by the subjects themselves through questionnaires. The subjective rating on vision performance includes vision at distance and near, stability of perceived vision at distance and at near. (Appendix 1)

References

1. Saw SM, Shankar A, Tan SB,Taylor H, Tan DT, Stone RA, Wong TY. A cohort study of incident myopia in Singaporean children. Invest Ophthalmol Vis Sci.2006;47:1839-44.
2. Lam CS, Goldschmidt E, Edwards MH. Prevalence of myopia in local and international schools in Hong Kong. Optom Vis Sci. 2004;81:317-22.
3. Lam CS, Lam CH, Cheng SC, Chan LY. Prevalence of myopia among Hong Kong Chinese schoolchildren: changes over two decades. Ophthalmic Physiol Opt. 2012;32:17-24.
4. Vongphanit J, Mitchell P, Wang JJ. Prevalence and progression of myopic retinopathy in an older population. Ophthalmology. 2002;109:704-11.
5. Xu L, Wang Y, Wang S, et al. High myopia and glaucoma susceptibility the Beijing Eye Study. Ophthalmology. 2007;114:216–20.
6. Lam CS, Tang WC, Tse DY, Tang YY, To CH. Defocus Incorporated Soft Contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: a 2- year randomised clinical trial. Br J Ophthalmol. 2014;98:40-5.

7. Appendix 1

Questionnaire: Evaluation of a new myopic control lenses

Name: _____ Date: _____

Record #: _____

Section A. Please estimate the time that you spend on the following activities.

School time

Hours per day	**(a) Weekdays: Mon-Fri**	**(b) Weekends: Sat -Sun**	**Hours per day on average = (5a + 2b)/2**
Wear our spectacles			
Do you wear other optical aids during this study? (e.g. contact lenses, other spectacles, etc.)	Yes (go to Q2)	No	
Contact lenses: _____			
Spectacles: _____			
Near work (e.g. reading, doing homework, smart-phone and i-pads, etc.)			
Mid-working distance activities (e.g. watch TV, computer, playing musical instruments, etc.)			
Outdoor activities			
Indoor activities			
Sleeping time			

Long holidays

Hours per day	**(a) Weekdays: Mon-Fri**	**(b) Weekends: Sat -Sun**	**Hours per day on average = (5a + 2b)/2**
Wear our spectacles			
Near work (e.g. reading, doing homework, smart-phone and i-pads, etc.)			
Mid-working distance activities (e.g. watch TV, computer, playing musical instruments, etc.)			
Outdoor activities			
Indoor activities			
Sleeping time			

Section B.

Please rate the performance of your current spectacles. (Please circle the choice and rating)

		Poorest	→	acceptable	→	Fair	→	→	Good	→	Excellent
1	Vision at distance (clarity)	1	2	3	4	5	6	7	8	9	10
2	Vision stability at distance	1	2	3	4	5	6	7	8	9	10
3	Clarity of vision for intermediate distance (e.g. computer, watching TV)	1	2	3	4	5	6	7	8	9	10
4	Clarity of vision for near tasks (e.g reading, using smartphone)	1	2	3	4	5	6	7	8	9	10

5	Vision stability at near	1	2	3	4	5	6	7	8	9	10
6	Vision comfort	1	2	3	4	5	6	7	8	9	10
8	Vision during outdoor	1	2	3	4	5	6	7	8	9	10
9	Easiness of lens adaption	1	2	3	4	5	6	7	8	9	10
10	Overall performance	1	2	3	4	5	6	7	8	9	10

Do you have the following symptoms when wear this spectacles?

		Never	→	Seldom	→	Some-times	→	→	Often	→	Always
1	Blurred vison at far distance	1	2	3	4	5	6	7	8	9	10
2	Blurred vision at intermediate distance (e.g. computer)	1	2	3	4	5	6	7	8	9	10
3	Blurred vision at near (e.g. reading, smart-phone)	1	2	3	4	5	6	7	8	9	10
4	Ghosting image	1	2	3	4	5	6	7	8	9	10
5	Unstable vision at distance	1	2	3	4	5	6	7	8	9	10
6	Unstable vision at near	1	2	3	4	5	6	7	8	9	10
7	Difficulty or slowness in	1	2	3	4	5	6	7	8	9	10

	refocusing your eyes from one distance to other										
8	Eyestrain	1	2	3	4	5	6	7	8	9	10
9	Double vision	1	2	3	4	5	6	7	8	9	10
10	Dizziness	1	2	3	4	5	6	7	8	9	10
11	Headache	1	2	3	4	5	6	7	8	9	10

Other comments:

_____