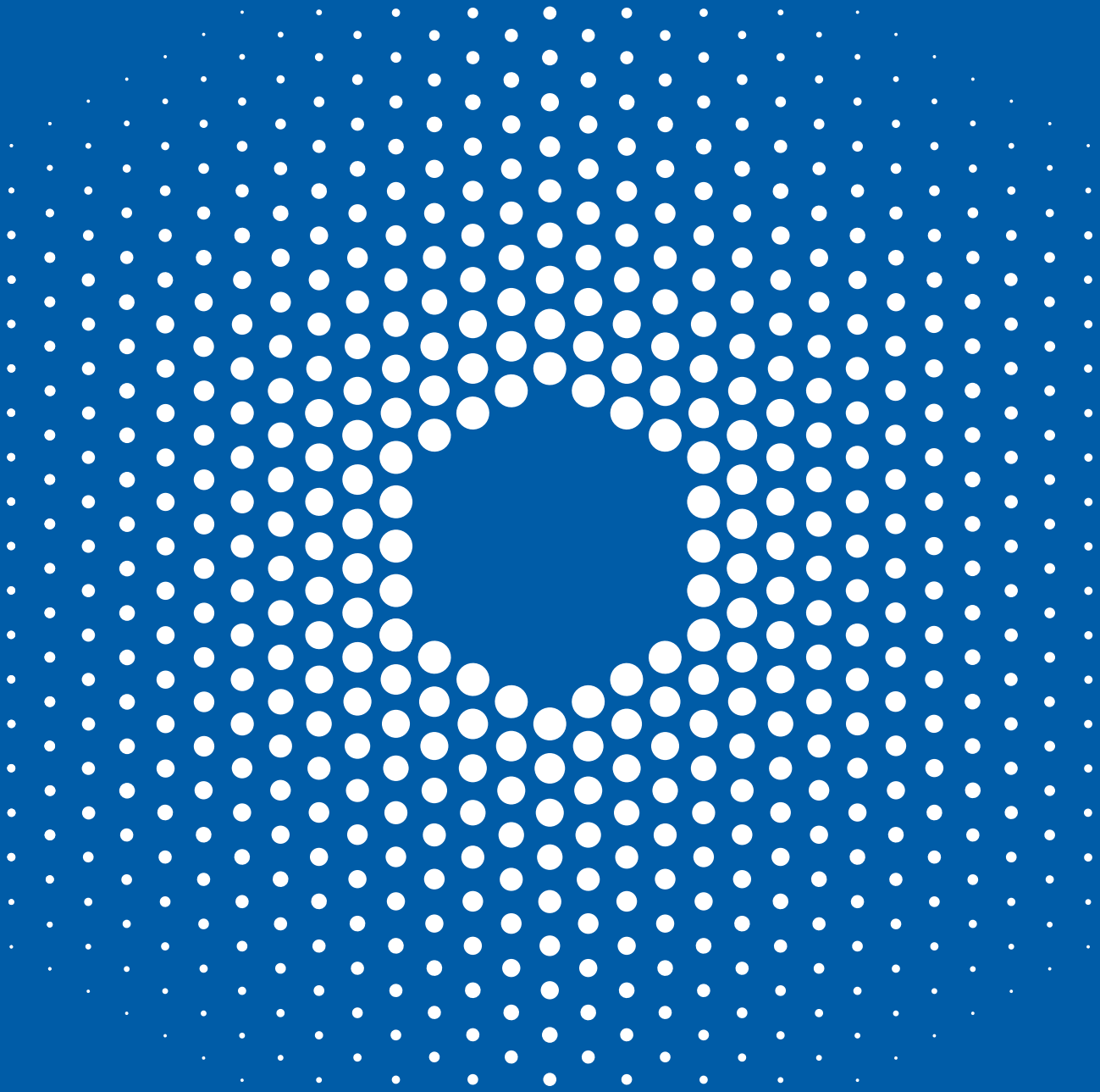
MiYOSMART



Handboek MiYOSMART

HOYA
FOR THE VISIONARIES

versie 07 - mei 2023

Inhoud

Retourformulier



Klantgegevens

Klantnummer: _____

Firmanaam: _____ Plaats: _____

Glazen retour:

Datum oogonderzoek: _____

- Refractie:

OD S _____ C _____ as _____

OS S _____ C _____ as _____

Cyclometing uitgevoerd: ❑ Ja ❑ Nee

Aslengte: _____

Datum bestelling 1e paar glazen: _____

Reden retour: _____

_____

_____

Nieuwe refractie/bestelling:

OD S _____ C _____ as _____

- OS S _____ C _____ as _____

Cyclometing uitgevoerd: ❑ Ja ❑ Nee

Aslengte: _____

Datum: _____

Ordernummer nieuw bestelde glazen:

Gewenningsproblemen: _____

_____

_____

Garantievoorwaarden

1. Sterkte verandering (SER) 0.75 D of meer binnen 12 maanden
2. Glazen zijn binnen 1 maand na meting aangeschaft
3. Cycloplegische refractie en aslengte meting verplicht
4. Bril wordt minimaal 12 uur per dag gedragen

Dit formulier opsturen naar HOYA Lens Nederland B.V., samen met de ingeleverde MiYOSMART glazen. Zonder dit formulier kunnen de glazen niet gecrediteerd worden.

HOYA
FOR THE VISIONARIES

1. Selectie en voorwaarden

A. Leeftijd
In het algemeen zijn myope kinderen in de leeftijd van 6 tot 18 jaar geschikt voor het dragen van MiYOSMART brillenglazen, maar de oogzorgprofessional dient te bepalen of iemand geschikt is.

B. Bijwerkingen
Er zijn geen bijwerkingen geassocieerd met het dragen MiYOSMART brillenglazen.[1]

C. Voorwaarden
Als er sprake is van strabismus, nystagmus of keratoconus is het advies om een orthoptist/oogarts in te schakelen.

D. Sport en activiteiten
Tijdens de gewenningsperiode dient de brildrager het volgende te vermijden:
- Intensieve contactsporten, zoals voetbal
- Het besturen van voertuigen, bijvoorbeeld een fiets of scooter
- Fysieke activiteiten of gymnastieklessen op school
- Klimmen, op een hoge trap staan of op andere plekken met hoogteverschillen

E. Vervanging en garantie
Indien de refractieafwijking (of het sferisch equivalent) ≥0.50D afwijkt van de huidige correctie is het aanbevolen om de glazen te vervangen. HOYA biedt een garantie op de brillenglazen indien binnen 12 maanden de stijging ≥ -0.75D bedraagt (vervanging van 2 MiYOSMART brillenglazen voor 2 nieuwe MiYOSMART brillenglazen zonder kosten).

Voorwaarden voor deze garantie:

- het protocol (pag. 3-5) is gevolgd
- de glazen zijn binnen 1 maand na de meting aangeschaft
- cycloplegische refractie en aslengte meting zijn verricht
- de bril is minimaal 12 uur per dag gedragen.

Bij een verzoek tot omruiling dient het te downloaden formulier gebruikt te worden.
Het formulier is ook toegevoegd achter in dit handboek.

F. Gewenning
Het duurt altijd enige tijd om aan een nieuwe bril te wennen. Hoe lang precies, is per persoon verschillend, maar brildragers moeten er rekening mee houden dat het één tot twee weken kan duren om volledig gewend te raken aan de MiYOSMART brillenglazen.

G. Gewenningsgarantie
Indien de klant niet kan wennen aan de MiYOSMART brillenglazen, tot 4 weken bij dagelijks gebruik, dan vervangt HOYA Lens Nederland B.V. in overleg met de afnemer deze glazen eenmalig voor een ander paar binnen het HOYA glasprogramma. De creditering vindt plaats na ontvangst van het oorspronkelijke paar MiYOSMART brillenglazen met een volledig ingevulde Distroptiek retourbon of HOYA retourenvelop. Voorwaarde is dat het protocol (pag. 3-5) is gevolgd.

1. Lam CSY, Tang WC, Lee RPK, Chun RKM, To CH. A randomized clinical trial for myopia control – use of myopic defocus spectacle lens. 8th International Congress of Behavioral Optometry (ICBO), 26-29 of April 2018. Sydney, Australia.

2. MiYOSMART protocol; onderzoek, aanmelden, behandelen

1.1. Eerste bezoek: wanneer starten met behandelen?

Tijdens de opleiding zijn de verschillende indicatoren behandeld om te kunnen bepalen of er gestart dient te worden met de behandeling van progressieve myopie, zoals leeftijd, levensstijl, etniciteit, snelheid van de progressie, aslengte, accommodatie lag en de oogheelkundige en optische geschiedenis van het kind en de ouders. De oogzorgprofessional dient te bepalen of iemand geschikt is en wanneer er gestart kan worden met behandelen. Het protocol is gebaseerd op de richtlijnen van het IMI (International Myopia Institute). In de bijlage staat een toelichting op het protocol, in het handboek MiYOSMART is nog meer informatie terug te lezen.

1.2 Anamnese

A. Oogheelkundige en optische geschiedenis kind

1. Klachten
2. Leeftijd ontstaan myopie, snelheid van myopie progressie (D/jaar)
3. Myopie behandeling verleden (indien van toepassing)
4. Buiten activiteiten (uur/dag) (met bril ja/nee)
5. Dichtbijwerk (uur/dag) (met bril ja/nee)
6. Huidige bril: hoe oud? sterkte?

B. Oogheelkundige en optische geschiedenis ouders

1. Huidige brilsterkte
2. Verloop myopie progressie (op welke leeftijd is myopie ontstaan, etc.)
3. Oogheelkundige aandoeningen

1.3 Vooronderzoek

A. Vooronderzoek

1. VOD/VOS/VODS zonder en met de eigen bril voor veraf en dichtbij
2. Pupilreacties en pupilgrootte
3. Covertest
4. Oogbewegingen
5. Gezichtsveld (optioneel, gebaseerd op klachten en geschiedenis ouders)
6. Kleurentest (optioneel, als het nog niet eerder gecontroleerd is)

B. Refractie en visus

1. Subjectieve refractie VOD/VOS/VODS veraf en dichtbij
2. Cycloplegische refractie (autorefractie/skiascopie)
3. Visus in dimlicht en met hoog/laag contrast (optioneel)

C. Visuele functies (met nieuwe correctie)

1. Stereopsis
2. Accommodatie-amplitude monoculair en binoculair
3. Accommodatie-lag (MEM skiascopie of NOTT skiascopie)

D. Gezondheid van het oog

1. Voorste oogsegment (spleetlamp)*
2. Funduscopie*
3. Aslengte**
4. Corneatopografie*
5. Oogdruk*

E. Analyse en communicatie

1. Kiezen behandelstrategie
2. Communicatie ouders/kind
   a. Prognose
   b. Behandeleffectiviteit
   c. Risico's en bijwerkingen
   d. Advies levensstijl
   e. Kosten

* Ter uitsluiting van secundaire myopie en complicaties.[1]

** Het NOG myopie panel (2020)[2] geeft in hun standpunt over de behandeling voor myopie progressie aan dat het vervolgen en analyseren van de progressie van myopie primair moet worden gestuurd op de aslengte. Indien sturing op aslengte niet mogelijk is adviseren zij het kind te verwijzen naar een zorgpraktijk/instelling waar dit wel mogelijk is.

1.4 Nazorg na twee weken

Het 1e controlebezoek vindt plaats als de bril twee weken is gedragen. Deze controle is nodig om de bril te controleren, te beoordelen of er nog goed door het midden van de optische zone wordt gekeken en om de gewenning te bespreken. Hiervoor wordt een standaard vragenlijst gebruikt, waaruit kan worden opgemaakt hoe de brildrager reageert op de MiYOSMART brillenglazen en of er eventueel sprake is van gewenningsproblemen.

Vragenlijst Gewenning en Prestaties van de nieuwe bril
(beoordeel de nieuwe bril door bij de vragen één cijfer van 1 – 5 te omcirkelen)

	Ervaring	Slecht	Matig	Acceptabel	Goed	Uitstekend
1	Scherp zicht op afstand	1	2	3	4	5
2	Scherp zicht op de tussenafstand (zoals computer, tv kijken)	1	2	3	4	5
3	Scherp zicht dichtbij (zoals lezen, smartphone, tablet)	1	2	3	4	5
4	Stabiliteit van het zicht	1	2	3	4	5
5	Comfort van kijken	1	2	3	4	5
6	Zicht tijdens buiten activiteiten	1	2	3	4	5
7	Gewenning van de bril (montuur + glazen)	1	2	3	4	5
8	Algemene kwaliteit van de bril (montuur + glazen)	1	2	3	4	5
Totaal						

Resultaten

A. Als één van onderstaande 3 vragen van de vragenlijst met ja is beantwoord, vul dan ook deel B in en plan een nieuwe controle afspraak.
1. De algemene kwaliteit (vraag 8) is met 1 of 2 beoordeeld
2. De totaalscore is minder dan 16 punten
3. Een van de vragen is beoordeeld met een 1

B. In hoeverre is er sprake van de volgende ervaringen of symptomen tijdens het dragen van de nieuwe bril?

		Nooit	Zelden	Soms	Vaak	Altijd
1	Moeite met omschakelen van dichtbij naar veraf of andersom	1	2	3	4	5
2	Wazig zien	1	2	3	4	5
3	Dubbelzien	1	2	3	4	5
4	Duizeligheid	1	2	3	4	5
5	Hoofdpijn	1	2	3	4	5

Andere opmerkingen: _____

_____

1.5 Controle elke zes maanden

A. Geschiedenis en achtergrond informatie
1. VOD/VOS/VODS zonder en met de bril voor veraf en dichtbij
2. Kijkcomfort/gewenning/klachten
3. Buiten activiteiten (uur/dag) (met bril ja/nee)
4. Dichtbijwerk (uur/dag) (met bril ja/nee)

B. Refractie en visus

1. Subjectieve refractie VOD/VOS/VODS dichtbij en veraf
2. Cycloplegische auto-refractie / skiascopie (indien nodig)
3. Visus in dimlicht en met hoog/laag contrast (optioneel)

C. Visuele functies

1. Stereopsis met huidige correctie
2. Accommodatie-amplitude monoculair en binoculair
3. Accommodatie-lag (MEM skiascopie of NOTT skiascopie)

D. Gezondheid van het oog

1. Voorste oogsegment (spleetlamp)*
2. Funduscopie*
3. Aslengte**
4. Corneatopografie*
5. Oogdruk*

E. Analyse behandeleffect

* Ter uitsluiting van secundaire myopie en complicaties.[1]

** Het NOG myopie panel (2020)[2] geeft in hun standpunt over de behandeling voor myopie progressie aan dat het vervolgen en analyseren van de progressie van myopie primair moet worden gestuurd op de aslengte. Indien sturing op aslengte niet mogelijk is adviseren zij het kind te verwijzen naar een zorgpraktijk/instelling waar dit wel mogelijk is.

1. Skaridurg P1, Tilia D1, Morton M1, Weng R1, Jong M1, Zhu F2. Guidelines for Myopia Management. Brien Holden Vision Institute; Shanghai Eye Disease Prevention and Treatment Center, https://guidelines.brienholdenvision.org , accessed 16.08.1018.
2. Standpunt NOG 2020. https://www.oogheelkunde.org/sites/www.oogheelkunde.org/files/richtlijnen/Behandeling%20van%20progressieve%20myopie%20op%20kinderleeftijd_standpunt%20NOG%202020.pdf (geraadpleegd op 2-2-2021).

Toelichting MiYOSMART protocol

1.3 A: Vooronderzoek

- Het meten van de pupilgrootte is nodig om vast te stellen welke behandelingen wel of niet geschikt zijn. Voor MiYOSMART zijn er geen beperkingen met betrekking tot de pupilgrootte.
- Het beoordelen van pupilreacties en oogbewegingen zijn nodig om neurologische aandoeningen uit te sluiten.
- De covertest is om latent en/of manifest strabismus vast te stellen. Een esoforie met een accommodatie lag is vaker geassocieerd met een snellere toename van de myopie. Door de accommodatie lag ontstaat er meer (perifere) hyperope defocus. Dit is een risicofactor voor myopie progressie.
- Indien er manifest strabismus aanwezig is, is voorzichtigheid geboden bij het voorschrijven van MiYOSMART. Raadpleeg altijd een orthoptist in het geval van strabismus.

1.3 B: Refractie en visus

- Cycloplegische refractie is noodzakelijk om pseudo-myopie uit te sluiten en overcorrectie van de myopie door accommodatie te voorkomen.
- Visus in dimlicht kun je uitvoeren indien er visusklachten aanwezig zijn maar er een goede visus behaald wordt, de visusklachten kunnen dan komen door contrastverlies. Dit kan meespelen in de keuze van de behandelstrategie.

1.3 C: Visuele functies

- Een pre-myoop kan specifieke stoornissen in het binoculair zien vertonen, waaronder verminderde accommodatie, verhoogde accommodatie lag en een hogere AC/A verhouding. Door een verhoogde accommodatie lag ontstaat er meer (perifere) hyperope defocus. Dit is een risicofactor voor progressieve myopie. Een verhoogde accommodatie lag geeft niet altijd visusklachten dichtbij.
- Door het meten van de stereopsis kan er bepaald worden of iemand samenwerking tussen de ogen heeft en hoe goed deze samenwerking is. Raadpleeg een orthoptist als er geen of een slechte samenwerking tussen de ogen is.

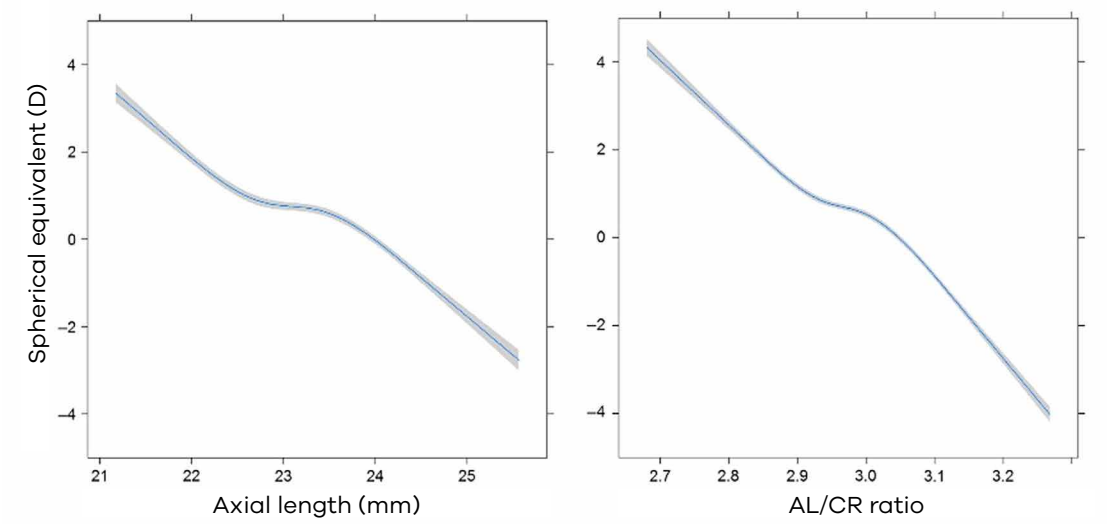
Het effect van managen op deze stoornissen op de ontwikkeling van myopie is nog niet bekend.[1]

1.3 D: Gezondheid van het oog

- Plot de aslengte op de groeicurve kaart van Tideman om het risico van (hoge) myopie in te schatten.
- Corneatopografie is nodig indien de myopie niet overeen komt met de aslengte (curve 1). Bijvoorbeeld als iemand een lage myopie heeft en in verhouding een hoge aslengte, kan het zijn dat iemand een vlakke cornea heeft. Zie AL/CR ratio curve 1.

Rekenvoorbeeld:
Myopie (SE): S-1.75 AL (mm): 25.32

Gemiddelde corneakromming (mm): 8.08
AL/CR ratio= 3,13 (25,32/8,08)



Curve 1: links verhouding aslengte (mm) en sferisch equivalent (d), rechts AL/CR ratio (Tideman) [2]

- Ook is het uitvoeren van een corneatopografie aan te bevelen indien er voor behandeling met contactlenzen gekozen/overwogen wordt.

1.3 E: Analyse en communicatie

a. Prognose: Geen enkele huidige myopie controle behandeling kan de progressie van de myopie permanent stoppen of omkeren. Over het algemeen zullen myope kinderen die een traditionele enkelvoudige bril of contactlenzen dragen, in myopie blijven toenemen met ongeveer 0,50 tot 1,00 dioptrieën per jaar. Verwacht wordt dat myopie controle behandelingen het tempo van de progressie zullen vertragen. Het effect van de myopie controle behandeling voor een individueel kind kan hoger of lager zijn dan het gemiddelde.[3]

b. Het gemiddelde behandeleffect van MiYOSMART is over een periode van 2 jaar 60%.[4] De vertraging van de myopie progressie hield ook in het derde jaar onderzoek aan[5]. De bevindingen van de 6-jarige follow-up studie toonden aan dat voor kinderen die MiYOSMART brillenglazen dragen **het myopiecontrole-effect in de loop van de tijd aanhoudt**. Tevens bevestigde de studie dat kinderen die stoppen met het dragen van MiYOSMART brillenglazen **geen reboundeffect ondervinden**, ten opzichte van de initiële progressie van myopie tijdens het gerandomiseerde gecontroleerde onderzoek over 2 jaar of ten opzichte van de algemene populatie.[6]

c. Mogelijke risico's en bijwerkingen: Ouders moeten worden geïnformeerd over mogelijke risico's en bijwerkingen geassocieerd met myopie controle behandelingen:

1. Contactlenzen: Het belangrijkste risico verbonden aan contactlenzen is microbiële keratitis, die in een klein percentage van de gevallen kan resulteren in een verminderd gezichtsvermogen. Het aantal nieuwe gevallen van microbiële keratitis bij kinderen die 's nachts Ortho-K-lenzen dragen, is 13 in 10.000 per jaar. Voor zachte contactlenzen bedraagt het aantal microbiële keratitis (MK) bij volwassen daglensdragers 2 per 10.000 per jaar; en 12 per 10.000 per jaar in herbruikbare zachte lenzen. Deze percentages van MK zijn niet specifiek bestudeerd bij kinderen; maar het percentage van de corneale infiltratieve events is ongeveer 15 per 10.000 per jaar voor kinderen leeftijd 13-17 jaar. Het percentage microbiële keratitis voor kinderen van 8-12 jaar die zachte contactlenzen dragen, lijkt minder te zijn dan die van volwassenen of tieners, maar kan met de beschikbare gegevens niet nauwkeurig worden ingeschat.
2. Ortho-K en multifocale zachte contactlenzen: In vergelijking met een bril kunnen kinderen licht wazig zien of veranderingen in het scherp stellen ervaren met Ortho-K of multifocale zachte contactlenzen.
3. Atropine: De meest voorkomende bijwerkingen geassocieerd met het gebruik van atropine oogdruppels zijn een tijdelijk prikkend of brandend gevoel, wazig zicht en lichtgevoeligheid. Lagere doseringen kunnen leiden tot minder van deze bijwerkingen. Effecten van langdurig gebruik zijn onbekend.[3]
4. MiYOSMART: Er is een verwaarloosbaar effect op de gezichtsscherpte gemeten. Er zijn uiteindelijk geen ongemakken of grote verschillen aangetoond in vergelijking met enkelvoudige glazen.[4]

d. Advies levensstijl geven

1. Kinderen moeten worden aangemoedigd om hun myopie-correctie voltijds te dragen, aan gezien in sommige studies is aangetoond dat een ondercorrectie van myopie de progressie van myopie kan stimuleren.
2. Ouders moeten worden geïnformeerd dat langdurig nabij werk (45 min), boek of digitaal, de ontwikkeling en progressie van myopie kan beïnvloeden. Een korte leesafstand is in ver band gebracht met een grotere kans op myopie. Buitenactiviteit wordt daarentegen ge associeerd met een verminderde incidentie van myopie bij kinderen, inclusief diegenen die meestal lange tijd dichtbij kijken.
3. Dit suggereert niet dat kinderen niet mogen deelnemen aan activiteiten op korte afstand, maar dat zij deze bewuster doen met regelmatige pauzes, passende leesafstanden (minimaal 30 cm) en fixatie veranderingen tijdens het lezen en kijken op een beeldscherm, waarbij ook voldoende tijd buitenshuis wordt aangemoedigd.
4. In Nederland wordt de 20-20-2 regel geadviseerd.
5. Zowel binnen- als daglicht maximaliseren en de buitentijd verhogen.[3]

1.4: Nazorg en gewenning

Wij adviseren deze controle door de verstrekkende opticien uit te laten voeren.

1.5 A: Anamnese

- Risico analyse doorlopen zorgt ervoor dat je inzicht krijgt in de levenstijlfactoren, waardoor je hier weer op kunt sturen indien nodig.

1.5 B: Refractie en visus

- Cycloplegische refractie is nodig indien de sterkte subjectief ≥S0.50 dpt afwijkt van de huidige brilsterkte of indien er een nieuwe bril wenselijk is.
- Visus in dimlicht als er visusklachten zijn ondanks een goede visus OD/OS/ODS

1.5 C: Visuele functies

- Na het ontstaan van myopie bestaat het vermoeden van accommodatieve stoornissen een kenmerk zijn van myopie en geen oorzaak.[1]

1.5 D: Gezondheid van het oog

- De aslengte is belangrijk om het succes van de behandeling te kunnen bepalen en het verloop te monitoren. Een behandeling is succesvol te noemen als de aslengte niet meer dan:
  - 0.25mm groeit in de leeftijd van 6-9 jaar
  - 0.15mm in de leeftijd van 10-13 jaar
  - 0.10mm in de leeftijd van 14-18 jaar.

Als er toch meer aslengte groei is, moet er overwogen worden om de therapie aan te passen. Bijvoorbeeld overstappen naar een hogere dosering atropine of een combinatietherapie instellen. (protocol Erasmus MC 2020)

- Advies 1x per jaar de fundus na te laten kijken.

1.5 E: Analyse behandeleffect

- zie 1.5D

Referenties:

1. Nicola S. Logan; Hema Radhakrishnan; Fiona E. Cruickshank; Peter M. Allen; Praveen K. Bandela; Leon N. Davies; Satoshi Hasebe; Safal Khanal; Katrina L. Schmid; Fuensanta A. Vera-Diaz; James S. Wolffsohn. IMI Accommodation and Binocular Vision in Myopia Development and Progression. Investigative Ophthalmology & Visual Science April 2021, Vol.62, 4. doi:https://doi.org/10.1167/iovs.62.5.4
2. Tideman , J. W. L., Polling, J. R., Vingerling, J. R., Jaddoe, V. W. V., Williams, C., Guggenheim, J. A., & Klaver, C. C. W. (2018). Axial length growth and the risk of developing myopia in European children. Acta Ophthalmol, 96(3), 301-309. doi:10.1111/aos.13603
3. Gifford KL, Richdale K, Kang P, Aller TA, Lam CS, Liu YM, et al. IMI - Clinical Management Guidelines Report. Invest Ophthalmol Vis Sci. 2019;60(3):M184-M203. https://iovs.arvojournals.org/article.aspx?articleid=2727312
4. Lam CSY, Tang WC, Tse DY, Lee RPK, Chun RKM, Hasegawa K, Qi H, Hatanaka T, To CH. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. British Journal of Ophthalmology. Published Online First: 29 May 2019. doi: 10.1136/bjophthalmol-2018-313739
5. Carly SY Lam, Wing Chun Tang, Paul H Lee, Han Yu Zhang, Hua Qi, Keigo Hasegawa, Chi Ho To. Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: results of a 3-year follow-up study. DOI: 10.1136/bjophthalmol-2020-317664
6. Lam, C.S.Y., Tang, W.C., Zhang, H.Y. et al. Long-term myopia control effect and safety in children wearing DIMS spectacle lenses for 6 years. Sci Rep 13, 5475 (2023). https://doi.org/10.1038/s41598-023-32700-7

3. Montuurkeuze en aanpassing

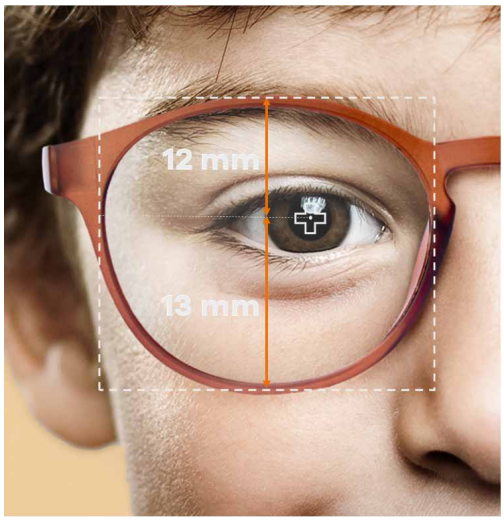
Omdat het gezicht van kinderen nog verandert als ze ouder worden, is het raadzaam om daar bij het uitzoeken van een montuur rekening mee te houden. Adviseer met name metalen of kunststof randbrillen in verband met de kwestbaarheid van nylors en glasbrillen.

Monturen die geschikt zijn voor kinderen hebben de volgende kenmerken:[1,2]

1. Sluit overal goed aan op de neus
2. Smaller voorstuk
3. Kortere veerlengte
4. Lagere neusbrug
5. Kortere bocht achter het oor
6. Grotere hoek tussen de voorkant en de veer zodat de veren niet in de slaap drukken
7. Kleinere diameter van het glas
8. Kortere hoornvliesafstand
9. Kleine inclinatiehoek (ideaal dichtbij nul)

Deze maattabel[3] is een inschatting voor de montuurmaat voor een kind:

Leeftijd kind (jaren)	Montuur maat (mm)
0 tot 1	35 tot 37
1 tot 2.5	37 tot 38
2.5 tot 4	40 tot 42
4 tot 7	43 tot 45
7 tot 10	45 tot 47
10 tot 16	47 tot 52



- Kies een montuur waarbij de ogen halverwege de montuurhoogte of iets daarboven gericht zijn.
- Meet het glas in zoals bij multifocaal: monoculair gemeten (verticale) hoogte en (horizontale) pupilafstand. Accepteer wanneer er een verschil is in monoculaire pd en hoogte OD/OS.
- Zorg voor minimaal 12 mm boven het doorkijkpunt tot aan de rand van het brillenglas.
- Montuur hoogte (B-maat): ≥ 20 mm (tot aan de binnenranden van het montuur).
- Optisch centrum van het glas afstemmen op het centrum van de pupil.
- Manuele aanpassing van de PD (CD) is noodzakelijk bij voorschrijven prisma (decentratie: per prisma =0.25mm).

Om er zeker van te zijn dat het gekozen montuur geschikt is voor de MiYOSMART glazen, adviseren wij om te controleren of de gemeten waarden van de pantoscoptische hoek (montuurinclinatie), de hoornvliesafstand en de montuurdoorbuiging passen binnen de optimale aanpas parameters.

- Hoornvliesafstand: 10 mm of minder
- Montuurdoorbuiging: 0-5°
- Pantoscoptische hoek: ongeveer 0°

1. Hughes E. Key considerations when dispensing children spectacles. Dispensing Optics. January 2014.
2. Obstfeld H. Spectacle Frames and their Dispensing. Bailliere Tindall. 1996.
3. https://tomatoglasses.me/pages/sizing-advice , accessed online 05.07. 2018

4. Slijpadviezen

MiYOSMART-brillenglazen zijn gemaakt van polycarbonaat. Dit vereist een andere inslijpprocedure in vergelijking met andere kunststof brillenglazen. Als u niet bekend bent met het verwerken van polycarbonaat brillenglazen, is het raadzaam deze richtlijn te volgen om ervoor te zorgen dat ze zo goed mogelijk passen in het gekozen montuur.

1. Slijp MiYOSMART brillenglazen met het polycarbonaat slijpprogramma.

- In de meeste slijpmachines vindt u de letters PC om het polycarbonaat glasprogramma aan te duiden. Dit programma maakt gebruik van droogslijpen (zonder water), dat essentieel is voor polycarbonaat glazen.
- Zoet de glazen af onder een hoek van 45 graden en een breedte van 0.2-0.5mm om ervoor te zorgen dat de glasranden niet te scherp zijn.

2. Polijst de glasranden, ongeacht het montuurtype

- Polycarbonaat glazen moeten altijd gepolijst worden.
- Gebruik de droge polijstmethode en gebruik de laagst mogelijke druk en snelheid van de polijstmachine. Gebruik indien mogelijk het polijstprogramma dat beschikbaar is in de slijpautomaat die is ontworpen voor polycarbonaat glazen.
- Hogere snelheid zorgt ervoor dat de temperatuur van het glas stijgt (door wrijving), wat kan leiden tot barsten in de coating of op de randen van het glas. Dit is mogelijk niet direct merkbaar en kan over een langere periode verschijnen.
- Gebruik geen chemische polijstmiddelen. Deze kunnen oplosmiddelen bevatten, die het polycarbonaat kunnen beschadigen.

3. Schoonmaken van de glazen

- Gebruik geen aceton!
- Isopropyl alcohol kan gebruikt worden.
- Let op: als u oplosmiddelen gebruikt, laat dan geen druppels of spatten van het oplosmiddel op het glasoppervlak achter.
- Controleer altijd of de vloeistof die u gebruikt geschikt is voor polycarbonaat glazen.

4. Boren van de glazen

- Het is aan te raden de glasranden te polijsten voordat u gaat boren.
- Gebruik een zeer scherpe boor, bij voorkeur van hardmetaal.
- Het wordt aanbevolen om een lagere boorsnelheid te gebruiken, idealiter tussen 160-180 rpm.
- Boor met kleine stoten en boor niet in één keer door het glas.
- Vermijd harde druk bij het boren van de glazen. Lage druk zorgt voor een betere afwerking en vermindert het risico op barsten van het materiaal.
- Gebruik geen ruimers om het geboorde gat te vergroten, hierdoor zal het glas barsten.
- Zoet de glazen af rondom de geboorde gaten, het gebruik van kunststof bussen wordt aanbevolen.

5. Gebruik van borgmiddelen (zoals Loctite)

- Het wordt afgeraden om borgmiddelen te gebruiken.
- Als het gebruik van borgmiddelen voor schroefdraad nodig is, zorg er dan voor dat er geen borgmiddel op het glas achterblijft.

6. MiYOSMART glazen in het montuur monteren

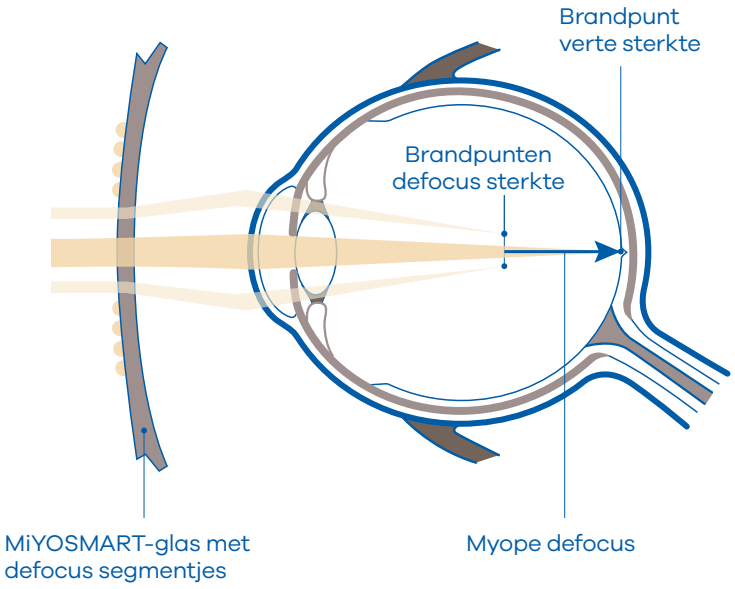
- Zorg ervoor dat de ronding van het montuur het glas niet buigt. Het wordt aangeraden om de vorm van het montuur handmatig aan te passen, zodat deze de basiscurve van het glas volgt.
- Monteer de glazen in een metalen montuur zodat ze los aanvoelen.
- Bij montage in een kunststof montuur wordt geadviseerd om bij elk bezoek aan de winkel te controleren of de glasspanning niet is toegenomen als gevolg van het natuurlijk krimpen van kunststof monturen.
- Reinig bij een metalen frame de facetranden aan de binnenzijde (waar de glazen komen) verwijder alle kleine klontjes verf of vuil. Deze veroorzaken spanningspieken op het glas en kunnen op de lange termijn problemen veroorzaken.
- Als het montuurtype een nylor is, zorg er dan voor dat de nylordraad niet te strak zit en druk op de onderkant van de groef uitoefent, vooral in de hoekgedeelte van het glas.
- Zorg ervoor dat het uiteinde van de nylondraad niet te veel tegen de rand van de lens drukt.

5. Veelgestelde vragen

1. Wat is D.I.M.S.-technology?
D.I.M.S. staat voor Defocus Incorporated Multiple Segments. Deze technologie is de basis voor MiYOSMART, HOYA's glas om progressieve myopie te behandelen.

2. Wat zijn de voordelen van MiYOSMART glazen?
Het is een veilige en niet-invasieve behandeling om de refractieafwijking van de brildrager te corrigeren, terwijl de progressie van myopie wordt vertraagd. Ook kunnen brildragers met MiYOSMART probleemloos alle activiteiten ondernemen die ze gewend zijn, omdat de brillenglazen slagvast zijn. De brillenglazen zien er door hun gladde oppervlak vrijwel identiek uit als standaard enkelvoudige brillenglazen.

3. Op welk principe is D.I.M.S.-technology gebaseerd?
Voor MiYOSMART wordt gebruik gemaakt van het natuurlijke aanpassingsmechanisme van het oog dat 'emmetropisatie' wordt genoemd. De immature (in ontwikkeling zijnde) ooglens ontwikkelt zich dusdanig dat de refractie-afwijking vermindert in de loop van de ontwikkeling (kinderleeftijd). Door een myope defocus te creëren (lichtstralen bundelen vóór het netvlies), wordt de groei van de oogbol (aslengte) beïnvloed, wat in verband wordt gebracht met progressieve myopie.[1]



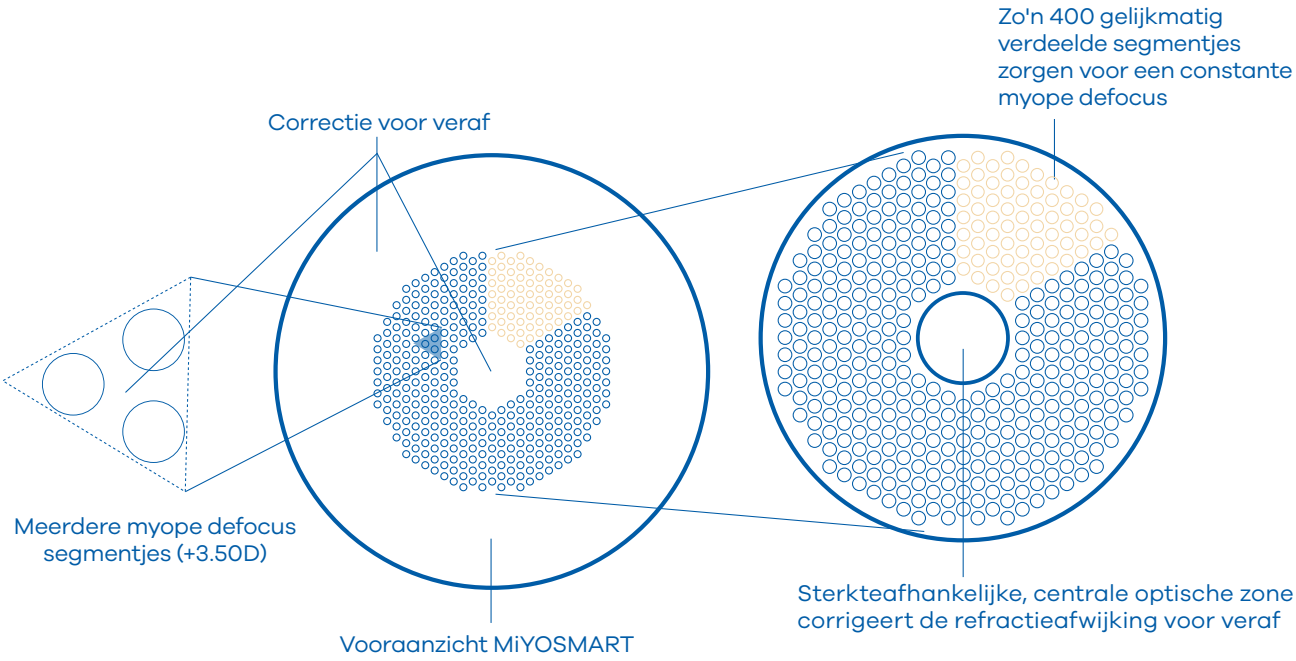
4. Hoe werkt MiYOSMART?
MiYOSMART met D.I.M.S.-technology is in basis een enkelvoudig brillenglas waarbij op de voorzijde bijna 400 kleine segmenten van 3.5D zijn aangebracht die een myope defocus creëren. Tussen de segmentjes is de benodigde vertesterkte aanwezig. Als het oog zich richt op de behandelzone met de defocus segmentjes ontvangt het tegelijkertijd de myope defocus én de benodigde vertesterkte. De verhouding van sterktes is hier ongeveer 50:50.

Er vallen gemiddeld 6 tot 7 defocus segmentjes door de pupilopening. Het brandpunt dat wordt gevormd door het licht, dat via de defocus segmentjes het oog binnenkomt, valt vóór het netvlies. Het is aangetoond in wetenschappelijk onderzoek dat hierdoor de groei van de aslengte vertraagt.[2,3,4] Het brandpunt dat gevormd wordt door de benodigde vertesterkte valt op het netvlies.

Deze structuur van het brillenglas maakt het mogelijk om gelijktijdig de groei van de aslengte te vertragen en scherp zicht te bieden.

Binnen een cirkel van 9,4 mm in het optisch centrum van het brillenglas bevinden zich geen defocus segmentjes. Binnen deze centrale zone is het mogelijk om de sterkte van het brillenglas goed te meten en de drager scherp zicht te geven.

Om progressieve myopie doeltreffend af te remmen moet de drager een constante myope defocus ervaren, ook als het beweegt. Hiervoor is een aanzienlijke hoeveelheid defocus segmentjes vereist die gelijkmatig over het oppervlak van het brillenglas verdeeld moeten zijn. HOYA is er in geslaagd om de D.I.M.S.-technology op een zodanige manier in het glas te integreren dat er, ondanks een grote hoeveelheid defocus segmentjes, een glad oppervlak ontstaat. Dankzij de innovatieve productietechnologie zien de MiYOSMART brillenglazen er net zo uit als standaard enkelvoudige brillenglazen.



5. Is het effect van MiYOSMART wetenschappelijk bewezen?

Een tweejarige gerandomiseerde controlestudie (RCT), uitgevoerd in China tussen 2014-2017 onder 160 kinderen in de leeftijd van 8-13 jaar, heeft aangetoond dat de D.I.M.S-technology de myopie progressie gemiddeld met 59%, en de groei van de aslengte met gemiddeld 60% afremt in vergelijking met de groep die standaard enkelvoudige glazen droeg. Uit de driejarige vervolgstudie is gebleken dat het beheersingseffect van myopie aanhield in het derde jaar bij de kinderen die de D.I.M.S.-glazen in de voorgaande twee jaar hadden gedragen. Dit werd ook aangetoond bij de kinderen die na de eerste twee jaar overschakelden van standaard enkelvoudige glazen naar D.I.M.S.-glazen.

Een zesjarige klinische vervolgstudie werd uitgevoerd op 90 kinderen in Azië. De resultaten vormden een uitbreiding van een driejarige follow-up studie, een voortzetting van een tweejarige gerandomiseerde controlestudie (RCT), die werden gepubliceerd in het British Journal of Ophthalmology en waarin sterke aanwijzingen naar voren kwamen dat de brillenglazen de progressie van myopie bij kinderen van 8-13 jaar doeltreffend vertraagden.

De bevindingen van de zesjarige vervolgstudie toonden aan dat voor kinderen die D.I.M.S.-glazen dragen het myopiecontrole-effect in de loop van de tijd aanhoudt. Tevens bevestigde de studie dat kinderen die stoppen met het dragen van D.I.M.S.-glazen geen reboundeffect ondervinden, ten opzichte van de initiële progressie van myopie tijdens het gerandomiseerde controlestudie over twee jaar of ten opzichte van de algemene populatie. Zie hoofdstuk 6 voor de studies.

6. Geldt dit ook voor westerse ogen?
Ja, bij extrapolatie van het COMET-onderzoek[6] komen geen statistische verschillen naar voren tussen multi-etnische groepen. De hogere prevalentie en mate van myopie bij Aziaten is waarschijnlijk geassocieerd met leefstijl en omgevingsfactoren.

7. Waarom is er +3.50D sterkte gebruikt?
Om effectief myopie progressie te behandelen, moet er constant myope defocus aanwezig zijn, ook tijdens oogbewegingen. Dit vereist een grote hoeveelheid defocus segmentjes over het gehele glasoppervlak. In de behandelzone, met een oppervlaktediameter van 33mm, bevinden zich bijna 400 +3.50D defocus segmentjes. Dit is de meest effectieve sterkte voor de behandeling van myopie progressie (zie de review artikelen achter in dit handboek).

8. Welke sterkte zit er tussen de defocussegmentjes?
De volledig voorgeschreven vertesterkte. Dat is de reden waarom de bildrager op ieder moment in elke kijkrichting goed door het brillenglas kan kijken. De bildrager kijkt zowel door het centrale deel met de volledige voorgeschreven sterkte als door de behandelzone. Er is getest en gecontroleerd bij welke verhouding een comfortabel gezichtsvermogen werd verkregen en tevens een effect op progressieve myopie werd bereikt. De hersenen concentreren zich op het scherpe beeld, niet op het wazige beeld. Dankzij de voorgeschreven sterkte kunnen bildragers goed zien, terwijl de bijna 400 defocus segmentjes het natuurlijke aanpassingsmechanisme van het oog beïnvloeden om progressieve myopie te vertragen. De ene helft van de lichtstralen valt samen op het netvlies (scherp) en de andere helft valt samen vóór het netvlies (myope defocus).

9. Ervaart de drager wazig zicht als gevolg van de defocus segmenten in het glas?
Uit de dragerstest[5] is gebleken dat er een verwaarloosbaar effect op de gezichtsscherpte aanwezig was. Er zijn uiteindelijk geen ongemakken of grote verschillen gerapporteerd tussen standaard enkelvoudige glazen en het MiYOSMART glas.

10. Heeft de pupilgrootte gevolgen voor het gezichtsvermogen met MiYOSMART?
Er zijn geen negatieve effecten gemeld met betrekking tot de pupilgrootte tijdens het dragen van MiYOSMART brillenglazen.

11. Een kinderbril zakt makkelijk af, is het niet lastig om de juiste hoogte te bepalen?
Nee, de centrale zone is vrij groot, 9.4mm en de behandelzone is 33mm. Volg de aanpasadviezen voor monturen.

12. Beïnvloedt het wegslijpen van een deel van de behandelzone de effectiviteit?
Het wegslijpen van een deel van de behandelzone heeft geen effect op de effectiviteit. Het wordt aanbevolen om voor MiYOSMART een montuur te gebruiken dat een minimale hoogte heeft van 20 mm (binnenrand montuur).

13. Zijn er gewenningsproblemen?
Er zijn geen gewenningsproblemen gerapporteerd tijdens het 2 jarige onderzoek dat uitgevoerd is door de Hong Kong Polytechnische universiteit (PolyU).[5]

14. Zijn er contra indicaties voor het voorschrijven van MiYOSMART?
Oogzorgprofessionals moeten voorzichtig zijn met aandoeningen zoals, strabismus, nystagmus en keratoconus.

15. Kan MiYOSMART gebruikt worden i.c.m. andere myopie management behandelingen?
In theorie ja, maar er zijn nog (geen) klinische studies die aantonen wat het effect is van combinatietherapie.

16. Zou een kind preventief MiYOSMART glazen moeten dragen?
In theorie ja, maar er zijn nog (geen) klinische studies die aantonen wat het effect is van preventief voorschrijven.

17. Welke coating is beschikbaar voor MiYOSMART?
Het brillenglas is voorzien van een eigen MiYOSMART anti-reflectie coating. Deze multi-layer coating is waterafstotend, makkelijk schoon te maken en duurzaam.

18. Hoe veilig is het materiaal van de brillenglazen voor kinderen?
MiYOSMART wordt gemaakt van dun, lichtgewicht 1.59 polycarbonaat materiaal, met een hoge slagbestendigheid. In een speciale test heeft het materiaal bewezen geschikt te zijn om een zeer sterke impact te kunnen weerstaan (6 ANSI Z87.1 High Velocity Impact Test). Tevens biedt het materiaal de benodigde UV-bescherming.

19. Zijn er instructies om polycarbonaat te slijpen?
HOYA biedt HELP (vormslijpen) op 1.59 polycarbonaat gratis aan.

20. Wat zijn de materiaal specificaties?

Materiaal	Covestro DPI-1821 VEA
Brekingsindex	1.59
Abbegetal	31
Soortelijk gewicht	1,20 g/cm^3
UV absorption	tot 380 nm
Hittebestendigheid	110°C

21. Wat is het leveringsbereik?
Sterkte: Plano tot -10,00D, max. cil -4,00D (tot een sterkte van -6,00D), max. prisma 3D, 3 prdpt per glas
Diameter: 60 – 65 – 70 – 75 mm (zie schema leveringsbereik).

22. Hoe is MiYOSMART te bestellen?
De brillenglazen zijn via HoyaiLog net zo eenvoudig te bestellen als andere, enkelvoudige brillenglazen. U hoeft alleen maar de monoculaire pupilafstand (PD) en de pupilhoogte (PH) door te geven. Houd ook rekening met een eventueel verschil in pupilhoogte. HOYA heeft de montuur parameters voor kinderen geanalyseerd om er zeker van te zijn dat deze waarden mogelijk zijn met MiYOSMART brillenglazen. Het ontwerp van de glazen is hiertoe optimaal aangepast. Controleer voordat je MiOSMART brillenglazen bestelt of de gemeten parameters binnen de volgende waarden vallen: montuurdoorbuiging 0-5°, hoornvliesafstand ≤10 mm en inclinatie dicht bij 0°.

1. https://www.polyu.edu.hk/cpa/excel/en/201804/viewpoint/v1/index.html,13.07. 2018.
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4. Tse DY, Lam CS, Guggenheim JA, Lam C, Li KK, Liu Q, To CH. Simultaneous defocus integration during refractive development. Invest Ophthalmol Vis Sci. 2007 Dec;48(12):5352-9.
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6. MiYOSMART Sun

1. Welke MiYOSMART Sun brillenglazen zijn/komen beschikbaar?
-MiYOSMART Chameleon: grijze meekleurende brillenglazen
-MiYOSMART Sunbird: grijze polariserende brillenglazen (juni/juli 2023)

2. Wat is de technologie achter MiYOSMART Chameleon?
'Molded Laminate Film Technology' bevindt zich onder het vooroppervlak en wordt geactiveerd door blootstelling aan de zon terwijl de optische prestaties van DIMS behouden blijven.

3. Waarom wordt het aangeboden in grijze kleur?
HOYA heeft een validatietest van het productconcept uitgevoerd voordat het product werd ontwikkeld. Het onderzoek werd uitgevoerd in China, Canada, Italië en het VK onder 800 ouders (elk 200) en 200 ECP's (elk 50). De meerderheid beschouwde grijze kleur als de meest geschikte en geprefereerde optie om te lanceren.[1]

4. Is het MiYOSMART Chameleon brillenglas dikker dan die van een helder MiYOSMART brillenglas?
De meekleurende laag verhoogt de dikte slechts met 40 micron.

5. Wat is de vermindering van de intensiteit van het licht met het MiYOSMART Chameleon brillenglas wanneer deze binnenshuis in heldere toestand is, in vergelijking met het standaard heldere MiYOSMART brillenglas?
De lichttransmissie wordt verminderd met ca. 3% in vergelijking met MiYOSMART heldere brillenglazen en minder dan 5% vermindering van lichttransmissie in vergelijking met geen brillenglazen.[2]

6. Zijn MiYOSMART zonneglazen aanvullende of primaire oplossingen?
– MiYOSMART Chameleon kan als primaire, stand-alone oplossing werken omdat het binnen en buiten kan worden gebruikt aangezien het zich snel aanpast aan het zonlicht. Op deze manier wordt myopie gecorrigeerd en de progressie ervan geremd, terwijl het kind ook wordt beschermd tegen intensief zonlicht. Het kan ook worden aangeboden als tweede paar naast MiYOSMART heldere brillenglazen, afhankelijk van de behoeften en gewoonten van het kind.
– MiYOSMART Sunbird is de ideale aanvullende oplossing voor MiYOSMART heldere brillenglazen.

7. Worden kinderen met meekleurende brillenglazen in de toekomst gevoeliger voor licht?
Er is geen bewijs dat het dragen van meekleurende glazen de lichtgevoeligheid op latere leeftijd verandert.

8. Is er extra contrastverlies door de basistint in de DIMS behandelingszone?
Aangezien de vermindering van transmissie in heldere toestand minder dan 3% is, verwachten we geen opmerkelijk contrastverlies.

9. Kunnen de klinische studiegegevens van een gemiddelde vermindering van 60% aslengtegroei worden gecommuniceerd? Wat is de verwachte impact van meekleurende brillenglazen op de werkzaamheid?
Op dit moment is er geen bewijs over hoe een vermindering van de transmissie van daglicht buitenshuis in het algemeen en specifieke golflengten van het zichtbare lichtspectrum de effectiviteit van optische behandelingsopties voor myopie beïnvloeden.[3] De vermindering van transmissie met minder dan 3% in niet-geactiveerde toestand is erg laag en wordt niet beschouwd als negatief beinvloedend.

Hoe langer optische behandelingsopties worden gedragen, hoe groter de verwachte effectiviteit van de behandeling zal zijn.[1]

De mogelijke remming van de myopie progressie door de langere draagtijd en daarmee de status van myope defocus te verlengen, zou positief kunnen worden beïnvloed door langdurige blootstelling aan daglicht wanneer de symptomen van intens zonlicht minder storend zouden zijn vanwege de ingebouwde zonbescherming.[1]

10. Is het volledige lichtspectrum niet belangrijk voor de ontwikkeling van myopie?
Het kan zijn dat het volledige zichtbare lichtspectrum, de lichtintensiteit en het gedrag van het kind van invloed zijn op de aslengte in plaats van een bepaalde golflengte zelf. De lichtintensiteit buiten is zelfs bij een bewolkte hemel of in de schaduw intensiever dan binnen. Zelfs met een zonnebril worden kinderen buiten nog steeds blootgesteld aan intenser licht dan binnen en hebben ze nog steeds het positieve effect van daglicht op bijziendheid.[4]

11. Waarom wordt momenteel aangenomen dat tijd buitenshuis doorbrengen de myopie progressie kan vertragen?
De rol van buiten zijn bij kinderen met myopie is nog onduidelijk, maar de aanbeveling is om ten minste 80 minuten per dag buiten in daglicht te verblijven.[3] De experts zeiden dat elke 45 minuten extra buiten doorbrengen 20% van het ontstaan van myopie kan voorkomen.

Het verschil in licht tussen binnen en buiten heeft te maken met lichtintensiteit, spectrale samenstelling, temporele frequentie en tijd en plaats zelf. Er wordt nog steeds nagedacht over de balans tussen binnen- en buitentaken en -activiteiten met betrekking tot het ontstaan van myopie en de progressie ervan, maar over het algemeen zijn kinderen die buiten zijn geneigd activiteiten op afstand te doen in plaats van activiteiten van dichtbij.[3]

12. Wat zijn de prestaties in de overgang van helder naar donker en van donker naar helder van MiYOSMART Chameleon?
MiYOSMART Chameleon meekleurende brillenglazen gaan in minder dan 30 seconden van helder naar 90% donker.
– De terugkleurtijd van volledige kleuring tot ongeveer 60% transmissie bedraagt 60 seconden en in 2 minuten kleuren ze terug naar maximale helderheid.[2]

13. In welke mate beschermen de glazen tegen UV?
Zowel MiYOSMART Chameleon als MiYOSMART Sunbird bieden 100% absorptie van UVA en UVB.

14. Welke coating wordt aangeboden met MiYOSMART Sun?
Dezelfde coating die wordt gebruikt voor de heldere MiYOSMART brillenglazen.

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4. Lanca C, Teo A, Vivagandan A, Htoon HM, Najjar RP, Spiegel DP, Pu SH, Saw SM. The Effects of Different Outdoor Environments, Sunglasses and Hats on Light Levels: Implications for Myopia Prevention. Transl Vis Sci Technol. 2019 Jul 18;8(4):7.

* Range of luminance transmittance for Category 2 is defined as 43 % ≥ τv > 18 % based on ISO 8980-3 (2022) standard.
** Data were obtained from tests conducted at room temperature (23 °C).

7. D.I.M.S.-onderzoeken

Clinical science

OPEN ACCESS

Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial

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ABSTRACT

Aim To determine if 'Defocus Incorporated Multiple Segments' (DIMS) spectacle lenses slow childhood myopia progression.

Methods A 2-year double-masked randomised controlled trial was carried out in 183 Chinese children aged 8–13 years, with myopia between −1.00 and −5.00 D and astigmatism ≤1.50 D. Children were randomly assigned to wear DIMS (n=93) or single vision (SV) spectacle lenses (n=90). DIMS lens incorporated multiple segments with myopic defocus of +3.50 D. Refractive error (cycloplegic autorefraction) and axial length were measured at 6month intervals.

Results 160 children completed the study, n=79 in the DIMS group and n=81 in the SV group. Average (SE) myopic progressions over 2 years were −0.41±0.06 D in the DIMS group and −0.85±0.08 D in the SV group. Mean (SE) axial elongation was 0.21±0.02 mm and 0.55±0.02 mm in the DIMS and SV groups, respectively. Myopia progressed 52% more slowly for children in the DIMS group compared with those in the SV group (mean difference −0.44±0.09 D, 95% CI −0.73 to −0.37, p<0.0001). Likewise, children in the DIMS group had less axial elongation by 62% than those in the SV group (mean difference 0.34±0.04 mm, 95% CI 0.22 to 0.37, p<0.0001). 21.5% children who wore DIMS lenses had no myopia progression over 2 years, but only 7.4% for those who wore SV lenses.

Conclusions Daily wear of the DIMS lens significantly retarded myopia progression and axial elongation in myopic children. Our results demonstrated simultaneous clear vision with constant myopic defocus can slow myopia progression.

Trial registration number NCT02206217.

INTRODUCTION

The increasing prevalence of myopia is reaching an alarmingly high level globally.[1 2] In many parts of East and Southeast Asia, as many as 70%–80% of young adults are myopic,[1–3] and as many as 20% of children are highly myopic, with refractions worse than −6 D.[2] Highly myopic eyes have higher risk of developing blinding complications such as retinal degenerations[4 5] and glaucoma.[6] It is no doubt that epidemic of myopia debilitates both at individual level and public health level.[7 8] In fact, myopia is now identified as one of immediate concerns by the WHO's Global Initiative for the Elimination of Avoidable Blindness.[8]

Several clinical interventions are currently used for slowing the progression of myopia.[9 10] A meta-analysis in efficacy comparison of different interventions for myopia control reported that pharmacological treatment is relatively more effective than optical methods using contact lenses or spectacles.[9 10] High-dose (1%) atropine[11] eye-drops are highly effective, but the associated side effects, such as photophobia and blurry vision, are not well tolerated. Lower dose (0.01%–0.1%)[12–14] atropine yields similar treatment effects with less side effects. Ideally, an intervention for myopia control should be as minimally invasive as possible, making spectacle lenses the ideal alternative option.

Animal studies have provided solid evidence that imposed myopic defocus (MD) inhibits eye growth whereas hyperopic defocus promotes eye growth.[15] Studies using chicks,[16 17] guinea pigs,[18] marmoset[19] and rhesus monkey[20] have demonstrated that myopic eye growth could be inhibited or reversed by applying MD using dual-power or multifocal lenses. Indeed, MD is likely be the key mechanism that underlies a number of current myopia control strategies, such as orthokeratology[21] and multifocal soft contact lenses.[22–24]

Several years ago, we designed a concentric dual-power soft contact lens called 'Defocus Incorporated Soft Contact' (DISC) lens for myopia control which imposes MD on both the central and peripheral retinas.[23] The clinical trial has shown the DISC lens wear significantly slowed myopia progression in schoolchildren by 25% over 2 years compared with the single vision (SV) contact lenses and 60% for a subgroup of children who have worn the lenses for more than 8 hours/day.[23] We have now designed a spectacle lens based on the MD mechanism for myopia control, and named it as Defocus Incorporated Multiple Segments (DIMS) spectacle lens. This lens provides the same optical stimulus as the DISC lens without the disadvantages inherent with contact lens wear. This study aims to investigate if the DIMS lenses can slow myopia progression in schoolchildren.

MATERIALS AND METHODS

Study design

This study was a prospective, randomised and double-masked clinical trial conducted between August 2014 and July 2017. The subjects were randomly allocated to wear either DIMS spectacle lenses (treatment group) or SV spectacle lenses

(control group). Spherical equivalent refraction (SER) and axial length (AL) were measured at baseline and every 6 months over 2 years. The changes in SER and AL between two groups were compared over the study period. Data collection and eye examinations were carried out in the Centre for Myopia Research at the Hong Kong Polytechnic University. Written assent and informed consent were obtained from the children and their parents before participation.

Subjects

Phone screening and visual screening were performed to determine whether the child met the study criteria. One hundred and eighty-three schoolchildren were recruited between August 2014 and July 2015. Inclusion criteria were:

- Hong Kong Chinese.
- 8–13 years old.
- SER: −1.00 to −5.00 dioptres (D).
- Astigmatism and anisometropia of 1.50 D or less.
- Monocular best corrected visual acuity (VA) of 0.00 logMAR (6/6) or better.
- Acceptance of random group allocation and the masked study design.

Exclusion criteria were:

- Strabismus and binocular vision abnormalities.
- Ocular and systemic abnormalities.
- Prior experience of myopia control.

Randomisation

Simple randomisation was implemented by the unmasked investigator (UI) by putting subject file numbers (1–200) in a spreadsheet of Excel (Microsoft Office) and creating a column of random numbers for the group allocation. Eligible subjects were then assigned to either group by following a random software sequence generated from Excel.

Sample size calculation

To achieve a 90% power to detect a 0.50D difference (0.70D of SD)[23] in myopia progression between two groups with an alpha level of 0.01 (2-tailed); the minimum subject number required in each group was 59. Assuming a dropout rate of about 15%, at least 70 subjects were required in each group.

Intervention and control

The children in the treatment group wore the DIMS spectacle lenses while those in the control group wore ordinary SV spectacle lenses.

The DIMS lens is a custom-made plastic spectacle lens. It comprises a central optical zone (9 mm in diameter) for correcting distance refractive errors, and an annular multiple focal zone with multiple segments (33 mm in diameter) having a relative positive power (+3.50 D) (figure 1). The diameter of each segment is 1.03 mm. This design simultaneously introduces MD and provides clear vision for the wearer at all viewing distances. There are multiple foci from MD at a plane in front of the retina, which would be received as blur images on the retina.

The final distance prescription was determined by the UI using cycloplegic subjective refraction measured by the masked investigator (MI). The lenses were replaced with an updated prescription when the change of SER was more than 0.50 D.

Masking and wear compliance

We adopted the same study protocol in our previous randomised controlled trials using progressive addition lenses[25] and the DISC lenses.[23] The UI was responsible for group allocation, spectacle-dispensing work, measuring visual performance of lenses, record keeping, data entry and compliance checking. The MI was responsible for refraction and related eye data measurement. Both the children and their parents were masked to group allocation until data analysis was completed. The masking procedures fulfilled the Consolidated Standards of Reporting Trials requirements.[26] Prior to the data measurement by MI, the spectacles were removed from the children by the UI.

At spectacles delivery, the children were instructed to wear the spectacles in full-time mode, except during sleeping and taking shower. Wear compliance was monitored and checked by phone calls and questionnaires.

Outcome variables

Refraction and AL under cycloplegia were measured at baseline and at 6-month intervals for 2 years. The primary outcome was myopia progression, which was the difference between the mean cycloplegic SER at the baseline and subsequent 6-month visits for 24 months. The secondary outcome was the change of AL,

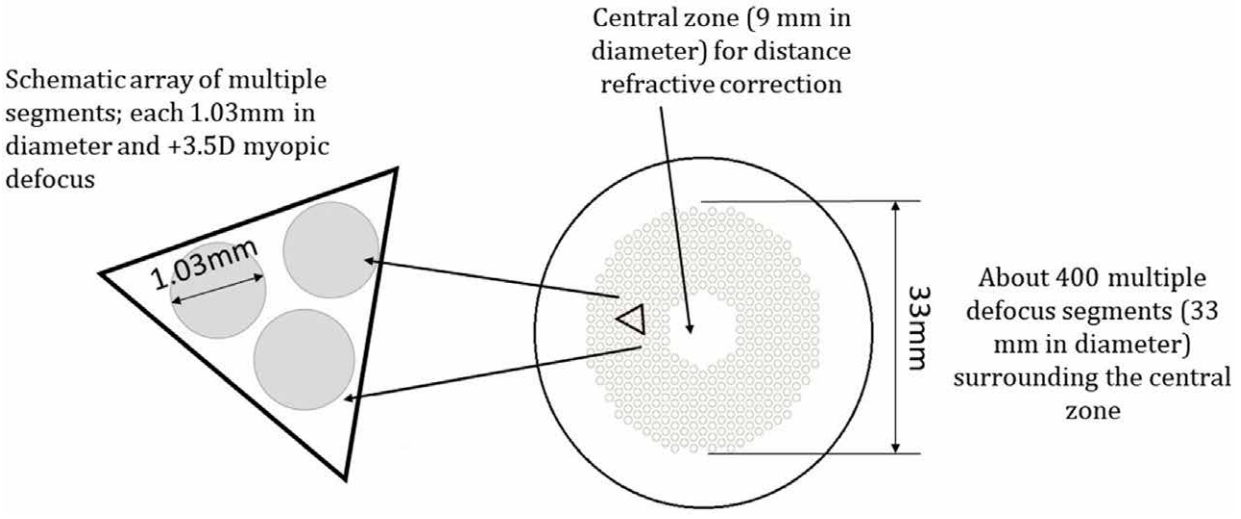

Figure 1 The design of the Defocus Incorporated Multiple Segments (DIMS) spectacle lens.

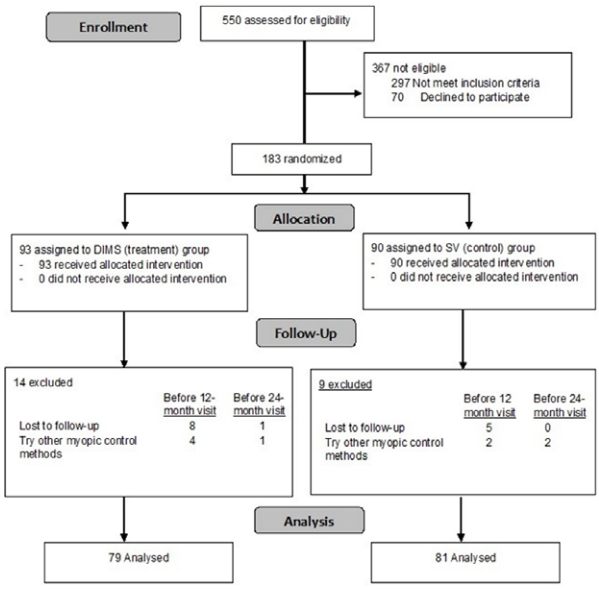

Figure 2 A flow diagram of the study design. DIMS, Defocus Incorporated Multiple Segments spectacle lens; SV, single vision spectacle lens.

which was the difference between the mean AL at the baseline and subsequent 6-month visits for 24 months.

One drop of Alcaine 0.5% followed by one to two drops of cyclopentolate HCL 1% were instilled to induce cycloplegia. Cycloplegia was confirmed by measuring the amplitude of accommodation using push-up method when accommodation was 2 D or less. Cycloplegic refraction was measured with an open-field autorefractor (Shin-Nippon NVision-K5001). AL was measured by partial coherence interferometry IOL Master (Carl Zeiss). Average of five measurements of autorefraction and AL for each eye were obtained for analysis.

Other measurements at each follow-up

Other outcomes such as distance and near VA, near phoria and accommodation lag were measured when the children were wearing full correction of distance at each 6-month follow-up.

Visual performance with the experimental lenses was also assessed. Distance and near VA, accommodation, phoria and stereopsis were measured when the subjects collected their spectacles. Vision quality, comfort and frequency of visual symptoms with lens wear were graded by the subjects themselves through questionnaires (online supplementary methods). Data between the two groups were compared.

Statistical analysis

There were no statistically significant differences between data from two eyes, only data of right eyes were used for analyses. Unpaired t-tests were used to compare baseline characteristics between groups when normality assumptions were preserved. Otherwise, Mann-Whitney U test for continuous data and the χ^2 test for categorical data were used.

Myopia progression over 2 years was calculated as the difference between SER at the baseline and the 2-year visits. For the subjects completed the study, the changes in SER and AL between two groups were compared using unpaired t-tests. The efficacy of myopia control of DIMS lens (%) was determined by dividing the difference in myopia progression (or axial elongation) between two groups with the myopia progression (or axial elongation) in the SV group, then multiplied by 100%.

Data analysis also followed the intention-to-treated approach for the subjects lost to follow-up. Generalised estimating equations (GEE) were adopted for handling missing data. GEE, with one within-subject factor (time), one between-subject factor (group: DIMS or SV) and their interactions, was used to determine the treatment effect on two main outcomes adjusted for some covariates. These covariates included age, gender, baseline refractive error, near phoria, lag of accommodation, number of myopic parents, time spent on near works and outdoor activities. The significant covariates ($p<0.05$) were tested for their correlation with the changes of SER and AL independently using Pearson correlation analysis.

RESULTS

Subject profile

Figure 2 is a flow diagram illustrating the number of subjects recruited, enrolled and dropped out. One hundred and eighty-three eligible schoolchildren participated and were randomly allocated to the DIMS group (n=93) and the SV group (n=90). One hundred and sixty subjects successfully completed the study: 79 (85%) children in the treatment group and 81 (90%) in the control group. The dropout rate was slightly higher in the treatment group (15%) than the control group (10%) (online supplementary eTables 1 and 2). Fourteen out of 23 children dropped out early soon after the baseline data collection.

Both groups showed an overall good compliance and could wear the spectacles full time. The mean daily lens-wearing time in the DIMS group and SV group was 15.5±2.6 and 15.3±2.1 hours, respectively, and was not significantly different.

Baseline characteristics

There were no statistically significant differences between the DIMS and SV groups in the baseline characteristics ($p>0.05$) (table 1). The mean initial myopia in the DIMS and SV groups was −2.93±1.04 D and −2.70±0.98 D, respectively. The mean initial AL was 24.85±1.59 mm and 24.72±1.30 mm in the DIMS and SV groups, respectively.

Changes in the refraction and AL

Completed subjects

For subjects who completed the 2-year trial (table 2), the mean myopia progression (SE) over 2 years in the DIMS group (n=79) and the SV group (n=81) was −0.38±0.06 D and −0.93±0.06 D, respectively. The total increase in AL was 0.21±0.02 mm and 0.53±0.03 mm, respectively. Schoolchildren wearing DIMS lenses had myopia progression significantly reduced by 59% (mean difference −0.55±0.09 D, $p<0.0001$) and axial elongation decreased by 60% (mean difference 0.32±0.04 mm, $p<0.0001$) compared with those wearing SV lenses.

All enrolled subjects

Changes in SER

The mean myopia progression over 2 years in the DIMS group (n=93) and the SV group (n=90) was −0.38±0.06 D and −0.85±0.08 D, respectively. Children wearing DIMS lenses had significantly less myopia progression by 55% (mean difference −0.47±0.09 D, $p<0.0001$).

The tests of model effect (online supplementary eTable 3) indicated that group, time and age ($p<0.05$) had significant association with the magnitude of myopia progression. After model

Table 1 Baseline demographics data of all and the completed subjects

Baseline demographic data, mean (SD)	Mean (SD)			
	All		Completed	
	DIMS (n=93)	SV (n=90)	DIMS (n=79)	SV (n=81)
Age at enrolment (years)	10.19±1.46	10.01±1.44	10.20±1.47	10.00±1.45
Gender				
Male, % (n)	59.1 (55)	55.6 (50)	58.2 (46)	54.3 (44)
Female, % (n)	40.9 (38)	44.4 (40)	41.8 (33)	45.7 (37)
Cycloplegic autorefraction in SER (D)	−2.93±1.04	−2.70±0.98	−2.97±0.97	−2.76±0.96
Axial length (mm)	24.85±1.59	24.72±1.30	24.70±0.82	24.60±0.83
Corneal power at steep meridian (D)	44.46±1.67	44.39±1.69	44.5±1.61	44.5±1.65
Corneal power at flat meridian (D)	43.14±1.41	43.09±1.45	43.2±1.41	43.2±1.44
Near phoria, Δ	−1.96±3.93	−0.98±3.53	−2.16±4.07	−0.15±3.28
Accommodation lag (D)	0.97±0.49	1.06±0.40	0.98±0.42	1.04±0.35
Myopics parents, n				
0	3	6	2	5
1	22	23	18	20
2	68	61	59	56

Δ, prism dioptres; AL, axial length; D, dioptres;DIMS, Defocus Incorporated Multiple Segments spectacle lens; SER, spherical equivalent refraction; SV, single vision spectacle lens.

adjustment, the mean myopia progressions were −0.41±0.06 D in the DIMS group and −0.85±0.08 D in the SV group (online supplementary eTable 4). Children wearing DIMS lenses had significantly less myopia progression by 52% (mean difference −0.44±0.09 D, p<0.0001). Controlling for covariates did not greatly change the treatment effect compared with the unadjusted means. The DIMS lens had the greatest effect on slowing myopia progression in the first 6 months, after that, the magnitude slightly decreased at 12-month visit and was sustained to the 24-month visits (figure 3).

For Pearson correlation analysis, the changes in SER significantly correlated (r^2=0.22, p<0.001) with subject's age in the DIMS group (online supplementary eFigure 1). Myopia progression was slightly slower in older children who wore DIMS lenses. In SV group, no significant correlation was found (r^2=0.04, p>0.05).

Table 2 Changes in the cycloplegic spherical equivalent refraction and axial length (from baseline) in the DIMS and the SV groups

	DIMS (n=79)	SV (n=81)	Mean difference (SE)
Time/visit	SER changes in dioptres, mean (SE)		
6 months	−0.13±0.03	−0.37±0.04	−0.24±0.05*
12 months	−0.17±0.05	−0.55±0.04	−0.38±0.07*
18 months	−0.31±0.06	−0.72±0.05	−0.42±0.08*
24 months	−0.38±0.06	−0.93±0.06	−0.55±0.09*
Time/visit	Changes in AL (mm), mean (SE)		
6 months	0.03±0.01	0.20±0.01	0.16±0.02*
12 months	0.11±0.02	0.32±0.02	0.21±0.02*
18 months	0.15±0.02	0.43±0.02	0.27±0.03*
24 months	0.21±0.02	0.53±0.03	0.32±0.04*

*Statistically significant difference between two experimental groups (unpaired t-tests, p<0.0001).
Δ, prism dioptres;D, dioptres;DIMS, Defocus Incorporated Multiple Segments spectacle lens; SER, spherical equivalent refraction; SV, single vision spectacle lens.

Changes in AL

The total increase in AL over 2 years was 0.21±0.02 mm and 0.56±0.02 mm in the DIMS and SV groups, respectively. The DIMS lenses significantly slowed axial elongation by 63% (mean difference 0.35 (0.04) mm, p<0.0001) as compared with the SV lenses. Group, time and age were found to be associated with AL changes. Model-adjusted mean changes in AL±SE were 0.21±0.02 mm and 0.55±0.02 mm in the DIMS and SV groups, respectively. The DIMS lens showed a significant effect on slowing axial elongation by 62% (mean difference 0.34±0.03 mm, p<0.0001).

For individual subjects

Seventeen (21.5%) out of 79 children wearing DIMS lenses had no myopia progression over 2 years (online supplementary eFigure 2), which was higher than the SV group (6 of 81, 7%). Likewise, 14% of the children wearing DIMS lenses had no axial elongation whereas all children in the SV group had axial elongation (online supplementary eFigure 3).

Visual performance with lens wear

There were no statistically significant differences between the two lens types in influencing VA and accommodation (unpaired t-test, p>0.05) (online supplementary eTable 5), except stereoacuity (p=0.04). However, the mean difference was only 5 s of arc, which is not clinically significant.

DISCUSSION

Children wearing the DIMS spectacle lenses had myopia progression significantly reduced by 52% and axial elongation by 62%

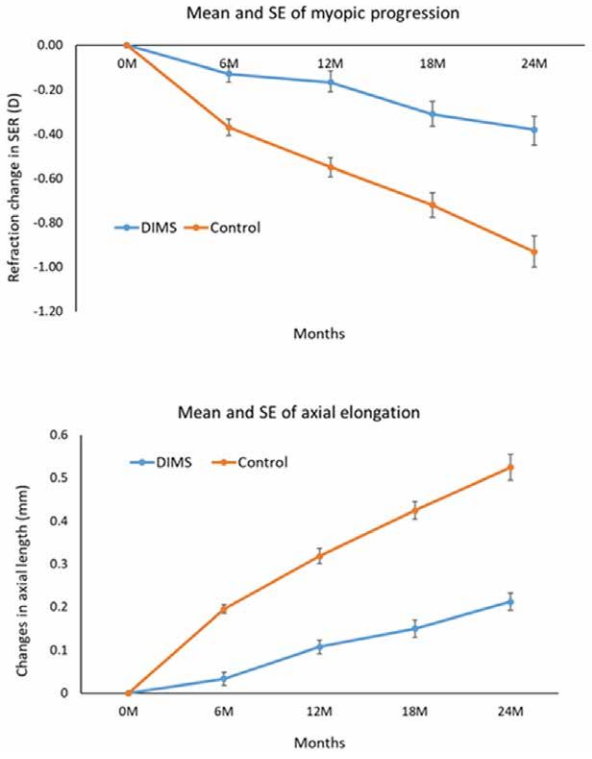

Figure 3 Model-adjusted mean and SE of myopia progression and axial length from baseline to 24 months. DIMS, Defocus Incorporated Multiple Segments; SER, spherical equivalent refraction.

over 2 years when compared with those wearing SV lenses. The greatest treatment effect was observed during the first 6 months of lens wear. It was due to the higher myopia progression in the SV group during this time, otherwise the treatment effect was quite consistent over the 2 years (figure 3, online supplementary eTable 4). The treatment effect with the DIMS lens was similar to that achieved with 6–8 hours daily wear of DISC lens, at around 50%–60%.[23] These findings are consistent with our previous animal studies[17 18] and the clinical trial of the DISC lens,[22] that the principle of employing MD does retard eye growth and myopia progression.

The DIMS lens design showed much better effect on slowing childhood myopia progression than existing progressive addition lenses (10%–35%),[25 27–31] spectacle lens with peripheral defocus[32] and contact lens[33] (34%) designed for reducing relative peripheral hyperopia (online supplementary eTable 6). The efficacy of myopia control is comparable to those of orthokeratology (60%),[10 21] prismatic bifocal spectacle lenses (about 50%)[34] and bifocal soft contact lenses (50%–60%)[10 23 35] and relatively less when compared with high and low-dose atropine (70+%).[11–14]

The DIMS lenses have slowed myopia progression, and have stopped myopia progression in some children (online supplementary eFigures 2 and 3). 21.5% of children in the DIMS group had no myopia progression over 2 years whereas only 7.4% in the control group. About 13% of children in the DIMS group still showed considerable progression in terms of refraction (>1 D). Such variations in retardation effect have been observed with prismatic bifocal spectacles, Cheng *et al*[34] showed that prismatic bifocals were more effective in the children with low accommodative lag. Also, they found that age, initial myopia and parental myopia were associated with the treatment effect. In contrast, in our study the magnitude of treatment effect was not dependent on lag of accommodation, initial myopia nor parental myopia.

Analysis of model effects indicated that age was the only associated factor that exhibited significant effect on myopia progression, and the effect of myopia control with DIMS lenses was greater in older children (aged 10–13) (online supplementary eFigure 1). About 80% of the DIMS wearers who had considerable myopia progression were younger children aged 8–9 years. We speculate that variations in treatment effect of the DIMS lenses may be due to different retinal profile or peripheral refraction among the children.[36] If there is a high amount of peripheral hyperopia, the amount of effective MD at the peripheral retina will be less, and thereby minimising the treatment effect.

In our previous study, wearing time was found to be a significant factor in determining the treatment effect of DISC lenses.[23] No such correlation was found in the present study. This is probably a result of the overall higher compliance, that the subjects were able to wear their assigned spectacle lenses constantly, with over 15 hours/day. The dropout rate in this study was much lower (13%) than that in our previous study using the DISC lenses (42%).[23]

The findings of visual performance (online supplementary eTable 5 and eFigure 4) showed that the DIMS lens could provide good vision at distance and near comparable to conventional SV spectacle lenses. Although some subjects initially noticed the slight blurriness at the mid-peripheral field, they fully adapted to the lenses in a few days. The symptoms (score below 2) such as ghost image, dizziness and headache seldom occurred during DIMS lens wear (online supplementary eFigure 5). No treatment-related adverse event was reported.

The current report includes only the first 2-year result, when the third year of the study is ongoing. Also, the current study is limited to Chinese children, further study will be needed to determine the treatment effect of the DIMS lenses in other ethnic populations. DIMS and SV lens could hardly be differentiated by their appearance unless the lens was tilted and the multiple segments may be observed from the reflection of a light source. Most children were not aware of the multiple segments features. A few children in the treatment group might recognise the multiple segments but they had no particular difficulties in using the lens as their previous spectacle lenses. Nevertheless, the study could not be totally masked for some subjects. Our study did not include children with over −5 D of myopia. The retardation effect on myopia progression in high myopes was yet to be determined. Further investigation is also required, in particular, to determine its optimal effectiveness in preventing myopia progression and incidence.

CONCLUSIONS

Daily wear of the DIMS lens significantly slowed myopia progression and axial elongation in myopic schoolchildren as compared with wearing SV spectacle lenses. They provided good vision while presenting simultaneous MD to the eyes. This intervention is simple to use and is the least invasive method compared with pharmacological or contact lens treatments. The DIMS spectacle lens offers an alternative treatment modality for myopia control.

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Contributors All the authors listed have been involved in the undertaking of the clinical trial with emphasis on various aspects, from the conception of the lens design, fabrication of the lens and registration of the clinical trial and preparation of clinical protocol to data collection and analysis, interpretation and conclusions. A few manuscripts are now in preparation by the author team.

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Competing interests None. Patents titled 'Spectacle Lens' in China (CN104678572 B) and in USA (US10268050 B2) were issued on 27 April 2018 and 23 April 2019 respectively.

Patient consent for publication Not required.

Ethics approval All aspects of the study met the tenets of the Declaration of Helsinki and were approved by the Human Subjects Ethics Subcommittee of the Hong Kong Polytechnic University.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data are available upon request.

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Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: results of a 3-year follow-up study

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ABSTRACT

Aims To determine myopia progression in children who continued to wear the defocus incorporated multiple segments (DIMS) lenses or switched from single vision (SV) to DIMS lenses for a 1-year period following a 2-year myopia control trial.

Methods 128 children participated in this study. The children who had worn DIMS lenses continued to wear DIMS lenses (DIMS group), and children who had worn SV lenses switched to wear DIMS lenses (Control-to-DIMS group). Cycloplegic spherical equivalent refraction (SER) and axial length (AL) were measured at 6-month interval. Historical controls were age matched to the DIMS group at 24 months and used for comparing the third-year changes.

Results Over 3 years, SER and AL changes in the DIMS group (n=65) were −0.52±0.69D and 0.31±0.26 mm; these changes were not statistically significant over time (repeated measures analysis of variance, p>0.05). SER (−0.04±0. 38D) and AL (0.08±0.12 mm) changes in the Control-to-DIMS group (n=55) in the third year were less compared with the first (mean difference=0.45 ± 0.30D, 0.21±0.11 mm, p<0.001) and second (0.34±0.30D, 0.12±0.10 mm, p<0.001) years. Changes in SER and AL in both groups over that period were significantly less than in the historical control group (DIMS vs historical control: mean difference=−0.18±0.42D, p=0.012; 0.08±0.15 mm, p=0.001; Control-to-DIMS versus historical control: adjusted mean differences=−0.30±0.42D, p<0.001; 0.12±0.16 mm, p<0.001).

Conclusions Myopia control effect was sustained in the third year in children who had used the DIMS spectacles in the previous 2 years and was also shown in the children switching from SV to DIMS lenses.

INTRODUCTION

The prevalence of myopia is growing alarmingly worldwide, especially in East Asian populations.[1–3] High myopia is associated with an increased risk of sight-threatening eye disease[4–6] creating a long-term burden on economies and public healthcare.[7 8] There is no doubt that myopia is a significant public health issue and a global concern.[8] Effective interventions for myopia management and reduction would alleviate this problem.

Currently, a variety of modalities are used for myopia control in children.[9–11] High-dose (1%) atropine eye-drops seem the most effective in myopia control, but the associated side effects, such as photophobia and blurred near vision, hinder its wide clinical application.[12] In recent years, some studies have reported that low-dose (0.01%) atropine treatment has yielded positive results with minimal side effects and low myopic rebound.[13–15] Optical treatments, including orthokeratology,[16–18] executive top bifocal spectacles[19] and multifocal soft contact lenses incorporating myopic defocus[20–24] have also shown promising results in slowing myopia progression. However, each method has limitations.[11]

The defocus incorporated multiple segments (DIMS) spectacle lens is designed to control myopia in children, based on the principle of myopic defocus and simultaneous vision. It is a dual-focus spectacle lens consisting of a central optical zone for correcting distance refractive error, and a batch of tiny circular segments with a relative positive power of 3.50D equally distributed throughout the mid-peripheral area in a honeycomb pattern.[25] Thus, the DIMS lens imposes myopic defocus while providing clear vision for the wearer simultaneously at all viewing distances. A 2-year double-masked randomised controlled trial (RCT) (ClinicalTrials.gov: NCT02206217) showed that DIMS lens wear slowed childhood adjusted myopia progression significantly by 52% and axial elongation by 62% compared with regular single vision (SV) spectacle lenses wear over 2 years.[25]

Our aims here are to determine (1) if myopia retardation (as measured by changes in spherical equivalent refraction (SER) and AL) continues in the third year of DIMS wear and (2) if myopia retardation is exhibited in the first year of DIMS wear by the original SV control group; both groups will be compared with a new historical control group.

MATERIALS AND METHODS

Study participants

Ethnic Chinese children who had completed the 2-year RCT[25] (NCT02206217, between August 2014 and July 2017) were invited to participate in this third-year follow-up study. Written assent and informed consent were obtained from the children and their parents respectively before participation.

Children who had worn DIMS lenses in the RCT continued to wear DIMS lenses in the third year (DIMS group). The children in the original control group were offered the DIMS treatment

and this gave us the opportunity to evaluate if the DIMS lenses could provide myopia control in the Control-to-DIMS group similar to that observed in the original DIMS group.

Study procedures and data collection

The primary and secondary outcomes were the changes in SER and axial length (AL). The procedures of data measurement followed those in the trial of DIMS lenses.[25] SER and AL were measured at 6-month intervals. SER was measured by cycloplegic autorefraction using an open-field autorefractor (Shin-Nippon NVision-K5001, Ajinomoto Trading Inc.). AL was measured by partial coherence interferometry using an IOL Master (Carl Zeiss Meditec). Cycloplegia was induced by instillation of one drop of alcaine 0.5%, followed by one to two drops of cyclopentolate HCL 1%. The measurements were taken 30 min after the instillation of eye drops, and cycloplegia was considered achieved when the amplitude of accommodation was less than 2.00D as measured using an RAF rule. An average of five autorefractions and AL measurements for each eye was used for data analysis.

The historical control group

Since the children originally in the control group switched to wear DIMS lenses in the third year, they could not be used as the 'control' to assess effectiveness on myopia control. Therefore, we obtained a historical control group by reviewing clinical records from the Optometry Clinic, PolyU for 2017–2019. The criteria for selection were based on the inclusion and exclusion criteria in the original RCT. Subjects were healthy myopic ethnic Chinese children who attended eye examinations in the clinic with at least 12-month follow-up data. They had not received any myopia interventions and were matched for age (between 10 and 15 years) and SER ranges (−1.00 to −5.50D) with the DIMS subjects at the end of the 2-year RCT. Annual myopia progression and AL changes in this group of children were calculated and compared with the third-year changes in the DIMS and Control-to-DIMS groups.

Statistical analysis

All statistical analyses were performed using SPSS V.20.0. Baseline characteristics and the changes in SER and AL are presented as mean±SD. The right eye data only were used for analysis as there was no statistically significant difference between the left and the right eye data.

Following Kolmogorov-Smirnov tests for distribution, unpaired t-tests, Mann-Whitney U tests or repeated measures analysis of variance (ANOVA) tests were used as appropriate. Pearson's correlation coefficient analyses were used to determine relationships between continuous variables and χ^2 tests for categorical data.

For both the DIMS group and Control-to-DIMS group, myopia progression and changes in AL in years 1, 2 and 3 were calculated and compared by repeated measures ANOVA and post hoc pairwise comparisons using Bonferroni corrections were performed for determining where the differences laid. Myopia progression and change in AL were calculated for the historical control group, for which we had one (12 months) set of data, and were compared with the third-year changes of two experimental groups by multiple linear regression approach with adjusting confounding covariates, such as age, sex, SER and AL.

RESULTS

Subject profile and baseline data

Figure 1 shows the number of subjects recruited and those lost to follow-up over 3 years. One hundred and sixty Chinese children completed the 2-year RCT and 128 of these agreed to participate in the third-year study. We compared the data between the subjects who joined and those who declined to join the third-year study for both the DIMS and Control-to-DIMS groups. No significant differences were found in terms of their age, gender, baseline myopia or AL, myopia progression or axial elongation in the previous 2-year trial ($p>0.05$) (online supplemental eTable 1).

At the end of the third year, 120 children (DIMS, n=65; Control-to-DIMS, n=55) completed the data collection. The mean age at enrolment (mean±SD) was 10.15±1.52 years and 10.24±1.42 years in the DIMS and the Control-to-DIMS groups, respectively. The baseline SER of the DIMS group and the Control-to-DIMS were −2.98±0.96D and −2.73±0.99D, respectively. The baseline AL of the DIMS and the Control-to-DIMS were 24.68±0.82 mm and 24.57±0.88 mm. There were no statistically significant differences between the two groups with respect to age at enrolment, gender proportion, baseline myopia or baseline AL ($p>0.05$).

Changes in SER and AL

Figure 2A and table 1 present the mean and cumulative changes in mean SER and AL from baseline to 36 months in both groups. Figure 2B shows the trend in changes in SER and AL changes in the third year.

The DIMS group

The mean changes in SER and AL in the DIMS group (n=65) were −0.52± 0.69D and 0.31± 0.26 mm over 3 years (table 1). The myopia progression and axial elongation did not change significantly

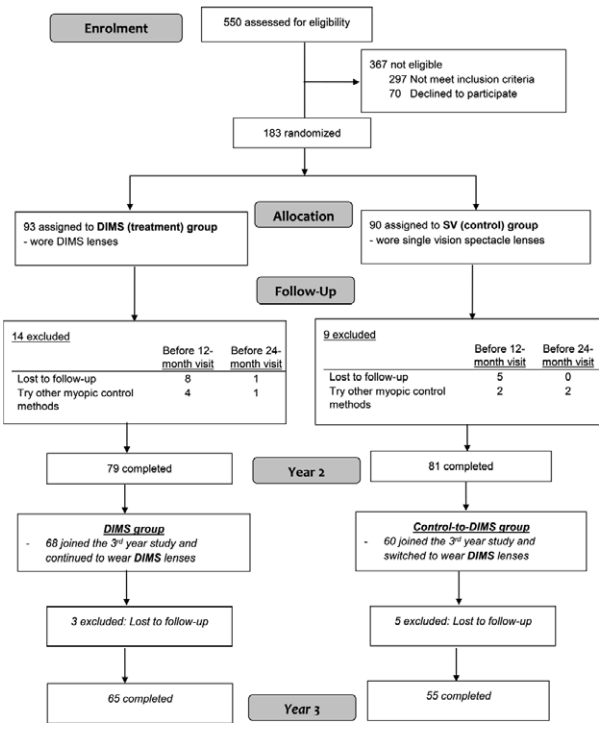

Figure 1 Subject numbers over 3 years. DIMS, defocus incorporated multiple segments; SV, single vision.

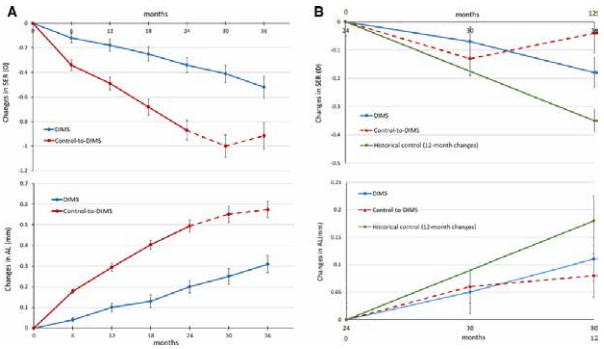

Figure 2 (A) Changes in spherical equivalent refraction (SER) and axial length (AL) from baseline to 36 months. The red dotted line represents the period (24–36 months) during which the previous single vision control group wore defocus incorporated multiple segments (DIMS) lenses. (B) The third-year changes in SER and AL in the DIMS and Control-to-DIMS groups. The green line shows the 12-month changes in SER and AL in the historical control group.

over time (repeated measures ANOVA, p>0.05). The mean annual changes in SER and AL in the DIMS group were −0.18± 0.25D and 0.10± 0.09 mm over 3 years.

The Control-to-DIMS group

In the Control-to-DIMS group (n=55), myopia progression and axial elongation were significantly different between the 3 years (repeated measures ANOVA, p<0.001). Post hoc analyses indicated that their myopia progression and axial elongation in the third year were significantly decreased compared with the first (mean difference=0.45±0.30D, 0.21±0.11 mm, p<0.001) and second years (mean difference=0.34±0.30D, 0.12± 0.10 mm, p<0.001) (figure 2A).

Table 1 Mean and cumulative changes in the cycloplegic SER and AL from baseline to 36 months in the DIMS group and Control-to-DIMS group

	Mean±SD			
	DIMS (n=65)	Control-to-DIMS (n=55)	DIMS (n=65)	Control-to-DIMS (n=55)
Time (months)	SER (D)		Changes in SER (D)	
0	−2.98±0.96	−2.73±0.99	–	–
6	−3.10±0.97	−3.07±1.02	−0.12±0.30	−0.34±0.33
12	−3.16±0.97	−3.22±1.08	−0.18±0.37	−0.49±0.40
18	−3.23±0.96	−3.41±1.09	−0.25±0.50	−0.68±0.52
24	−3.32±1.00	−3.61±1.15	−0.34±0.52	−0.87±0.59
30	−3.39±1.01	−3.73±1.23	−0.41±0.58	−1.00±0.67
36	−3.50±1.08	−3.65±1.34	−0.52±0.69	−0.92±0.81
Time (months)	AL (mm)		Changes in AL (mm)	
0	24.68±0.82	24.57±0.88	–	–
6	24.72±0.81	24.75±0.89	0.04±0.10	0.18±0.09
12	24.78±0.81	24.86±0.91	0.10±0.14	0.29±0.14
18	24.81±0.81	24.97±0.93	0.13±0.18	0.40±0.18
24	24.88±0.80	25.06±0.96	0.20±0.21	0.49±0.24
30	24.93±0.79	25.12±0.99	0.25±0.24	0.55±0.27
36	24.99±0.80	25.14±1.01	0.31±0.26	0.57±0.33

The grey blocks indicate the period of wearing DIMS lenses in the Control-to-DIMS group.
AL, axial length; Control-to-DIMS, subjects wore single vision spectacle lens during the 2-year randomised controlled trial and switched to wear DIMS lens; D, dioptres; DIMS, defocus incorporated multiple segments; SER, spherical equivalent refraction.

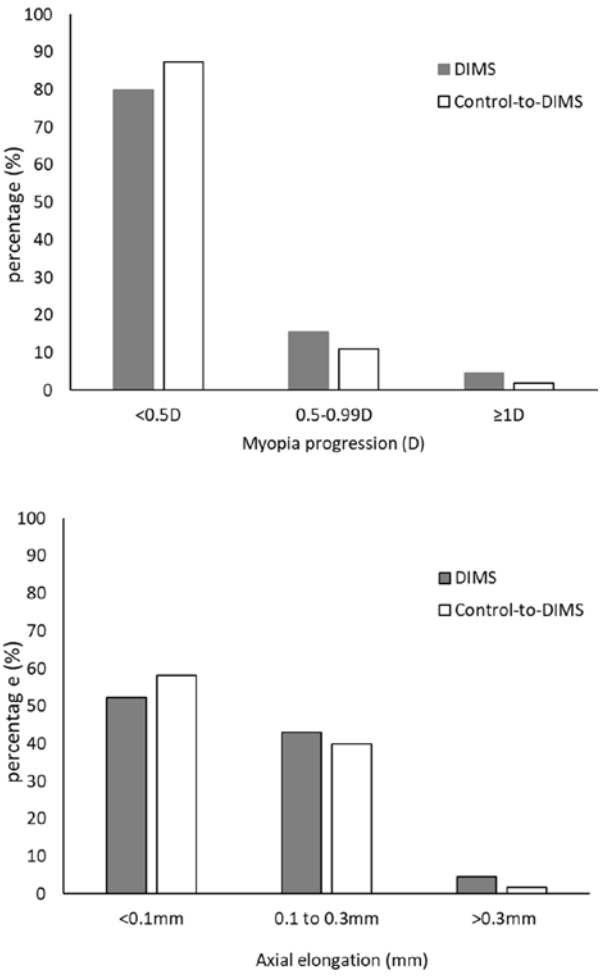

Figure 3 Distributions of myopia progression and axial elongation in the third year. DIMS, defocus incorporated multiple segments.

DIMS compared with Control-to-DIMS in SER and AL changes

There were no statistically significant differences in myopia progression and axial elongation in the third year between the Control-to-DIMS group and the DIMS group ((p>0.05) (figure 2B).

The myopia of 80% of the subjects in the DIMS group progressed by less than 0.5D in the third year, compared with 87% in the Control-to-DIMS group. Only 5% and 2% in the DIMS and Control-to-DIMS groups, respectively, had myopia progression more than 1D. 52% and 58% in the DIMS and Control-to-DIMS groups had axial elongation less than 0.1 mm (figure 3).

DIMS compared with the historical control group in SER and AL changes

The historical control group (n=76, 39 males and 37 females) had a mean age of 12.19±0.71 years, baseline SER and AL were −2.93± 1.33D and 24.77± 0.91 mm. Baseline characteristics of the historical control group did not differ statistically significantly from those of DIMS groups at 24 months (p>0.05) (online supplemental eTable 2).

The 12-month changes in SER and AL in the historical control group were −0.35± 0.40D and 0.18± 0.14 mm. The myopia progression in the DIMS group in the third year was significantly less than in the historical control group (mean difference=−0.18±0.42D, p=0.012). Axial elongation in the DIMS group was also less than in the historical control group (mean differences=0.08±0.15 mm, p=0.001).

Control-to-DIMS compared with the historical control group in SER and AL changes

There were no significant differences between the baseline data of the historical control group and the 24-month data in the Control-to-DIMS group, in terms of age, sex or AL, however, SER was significantly less in the historical control group than in the Control-to-DIMS group (p=0.003), the historical control group having been matched to the DIMS group (online supplemental eTable 3).

The children in the Control-to-DIMS group switched to wear DIMS spectacles in the third year. After adjusting for baseline SER, their myopia progression over that period was significantly slower than in the historical control group (mean differences=−0.30±0.42D, p<0.001). A similar result was found in the AL changes after controlling the cofounding factor (mean differences=0.12±0.16 mm, p<0.001).

DISCUSSION

Myopia progression and axial elongation were less in the subjects wearing DIMS lenses throughout the 3 years, first compared with the initial control group (which subsequently became the Control-to-DIMS group), and then in the last 12 months compared with the historical control group. In the DIMS group, myopia progression and axial elongation in the third year were similar to those in the first and second years (figure 2A—blue line).

Overall myopia progression

The mean changes in SER and AL in the DIMS treatment group over the 3-year period were −0.52±0.69D and 0.31±0.26 mm. These findings are comparable with the corresponding findings in the 3-year trial with dual power contact lenses by Chamberlain *et al*[24] (-0.51±0.64D and 0.30±0.27 mm) and the 3-year trial with multifocal soft contact lenses by Walline *et al*[26] (-0.60D, range −0.72 to −0.47D and 0.39 mm, range 0.32–0.46 mm). Our progression findings were nearly 50% less than reported by Cheng *et al*[19] in a 3-year trial with bifocal and prismatic bifocal spectacle lenses which included subjects with fast myopia progression (−1.25±0.10D for the bifocal treatment group, and −1.01±0.13D for the prismatic bifocal treatment group).

Myopia retardation in DIMS and Control-to-DIMS groups

The mean changes in SER and AL in the DIMS group were −0.18±0.37D and 0.10±0.14 mm in the first year and, −0.17±0.31D and 0.10±0.11 mm in the second year. In the first 2 years, myopia progression and axial elongation in the DIMS group were retarded by 0.53D and 0.29 mm compared with the original control group.

The mean annual SER and AL changes in the historical control group aged from 10 to 15 years were −0.35D and 0.18 mm; when compared with the DIMS group's third year changes in SER and AL, myopia progression and axial elongation in the DIMS group were retarded by 0.18D and 0.08 mm, respectively (figure 2B). The overall 3 years control effect in the DIMS group would be myopia retardation by 0.71D and AL decrease by 0.37 mm.

Cheng *et al*[19] reported that in a selected group of fast progressing myopic children wearing executive top bifocal spectacles with and without prisms, lowered myopia progression by 0.81D and 1.05D compared with SV spectacle lenses wearing children. Chamberlain *et al*[24] showed that a dual power soft contact lens significantly slowed myopia progression by 0.73D in children of various ethnicity aged 8–12 years. Walline *et al* reported in their BLINK clinical trial that children wearing high add power (+2.50D) multifocal contact lenses had 0.46D less myopia progression over 3 years.[26] The reduction of myopia progression by the wearing of DIMS lenses is comparable to the findings from these studies using bifocals, dual focus and multifocal soft contact lenses.

The subjects in the Control-to-DIMS group showed significant reductions in myopia progression and axial elongation after switching from SV to DIMS lenses wear (figure 2B). Their changes in SER and AL in the third year were comparable to the first-year changes in the DIMS group, even though these subjects were 2 years older. In comparison to the historical control group, their myopia progression and axial elongation in the third year, after adjustment were reduced by 86% and 61%, respectively.

In the third year, more than 80% of the Control-to-DIMS children had myopia progression less than 0.5D, and approximately 70% showed progression less than 0.25D. All these findings suggested that the myopia control effect was achieved even though the subjects started to wear DIMS lenses at an older age.

Limitations

A limitation of this study was that the cohort used in the analyses comprised the DIMS plus the Control-to-DIMS groups of children so that the study was no longer randomised. This follow-up study, however, did benefit from the comparison of the third-year myopia progression findings in the DIMS group with the Control-to-DIMS group. While there were no statistically significant differences between the DIMS group and the historical control group at the start of the third year, there was a statistically significant difference in SER between the historical control group and the Control-to-DIMS group at baseline. This was because the historical control group was matched with the DIMS group at 24 months for age and SER and as the Control-to-DIMS group had no treatment in the first 2 years it could be expected to have more myopic SER. Although adjustment was made in the comparison, this approach does not eliminate the effect that can result from known or unknown factors, such as different examiners, the number of myopic parents and time spent on near and outdoor activities, and potentially could lead to selection bias for estimating the treatment efficacy of the DIMS lens.

CONCLUSIONS

The DIMS spectacle lens slowed myopia progression and axial elongation in children throughout the 3 years of study and the myopia control effect was also demonstrated in the Control-to-DIMS group. These findings provided further evidence that DIMS lenses slowed myopia progression and axial elongation in children. The optimal age at which treatment should commence is still to be determined and further monitoring is required to ascertain the treatment effect over a longer period. We also plan to follow up on those children who discontinued wearing the DIMS lenses to determine if rebound occurs.

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Contributors Writing—Original Draft: CSYL, WCT; Writing—Review and Editing: CSYL, WCT, PHL; Conceptualisation: CHT, CSYL, HQ; Project administration: CSYL, CHT, KH; Investigation: WCT, HYZ; Methodology: CSYL, CHT, WCT; Visualisation: CSYL, CHT, WCT. All the authors listed have been involved in the undertaking of the clinical trial and follow up study including the conception of the lens design, fabrication of the lens, registration of the clinical trial, preparation of clinical protocol, data collection and analysis, interpretation of the findings and conclusions. A number of manuscripts are now in preparation by the author team.

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Patient consent for publication Not required.

Ethics approval The study obtained the human ethical approval from the Departmental Research Committee of the School of Optometry, The Hong Kong Polytechnic University. The reference number is HSEAR20140630003-03. All aspects of the study met the tenets of the Declaration of Helsinki and were approved by the Human Subjects Ethics Subcommittee of the Hong Kong Polytechnic University (PolyU).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The primary and secondary outcomes and the baseline demography of the participants in the 2-year RCT and the third year study can be made available. Please contact CSYL at carly.lam@polyu.edu.hk.

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Supplementary content

Title: Myopia Control Effect of Defocus Incorporated Multiple Segments (DIMS) spectacle lens in Chinese children – results of a 3-year follow up study

Authors: Carly Siu Yin Lam, Wing Chun Tang, Paul H Lee, Han Yu Zhang, Hua Qi, Keigo Hasegawa, Chi Ho To

Supplementary Results

eTable 1. Demographic data between the subjects who had joined and the subjects who had not joined the third year.

eTable 2. Comparison between the baseline data for the historical control group and the data at 24-month in the DIMS group

eTable 3. Comparison between the baseline data in the historical control group and the data at 24-month in the Control-to-DIMS group.

eTable 1. Demographic data between the subjects who had joined and the subjects who had not joined the third-year study

DIMS group	**joined study (n=65)**	**not joined study (n= 14)**	**p-value (t-test /chi-square test)**
Age at enrolment (years)	10.15 ± 1.52	10.43 ± 1.22	0.521
Sex Male, % (n) Female, % (n)	 57% (37) 43% (28)	 64% (9) 36% (5)	0.612
Baseline SER (D)	-2.98 ± 0.96	-2.93 ± 1.05	0.863
Baseline AL (mm)	24.68 ± 0.82	24.81 ± 0.84	0.594
Myopia progression (D) in previous 2 years	-0.34 ± 0.52	-0.55 ± 0.54	0.177
Axial elongation (mm) in previous 2 years	0.20 ± 0.21	0.27 ± 0.23	0.270
Control to DIMS group	**joined study (n=55)**	**not joined study (n= 26)**	**p-value (t-test /chi-square test)**
Age at enrolment (years)	10.15 ± 1.42	9.83 ± 1.35	0.089
Sex Male, % (n) Female, % (n)	 47% (26) 53% (28)	 62% (16) 38% (10)	0.261
Baseline SER (D)	-2.73 ± 0.99	-2.86 ± 0.91	0.573

Baseline AL (mm)	24.57 ± 0.88	24.73 ± 0.73	0.423
Myopia progression (D) in previous 2 years	-0.87 ± 0.59	-1.01 ± 0.62	0.330
Axial elongation (mm) in previous 2 years	0.49 ± 0.24	0.59 ± 0.23	0.080

eTable 2. Comparison between the baseline data for the historical control group and the data at 24-month in the DIMS group

	DIMS (n=65)	**Historical control group (n= 76)**	**p-value (t-test /chi-square test)**
Age	12.14 ± 1.52	12.19 ± 0.71	0.856
Sex Male, % (n) Female, % (n)	 57% (37) 43% (28)	 51% (39) 49% (37)	0.506
Baseline SER (D)	-3.32 ± 1.00	- 2.93 ± 1.33	0.054
Baseline AL (mm)	24.88 ± 0.88	24.77 ± 0.91	0.469

eTable 3. Comparison between the baseline data in the historical control group and the data at 24-month in the Control-to-DIMS group

	Control-to-DIMS (n=55)	**Historical control group (n= 76)**	**p-value (t-test /chi-square test)**
Age	12.24 ± 1.47	12.19 ± 0.71	0.793
Sex Male, % (n) Female, % (n)	 47% (26) 53% (28)	 51% (39) 49% (37)	0.722
Baseline SER (D)	-3.61 ± 1.15	-2.93 ± 1.33	0.003*
Baseline AL (mm)	25.06 ± 0.96	24.77 ± 0.91	0.081

*p value <0.05

Langst durende onderzoek[1] naar brillenglazen voor behandeling van progressieve myopie: 6-jarige klinische D.I.M.S. follow-up studie

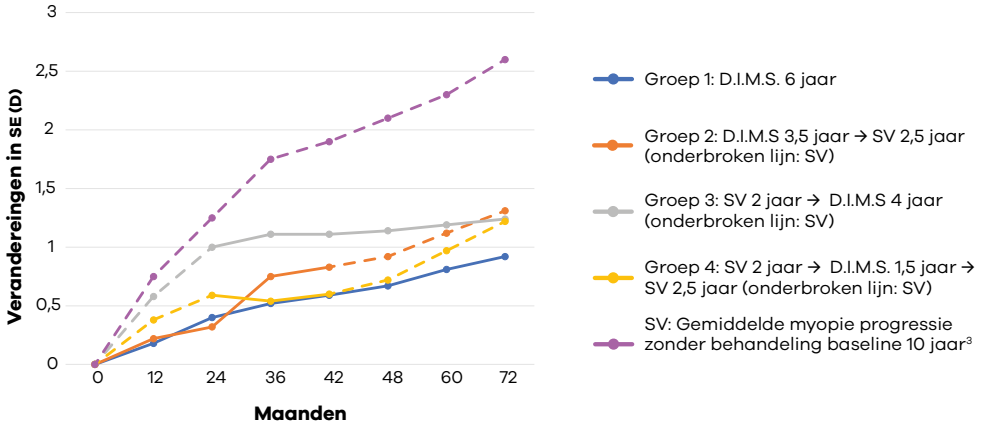
Conclusies

- In een 2-jarige klinische gerandomiseerde controlestudie (RTC)[2] is gebleken dat D.I.M.S. brillenglazen effectief zijn in het vertragen van de myopie progressie. Toen deze kinderen de D.I.M.S. brillenglazen gedurende een periode van 6 jaar bleven dragen, hield het myopiecontrole-effect aan. Zowel de myopie progressie als de aslengte verandering waren vergelijkbaar met de bevindingen in de 2-jarige RCT.
- Tevens bevestigde de studie dat kinderen die stoppen met het dragen van D.I.M.S. brillenglazen geen rebound-effect ondervinden, ten opzichte van de initiële myopie progressie tijdens de 2-jarige RCT of ten opzichte van de algemene populatie.

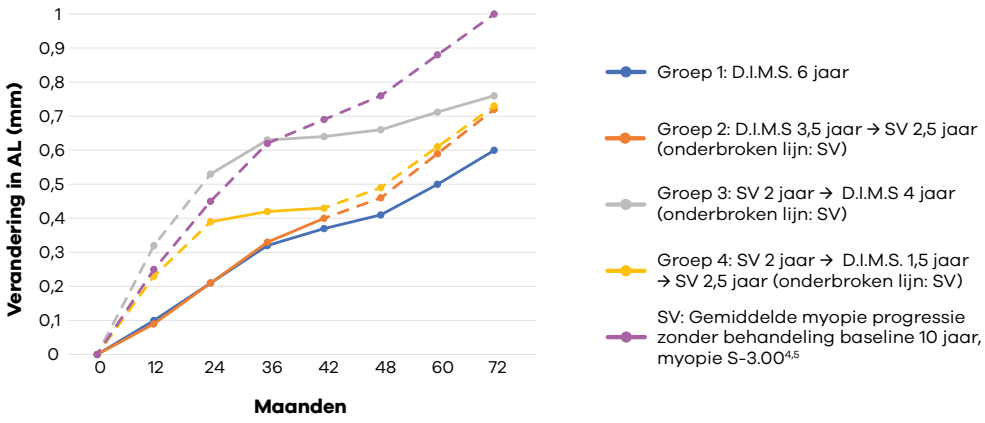
Onderzoeksgroepen

- Groep 1: Droeg in totaal 6 jaar D.I.M.S. brillenglazen (inclusief eerste 2 jaar van RCT).
- Groep 2: Droeg de eerste 3,5 jaar D.I.M.S. brillenglazen en ging daarna over op enkelvoudige brillenglazen (SV).
- Groep 3: Droeg enkelvoudige brillenglazen in de eerste 2 jaar van RCT en stapte daarna over op het dragen van D.I.M.S. brillenglazen.
- Groep 4: Droeg enkelvoudige brillenglazen in de eerste 2 jaar van RCT, stapte daarna over op het dragen van D.I.M.S. brilenglazen en stapte bij 42 maanden weer over op het dragen van enkelvoudige brillenglazen.

Verandering in SE over 6 jaar



Verandering in AL over 6 jaar



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Long-term myopia control effect and safety in children wearing DIMS spectacle lenses for 6 years

Carly Siu Yin Lam[1,2]✉, Wing Chun Tang[1], Han Yu Zhang[1,6], Paul H. Lee[3], Dennis Yan Yin Tse[1,2], Hua Qi[4], Natalia Vlasak[5] & Chi Ho To[1,2]

This study evaluated the long-term myopia control effect and safety in children wearing Defocus Incorporated Multiple Segments (DIMS) spectacle lenses. Participants who completed the 2-year RCT were followed for a total of 6 years; their cycloplegic refractions and axial length were measured. Group 1 (n = 36) wore DIMS spectacles for 6 years; Group 2 (n = 14) wore DIMS lens for the first 3.5 years and SV spectacles afterwards; Group 3 (n = 22) wore SV spectacles in the first 2 years and switched to DIMS; Group 4 (n = 18) wore SV spectacles in the first 2 years, switched to DIMS for 1.5 years and then SV spectacles again. Group 1 showed no significant differences in myopia progression (− 0.52 ± 0.66 vs. − 0.40 ± 0.72D) and axial elongation (0.32 ± 0.26 vs. 0.28 ± 0.28 mm, both $p > 0.05$) between the first and the later 3 years. In the last 2.5 years, DIMS lens groups (Groups 1 and 3) had less myopia progression and axial elongation than the single vision groups (Groups 2 and 4). There was no evidence of rebound after stopping the treatment. Post-wear visual functions in all groups were within norms. The results supported that DIMS lenses provided sustained myopia control without adverse effects over the 6-year study period.
Trial registration: clinicaltrials.gov; NCT02206217.

Myopia is now an alarming concern worldwide as it is estimated to impact more than half of the global population by 2050[1]. The prevalence of high myopia (− 5.00D or greater[2,3]) is expected to increase from 3% at present to 10% of the myopic population by 2050.[1] High myopia is associated with an increased risk of vision-threatening pathologies[2], such as myopic macular degeneration, which is one of the leading causes of low vision and blindness in different countries, such as European regions and China[4,5]. Thus the high prevalence of myopia brings significant public health and socio-economic problems[6,7].

Different strategies have been suggested to delay the onset of myopia and slow myopia progression in children. Atropine is one of the popular drugs used for controlling childhood myopia progression and has shown the most efficacy among different remedies[8]. Recent clinical trials have indicated that low-concentration (0.01%) atropine eyedrops have also obtained modest treatment effects with low myopic rebound and minimal side effects[9–11]. For optical interventions, orthokeratology[12–14], some spectacle lenses[15,16] and soft contact lenses[17–19] are specially designed to impose myopic defocus on the retina and have shown promising reductions in the progression rate of myopia and eye growth.

The Defocus Incorporated Multiple Segments (DIMS) spectacle lens is designed to control myopia by imposing myopic defocus with the principle of simultaneous vision. It is a dual-focus spectacle lens consisting of a central optical zone for correcting distance refractive error, and a batch of small circular segments of + 3.50D equally distributed throughout the mid-peripheral area in a honeycomb pattern[15]. Thus, the DIMS spectacle lens introduces myopic defocus and provides a clear vision for the wearer simultaneously at all distances. The 2-year double-masked randomized controlled trial (RCT) found that DIMS spectacle lens wear could slow childhood myopia progression significantly by 0.44D and axial elongation by 0.34 mm compared with regular single vision (SV) spectacle lenses wear over the evaluation period[15]. In the third year, the children in the treatment group continued to wear DIMS spectacles (DIMS group), and the results showed the slowing effect on myopia progression was sustained over 3 years[20]. On the other hand, the children in the control group switched to DIMS lens wear due to ethical concerns (Control-to-DIMS group). Their myopia progression and axial elongation in the

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3rd year were significantly decreased compared with those in the first and second years. Thus, a good myopia control effect was shown in the children when they changed from SV to DIMS spectacle lens wear. However, the long-term treatment effect and safety with DIMS spectacles were uncertain.

This study aimed to monitor the refractive error and axial length (AL) as well as the safety of the children who wore DIMS spectacle lenses for 6 years and to determine if wearing the DIMS spectacle lens slows myopia progression and axial elongation throughout this period. This study also determines the effect of stopping DIMS spectacle lens wear and the changes in refractive error and axial growth in those children who reverted to SV spectacle lenses. We also evaluate any rebound effects after discontinuation of DIMS spectacle lens wear.

Materials and methods

Participants and study design. Hong Kong ethnic Chinese children who completed both the 2-year RCT[15] and the 3rd year study of DIMS spectacle lenses[20] were invited to participate in this follow-up study. Comprehensive eye examination and related ocular data collection were performed over 6 years after the initial RCT commenced. The participants were asked what types of optical lenses and myopia interventions they had. The children who changed to other myopia control methods or had any ocular anomalies were excluded from this study.

There was the intention of continual follow-up visits at 6-month intervals after the 3rd year; however, the university campus was closed due to unexpected societal events and the COVID pandemic also hit, and all the children were released from the study at 3.5 years. Children and parents were advised that they could opt for their choices of spectacle lens wear. Any follow-up activities and data collection could not be performed until May 2020. The children were invited back for the sixth-year follow-up, regardless of their current choice of spectacle lens wear (DIMS or SV spectacles). Data collection was completed in October 2021.

Participants were divided into 4 groups (eTable 1). Group 1 wore DIMS spectacles from 0 to 6 years; Group 2 wore DIMS spectacles from 0 to 3.5 years and changed to wearing SV spectacles afterwards; Group 3 wore SV spectacles in the first 2 years and switched to DIMS spectacles afterwards; Group 4 wore SV spectacles in the first 2 years, switched to wear DIMS spectacles for 1.5 years and then switched to SV spectacles again. Changes in spherical equivalent refraction (SER) and AL over 6 years were analyzed and compared.

Study procedures and data collection. As for the previous RCT of DIMS spectacle lens, all data collection was carried out at the Centre for Myopia Research, The Hong Kong Polytechnic University. All procedures of the study followed the tenets of the Declaration of Helsinki. This study was approved by the Human Subjects Ethics Sub-committee of The Hong Kong Polytechnic University (HSEARS20191008002) before the commencement of the study. Written assent and informed consent were obtained from the children and their parents after explanations of the nature and possible consequences of the study.

The primary and secondary outcomes were SER (D) and AL (mm) changes. Data collection procedures followed those in the previous trials of DIMS lenses. SER was measured by cycloplegic auto-refraction using an open-field autorefractor (Shin-Nippon NVision-K5001, Ajinomoto Trading Inc.), whereas AL was measured by partial coherence interferometry using an IOL Master (Carl Zeiss Meditec). One drop of Alcaine 0.5% and then 1–2 drops of cyclopentolate HCL 1% were instilled to induce cycloplegia. An average of five autorefraction and AL measurements for each eye were used for data analysis.

Other measurements such as distance and near visual acuities (VA), distance and near phoria, stereoacuity and amplitude of accommodation (AA) were performed when the children were wearing full distance correction based on non-cycloplegic subjective refractions.

Statistical analysis. SPSS statistical analysis software, version 26 (IBM Corp., Armonk, NY, USA), was used for data analysis. The means and standard deviations (SD) of all continuous variables are presented unless otherwise stated. Only data from the right eyes were presented. Myopia progression over 6 years in each group was calculated as the difference between SER at 6 years and baseline. The cumulative myopia progression and axial elongation per 6 months over 6 years were calculated. The trend of changes in SER and AL was plotted against time. The changes in SER or AL between 3.5 and 6 years were the differences between SER or AL at the 6-year visit and the 3.5-year visit. The changes in SER and AL were compared among 4 groups.

Results

Participant number and demographic data. Figure 1 shows the number of participants and the loss to follow-up. 120 children who completed the 3rd year trial (DIMS, n = 65; Control-to-DIMS, n = 55) were invited to join this follow-up study. A total of 92 children (77%) enrolled, and 28 (23%) did not join or were excluded (eTable 2). Most of the children (n = 20) were not willing or too busy to come back for an eye examination; 3 children studied abroad and 4 children changed to other methods of myopia control (3 changed to orthokeratology and 1 child used atropine eye drops). Additionally, 1 child in the DIMS group was excluded due to suffering from ocular disease. Finally, 90 children completed the 6-year data collection.

Table 1 summarizes the demographic findings, mean SER and AL at different visits. No statistically significant differences were found in age, gender, SER and AL at baseline and year 3 ($p > 0.05$) between groups. All children wore their spectacles daily full-time (at least 15 h/day on average).

Changes in SER and AL over 6 years of DIMS spectacle lens wear. Table 2 summarises the mean changes while eTable 3 summarises the cumulative changes in SER and AL from baseline to 6 years. The children in Group 1 (n = 36) showed the least myopia progression and axial elongation which were − 0.92 ± 1.15D (mean ± SD) and 0.60 ± 0.49 mm. Group 1 sustained a similar rate of myopia progression throughout 6 years

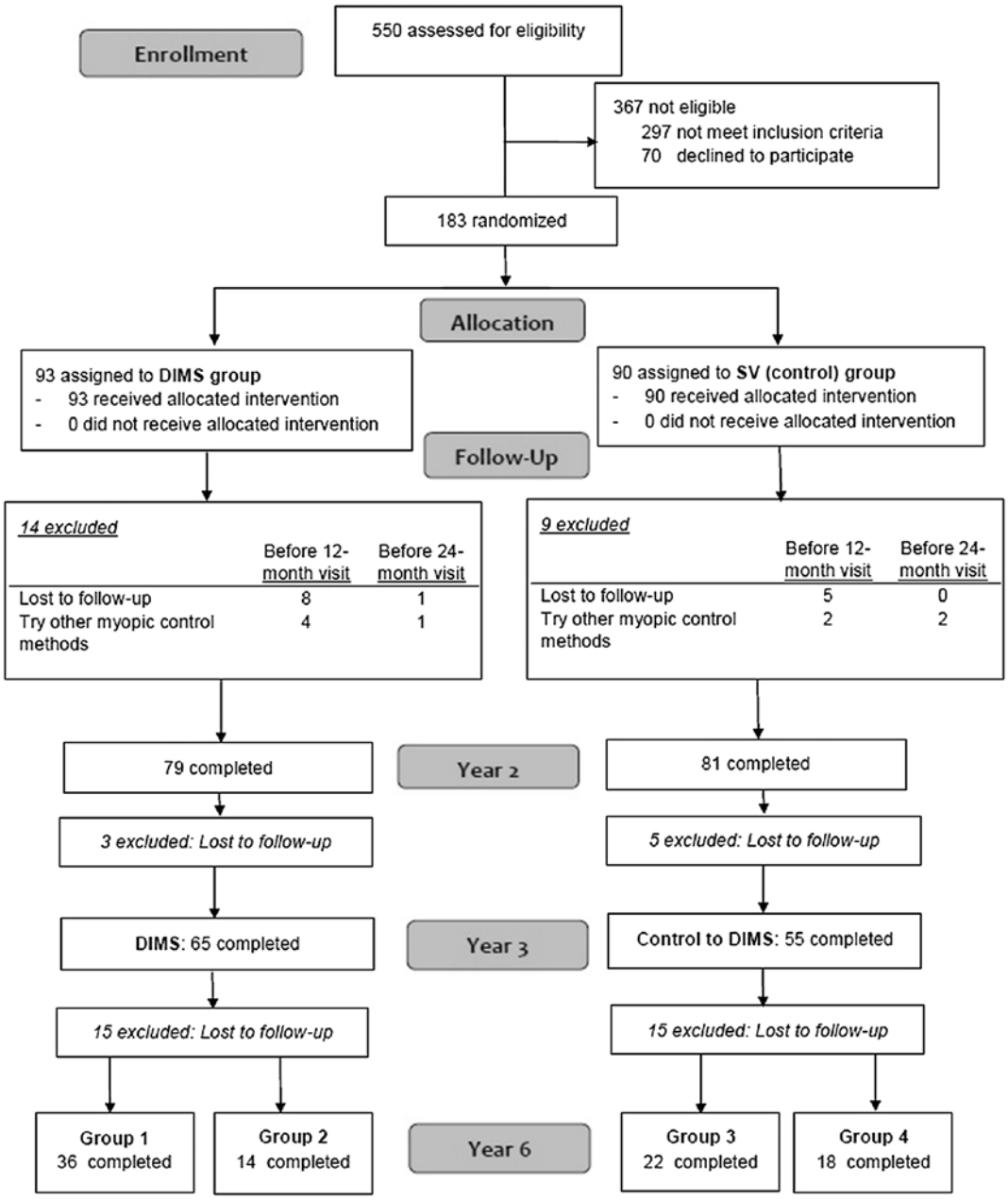

Figure 1. Flowchart showing treatment allocation and participant number in different stages of the DIMS study over 6 years. Both DIMS and Control-to-DIMS groups wore DIMS lenses in year 3. Group 1: wore DIMS lenses for 6 years, Group 2: wore DIMS lens for the first 3.5 years and SV spectacles afterwards. Group 3: wore SV spectacles in the first 2 years and switched to DIMS, Group 4: wore SV spectacles in the first 2 years and switched to DIMS for 1.5 years and then SV spectacles again.

Mean ± SD	Dropouts (N = 15)	DIMS		Dropouts (N = 15)	Control-to-DIMS		P
		Group 1 (N = 36)	Group 2 (N = 14)		Group 3 (N = 22)	Group 4 (N = 18)	
Age at enrolment, years	10.80 ± 1.57	9.75 ± 1.42	10.21 ± 1.53	9.73 ± 1.61	10.50 ± 1.41	10.33 ± 1.71	0.11
Gender, % (number)							
Male	60% (9)	47% (17)	79% (11)	60% (9)	45% (10)	50% (9)	0.38
Female	40% (6)	53% (19)	21% (3)	40% (6)	55% (12)	50% (9)	–
SER at baseline (D)	− 2.83 ± 0.98	− 3.04 ± 0.89	− 2.98 ± 1.13	− 2.92 ± 0.91	**− 2.68 ± 0.88**	**− 2.65 ± 1.18**	0.68
SER at 2-year (D)	− 3.07 ± 0.83	− 3.44 ± 1.02	− 3.29 ± 1.15	− 3.94 ± 1.15	**− 3.67 ± 0.95**	**− 3.24 ± 1.33**	0.09
SER at 3-year (D)	− 3.19 ± 0.86	− 3.57 ± 1.08	− 3.73 ± 1.30	− 4.05 ± 1.34	− 3.78 ± 1.19	− 3.19 ± 1.47	0.25
SER at 6-year (D)	–	− 3.96 ± 1.42	**− 4.28 ± 1.15**	–	− 3.92 ± 1.18	**− 3.87 ± 1.53**	
AL at baseline (mm)	24.38 ± 0.90	24.68 ± 0.76	25.00 ± 0.80	24.59 ± 1.05	**24.62 ± 0.79**	**24.42 ± 0.86**	0.40
AL at 2-year (mm)	24.54 ± 0.83	24.90 ± 0.77	25.20 ± 0.72	25.16 ± 1.15	**25.21 ± 0.89**	**24.80 ± 0.86**	0.11
AL at 3-year (mm)	24.65 ± 0.84	25.00 ± 0.77	25.33 ± 0.76	25.28 ± 0.28	25.30 ± 0.95	24.83 ± 0.85	0.14
AL at 6-year (mm)	–	25.28 ± 0.81	**25.71 ± 0.69**	–	25.43 ± 1.01	**25.14 ± 0.87**	–

Table 1. Summary of demographic data for the dropouts and the children who completed the 6-year follow-up study. The bold figures in the rows of SER and AL represent the time of wearing SV spectacle lenses and the unbold figures represent the time of wearing DIMS spectacle lenses.

	DIMS		Control-to-DIMS	
	Group 1 (N = 36)	Group 2 (N = 14)	Group 3 (N = 22)	Group 4 (N = 18)
Time/SER (D) ± SD				
6-month	− 0.11 ± 0.31	− 0.14 ± 0.30	**− 0.36 ± 0.31**	**− 0.30 ± 0.38**
12-month	− 0.07 ± 0.29	− 0.08 ± 0.28	**− 0.22 ± 0.28**	**− 0.08 ± 0.28**
18-month	− 0.11 ± 0.36	− 0.03 ± 0.24	**− 0.20 ± 0.25**	**− 0.07 ± 0.31**
24-month	− 0.11 ± 0.31	− 0.05 ± 0.23	**− 0.22 ± 0.22**	**− 0.14 ± 0.36**
30-month	0.02 ± 0.28	− 0.15 ± 0.29	− 0.13 ± 0.31	− 0.10 ± 0.23
36-month	− 0.15 ± 0.39	− 0.29 ± 0.39	− 0.02 ± 0.36	0.16 ± 0.41
42-month	− 0.12 ± 0.42	− 0.08 ± 0.34	− 0.00 ± 0.27	− 0.07 ± 0.36
72-month	− 0.30 ± 0.65	**− 0.48 ± 0.37**	− 0.13 ± 0.42	**− 0.63 ± 0.49**
Time/AL(mm) ± SD				
6-month	0.03 ± 0.10	0.04 ± 0.12	**0.19 ± 0.08**	**0.15 ± 0.08**
12-month	0.07 ± 0.07	0.06 ± 0.07	**0.13 ± 0.07**	**0.08 ± 0.09**
18-month	0.04 ± 0.07	0.02 ± 0.11	**0.12 ± 0.07**	**0.08 ± 0.09**
24-month	0.07 ± 0.06	0.07 ± 0.07	**0.10 ± 0.06**	**0.08 ± 0.08**
30-month	0.05 ± 0.07	0.07 ± 0.07	0.08 ± 0.07	0.05 ± 0.05
36-month	0.05 ± 0.06	0.06 ± 0.06	0.02 ± 0.09	-0.02 ± 0.08
42-month	0.04 ± 0.07	0.07 ± 0.06	0.01 ± 0.10	0.01 ± 0.09
72-month	0.25 ± 0.24	**0.31 ± 0.21**	0.12 ± 0.13	**0.30 ± 0.19**

Table 2. Changes in the cycloplegic spherical equivalent refraction (SER) and axial length (AL) between different visits in Groups 1–4. SER: spherical equivalent refraction, D = dioptres, AL: axial length. The bold figures represent the time of wearing SV spectacle lenses and the unbold figures represent the time of wearing DIMS spectacle lenses.

(Fig. 2), and no statistically significant difference ($p > 0.05$) in myopia progression was found between the first 3 years and 4 to 6 years. Myopia progression in the first 3 years was − 0.52 ± 0.66D (annual rate: − 0.17D/year) while progression between 3 and 6 years was − 0.40 ± 0.71D (− 0.13D/year).

Changes in SER and AL from 3.5 to 6 years. Figure 3 shows the changes in SER and AL between 3.5 and 6 years in different groups. Group 3 showed the least myopia progression and axial elongation in the last 2.5 years among the groups. Both the DIMS lens groups (Group 1 and Group 3) had less myopia progression and axial elongation than the single vision lens groups (Group 2 and Group 4). Between the groups wearing DIMS lenses, Group 3 children showed slower myopia progression and axial elongation in the last 2.5 years than Group 1, but only the changes of AL (0.13 ± 0.46 mm, $p = 0.023$) showed statistically significant differences. Group 2 and

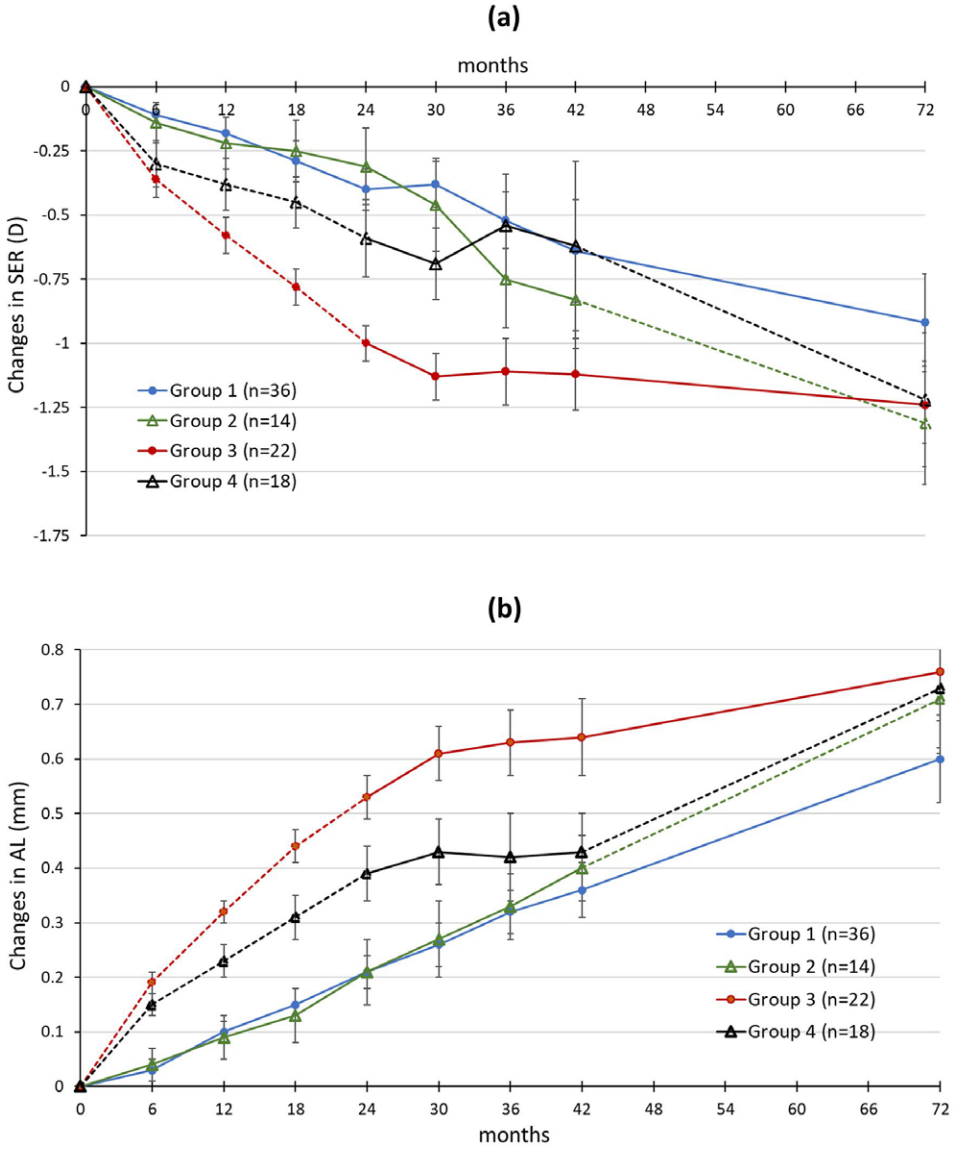

Figure 2. The mean and standard error of (**a**) myopia progression (changes in SER) and (**b**) axial elongation (changes in AL) from baseline to 6 years for Groups 1–4. The solid lines represent the time of wearing DIMS spectacle lenses and the dot lines represent the time of wearing single vision spectacle lenses.

Group 4 had similar changes in AL in the last 2.5 years. Although Group 4 exhibited faster myopia progression (Table 2) than Group 2, the differences were not statistically significant ($p > 0.05$).

The myopia progression and axial elongation between 3.5 and 6 years in Group 2 were − 0.48 ± 0.37D (− 0.19D/year) and 0.31 ± 0.21 mm (0.12 mm/year) and in Group 4 were − 0.63 ± 0.49D (-0.25D/year) and 0.30 ± 0.19 mm (0.12 mm/year). However, such an amount of myopia progression in Group 2 and Group 4 did not indicate a rebound effect. This can be observed that the duration of DIMS lens wear showed a flatter slope of myopia progression and axial elongation, and the slope of SV spectacle lens wear in the last 2.5 years did not show a faster progression rate when compared to those in the initial 2 years (Fig. 2). The treatment effect from DIMS spectacle lens was sustained.

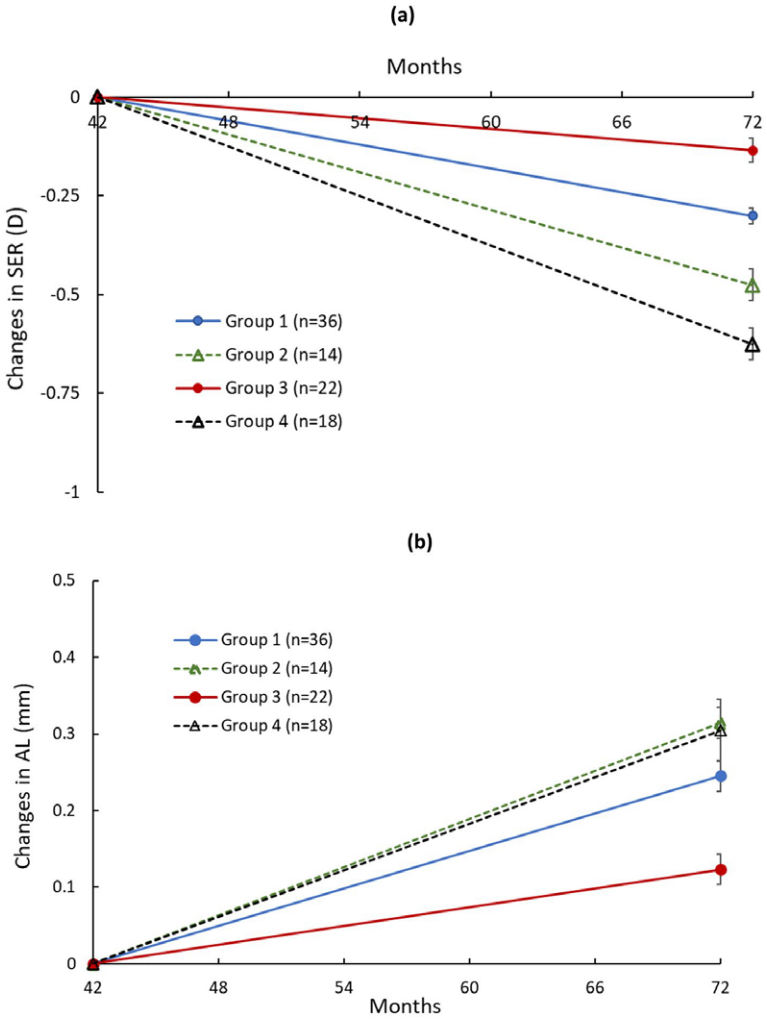

Figure 3. Changes in SER and AL between 3.5 to 6 years in Groups 1–4. The solid lines represent the time of wearing DIMS spectacle lenses and the dot lines represent the time of wearing single vision spectacle lenses.

Myopia progression in individuals. In Group 1 (eFigure 1) 8 out of 36 children (22.2%) did not have any myopic progression (0 to + 0.50D) over 6 years; 3 of them started the DIMS spectacles wear at the age of 9 years, 2 at 10 years old, and 3 at 11 or 12 years old. Five children showed 0.25 to 0.50D of myopia reduction. Twelve children (33%) had an axial elongation of less than 0.3 mm over 6 years (~ 0.05 mm/year). A small portion of the children had low responses to the treatment, 8% had more than 3.00D of myopia progression (0.50D/year on average) and 11% had more than 1.2 mm of axial elongation over 6 years (0.20 mm/year).

Age effect on slowing effect. Both myopia progression and axial elongation slowed with age for children in Group 1 (eFigure 2). eFigure 3 shows the changes in SER and AL over 6 years in different age groups, older children at enrolment gained better myopia control with DIMS lenses than younger children. And eTable 4 shows the mean changes in each age group.

Visual functions after 6-year lens wear. Table 3 shows visual functions at the 6-year visit. There were no statistically significant differences in best-corrected VA, distance and near phoria, stereopsis, and AA (Kruskal–Wallis test, $p > 0.05$) among the 4 groups. All findings of visual function tests were within normal ranges. Long-term wear of DIMS spectacle lenses did not cause any adverse effects on the visual functions.

Mean ± SD	Group 1 (n = 36)	Group 2 (n = 14)	Group 3 (n = 22)	Group 4 (n = 18)	Kruskal–Wallis test, *P* value
BCVA (distance), Log MAR	− 0.09 ± 0.16	− 0.13 ± 0.26	− 0.12 ± 0.20	− 0.05 ± 0.09	0.53
Distance phoria, Δ	− 1.36 ± 2.00	− 0.86 ± 1.75	− 1.45 ± 1.82	− 0.67 ± 1.19	0.46
Near phoria, Δ	− 3.86 ± 5.00	− 3.86 ± 3.46	− 4.23 ± 5.02	− 2.72 ± 3.97	0.59
Stereoacuity, seconds of arc	25.14 ± 8.32	25.00 ± 7.84	24.32 ± 7.12	24.17 ± 7.52	0.94
Monocular amplitude of accommodation (right eye), D	17.06 ± 3.06	15.64 ± 2.79	16.49 ± 2.74	16.21 ± 2.88	0.33
Binocular AA, D	18.31 ± 2.44	17.71 ± 2.30	18.18 ± 2.79	17.87 ± 2.67	0.61

Table 3. Post-trial visual functions.

Discussion

This study over 6 years (including the 2.5-year follow-up) on DIMS spectacle lens wear is one of the longest studies of myopia control intervention. The children who wore DIMS lenses over 6 years (Group 1) had − 0.92D of myopia progression (− 0.15D/year) and 0.60 mm of axial elongation (0.10 mm/year). There were no statistically significant differences in myopia progression during the first three years and the next three years. Although myopia progression slows with age, it was encouraging that the myopia control effect was still exhibited throughout the 6 years. On the other hand, the children (Group 2 and Group 4) who discontinued DIMS lens wear exhibited faster myopia progression and axial elongation compared to those who kept DIMS lens wear (Group 1 and Group 3). These findings support that the myopia control effect was sustained in the treatment groups. Both Group 1 and Group 3 were wearing DIMS spectacles for the last 2.5 years. The children in Group 3 wore the treatment lenses for 4 years (started after 2-year RCT) and started the treatment at an older age while those in Group 1 wore the DIMS lenses for 6 years. Surprisingly, Group 3 showed slower myopia progression and axial growth than Group 1.

A few RCTs of optical myopia interventions reported data over 3 years[13,18,19,21]. Cheng et al.[21] found that Chinese-Canadian children who wore ordinary executive bifocals and prismatic bifocals showed − 1.25 ± 0.10D and − 1.01 ± 0.13D over 3 years, respectively, i.e., the myopia progressions were about 0.41D/ year and 0.34D/ year. The progression findings in the DIMS wearing children showed about 56 to 63% less than them. However, the children in that study had fast myopia progression before enrolment. A 5-year study indicated that orthokeratology could effectively retard axial elongation in children[13]. The elongation over 5 years was 0.99 ± 0.47 mm for the orthokeratology group (0.20 mm/year). For soft contact lenses, a 3-year study[19] reported the absolute myopia progression and axial elongation in children wearing multifocal soft contact lenses were -0.60D and 0.39 mm (0.20D/year and 0.13 mm/year).

Only one clinical trial has been reported with data over 6 years[22]. The RCT of MiSight 1-day contact lenses showed myopia progression and axial elongation in the treatment group were − 0.51 ± 0.64D and 0.30 ± 0.27 mm (0.17D/year and 0.1 mm/year) over the first 3 years[11]. The children who completed the 3-year RCT were assigned to wear the treatment lenses for the other 3 years. The original control group changed to wear the same treatment lenses and exhibited a significant reduction in myopic progression from the previous SV 1-day contact lens wear. The results indicated that children who continued to wear dual-focus soft contact lenses showed myopia control effect sustained for up to 6 years. The prior treatment in the first 3 years did not affect later treatment efficacy (Table 4)[22]. Their mean myopia progression and axial elongation were − 0.92 ± 0.87D and 0.49 ± 0.39 mm, which were comparable to the findings from the children wearing the DIMS lenses continuously for 6 years (− 0.92 ± 1.15D and 0.60 ± 0.49 mm). Their study was carried out in multi-centres including children of different ethnicity whereas our study only included ethnic Chinese children. This might indicate that the race of the children might not be a factor to influence the efficacy of myopia control. Bullimore et al.[23] evaluated the findings of different studies of myopia control and also suggested that no matter what is the race of the children, the benefit of any myopia control treatment seems to be the same.

Whilst treatments of myopia control are effective, there is a concern about a rebound effect which is an accelerated myopia progression or eye growth after discontinuing treatment as compared to the untreated children of similar ages, even to the point of counteracting the prior myopia control effect[24]. Most studies investigated the presence of any rebound effect after stopping the treatment from 6 to 12 months. This study is the first study to observe the myopia progression rate over 2.5 years after the discontinuation of myopia control. Our results revealed that the mean myopia progression and axial elongation were about 0.22D/year and 0.12 mm/year after

Myopia control lenses	SER changes Mean ± SD (D)		AL changes Mean ± SD (mm)	
	first 3 years	3 to 6 years	first 3 years	3 to 6 years
Dual-focus contact lensy[22]	− 0.52 ± 0.64	− 0.45 ± 0.41	0.30 ± 0.28	0.22 ± 0.17
DIMS spectacle lens	− 0.52 ± 0.66	− 0.40 ± 0.72	0.32 ± 0.26	0.28 ± 0.28

Table 4. Comparison of SER and AL changes with a dual-focus contact lens.

stopping DIMS lens wear (combining Group 2 and Group 4), and such amount of myopia progression was clinically insignificant compared with children in the same age range[25–27].

Thus, we conclude that there was no evidence of a rebound effect. Similarly, MiSight contact lenses[28] and progressive additional lenses[29] showed negligible myopic rebound after switching to SV contact lenses and SV spectacles for one year, respectively. Conversely, discontinuation of high-dose atropine (≥0.1%)[30] led to more than 0.1 mm axial elongation than the control groups for one year, and discontinuation of orthokeratology lenses[31] led to more than 0.07 mm axial elongation than using SV spectacle lenses over 6 months. The reason for the myopic rebound in these methods is unclear. On the other hand, the myopic defocus signal from optical devices, such as DIMS spectacle lenses and dual-focus contact lenses, seems to be relatively stable in resisting rebound.

Fan et al.[32] reported the mean rate of myopia progression in Hong Kong children aged 5 to 16 years was − 0.63 D/year. Sankaridurg et al.[26] and Donovan et al.[27] reviewed the previous epidemiological studies on myopia prevalence extensively and constructed an equation for estimating the annual rate of myopia progression in Asian children (eTable 5). Both studies indicated that the younger the age the greater the myopia progression. Donovan's nonsensical quadratic model predicted that myopia progression does not slow but continues to accelerate at the age of 15 years[27]. In our study, all age subgroups in Group 1 showed a slower annual rate of myopia progression than the rate in those studies. A study on European children estimated the annual myopia progression at − 0.50 D for the age of fewer than 10 years and − 0.38 D for the age of 10 to 12 years[33]. The mean annual myopia progression in the purely DIMS group (Group 1: − 0.15D) was much less than the general populations of children with similar ethnicity and Europeans at similar ages.

Similar to the first 3 years[15,20], the 6-year results of Group 1 also indicated that the older children seemed to exhibit a better treatment effect with the DIMS spectacle lens wear. Children with a baseline age of 10 to 13 years had almost no myopia progression and less than 0.08 mm/year of axial elongation at 42 to 72 months (eFigure 3) and this amount of axial elongation has been suggested to be the physiological eye growth[34,35]. Age has been documented as an associated factor with myopia progression[25]. Thus myopia control using DIMS spectacle lenses could slow the faster myopia progression in earlier childhood and then maintain almost no myopia progression in the latter stages of their childhood.

A recent review of myopia control studies indicated that age is not a factor affecting the efficacy of myopia control modality[36]. However, our study found that the older children progressed slower than the younger ones. eFigure 3 shows the myopia progression of DIMS lens wearers of each age group from baseline to 6 years. The 8-year-old group always showed more myopia progression and axial elongation. In the 42 to 72 months, the myopic progression in the 8-year-old group was still faster than in other age groups. We have discussed this observation in two publications[37,38] that relative peripheral refraction (RPR) at the start of the treatment has some impact on myopia control outcomes. Most children with younger enrolment age (aged 8 years) in the 2-year RCT of DIMS lenses had myopic RPR at baseline[37,38]. They showed less myopia control effects compared with the other age groups who had baseline hyperopic RPR and this impact continues to older age despite continuation with treatment lenses. A possible explanation for the variation in myopia control effectiveness between ages could be due to the interaction of the RPR profile and the imposed myopia defocus during treatment. The myopia control effect depends on the counterbalance of the hyperopic defocus from the eye by the myopic defocus from the DIMS lens. The ideal situation is to shift the eye's hyperopic defocus to become myopic defocus. Myopic children with baseline myopic RPR when combined with the myopic defocus of + 3.5D from the treatment lens may be receiving too much myopic defocus at the mid-periphery retina, and this situation may result in an overall more blur peripheral image and such blur could be beyond the threshold of signal detection, and myopia control would therefore be less effective in this age group[37,38]. In the same way, Group 3 and Group 4 started to wear DIMS lenses at 24 months, these two groups showed better myopia control than Group 1. It could also be related to the RPR profile of Groups 3 and 4, having more hyperopic RPR than Group 1 who were shown to have more myopic RPR at the start of the treatment (eTable 6a,b,c). From these findings, we expect that there could be a cap on the amount of imposed myopic defocus that could slow eye growth and myopia progression. And this is uncommon in animal myopia research[37,38]. Also, the children in the older age groups became older than 16 years during that period, and their myopia may have become more stable as per normal eye development.

There were some limitations in this study. First, the children self-selected their choices of spectacle lens wear in the last 2.5 years, so there were four separate groups with different spectacles-wearing combinations during the 6 years. Therefore, the study was not randomized and had selection bias. However, it did benefit from the comparison of the myopia progression trend in the treatment groups with the groups stopping the DIMS lens wear in the last 2.5 years. Second, due to various reasons, it was not possible to continue with every 6-month monitoring and the study was interrupted until three and a half years after the onset of the study. In addition, the sample size in each group became smaller, and the attrition rate (25%) was relatively high due to the long follow-up period and the unexpected COVID pandemic which has caused reluctance for many participants to re-join the research. However, we believe it is a minor limitation as the comparison between the dropouts and those who completed the 6-year study showed no substantial differences (Table 1).

In addition, Group 3 and Group 4 showed differences in the rate of myopia progression (Fig. 2) in the first 2 years. Both groups were wearing SV spectacles in the 2-year RCT and they were expected to have a similar trend in SER and AL changes. There might be other subtle and unmeasured differences between these two groups, so such differences limit the comparison and interpretation of subsequent effect in the last 2.5 years. When considering the rebound effect, we extrapolated the progression trend from the original control group in the 2 years RCT and found that when children stopped the DIMS lens wear and revert to single vision lens wear, there was no sharp change in the rate of myopia progression (comparing the slopes of the first 2 years RCT control with the last 2.5 years of single vision lens wear). In assessing the rebound effect, data from the natural myopia progression for people who are uncontrolled, ideally matched for age and SER should be used for comparison. However, the current participants in all four groups have received certain degrees of intervention so their data in years 3.5

to 6 could not be treated as control. With only preliminary, single-group data, while there is a suggestion that there is no rebounding effect, further studies with bigger sample sizes are needed to confirm this observation.

Conclusions

Our study demonstrated that DIMS spectacle lenses provided a sustained effect of slowing myopia progression and axial elongation in myopic children who wore DIMS lenses for up to 6 years. On the other hand, children who discontinued the treatment did not show evidence of a rebound effect. The findings of visual functions indicated that long-term wear of DIMS spectacle lenses did not show any adverse effect, we conclude that DIMS spectacle lenses are safe to be used as a clinical intervention for childhood myopia control.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions
C.L., W.C.T. and H.Y.Z. wrote the main manuscript text. C.L. and W.C.T. prepared all the figures and tables. All authors reviewed the manuscript.

Competing interests
The authors declare no competing interests.

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8. Combinatietherapie

Deskundigen bereikten overeenstemming over het gebruik van combinatiebehandeling voor het behandelen van myopie

Samenvatting van het akkoord

- Kinderen moeten regelmatig worden gecontroleerd en hun sterkte verandering en aslengtegroei moeten worden gemeten en beoordeeld. Dit moet worden vergeleken met het behandelingsdoel en op basis hiervan moet er besloten worden om bij één behandeling te blijven of te beginnen met een lage dosis atropine in combinatie met een optische behandeling, op basis van de individuele behoeften van het kind.
- Als het verwachte behandeldoel met alleen MiYOSMART brillenglazen niet wordt bereikt, is er volgens de deskundigen een beter effect met een combinatiebehandeling.

Vijf bekende deskundigen in kinderoogheelkunde uit Azië en Europa

Deskundigen deelden en bespraken hun meningen over **het gebruik van combinatiebehandeling voor myopiecontrole** op basis van hun klinische ervaring en bereikten een akkoord

Tijdens deze bijeenkomst werd de combinatiebehandeling aangeduid als een combinatie van **optische en farmatherapeutische behandeling.**

Het risicoprofiel kan de besluitvorming over de behandeling beïnvloeden.

Oudere kinderen met een lager risico op hoge myopie
→ beginnen met een optische behandeling

Jongere kinderen met een hoog risicoprofiel en een sterkte verandering van >-0,50 dpt in de afgelopen zes maanden
→ gelijk starten met de combinatiebehandeling

Beoordelingstijdlijn voor kinderen met een combinatiebehandeling

Start van de behandeling*[1,2,3]

- Cycloplegische refractie
- Aslengtegroei
- Gezondheid van de ogen
- Visuele functie
- Risicobeoordeling

Eerste 2 weken van de start van de behandeling[1,2,3]

- Aanpassingscontrole
- Visuele functie
- Meer gedetailleerd onderzoek als er afwijkingen worden geconstateerd

Controle elke 6 maanden*[1,2,3]

- Cycloplegische refractie
- Aslengtegroei
- Gezondheid van de ogen
- Visuele functie

*Voor alle behandelmethodes voor myopiecontrole geld dat de volledige sterkte van de cycloplegische refractie moet worden voorgeschreven.

Behandeldoelen

Sterkte verandering maximaal

-0.75 dpt per jaar

AZIË

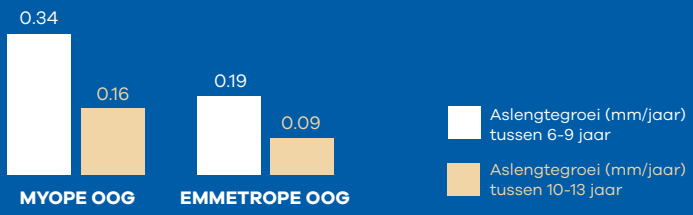
-0.50 dpt per jaar

EUROPA

Aslengtegroei

- Verhogingen van ongeveer 0,1 mm per jaar is een normale ooggroei.[3]
- Normale ooggroei is leeftijdsafhankelijk.
- Een groei van meer dan 0,20 mm per jaar duidt op het niet halen van het behandeldoel.*
- Het idee om de ooggroei van het emmetrope/fysiologische oog te gebruiken als doel voor aslengte verandering bij myopiecontrole is beschreven in verschillende artikelen, maar is nog niet algemeen vastgesteld.

Gemiddelde aslengtegroei bij Nederlandse kinderen naar leeftijd en refractie categorie[4]



De ervaring van de deskundigen met MiYOSMART glazen in combinatie met atropine

- Er zijn geen significante veranderingen waargenomen in de gezichtsscherpte of het binoculaire zicht tussen alleen MiYOSMART glazen of een combinatiebehandeling.[5]
- Er wordt geen verschil gevonden in de contrastgevoeligheidsmetingen met alleen MiYOSMART glazen of een combinatiebehandeling.[5]

MiYOSMART is niet in alle landen goedgekeurd voor myopiecontrole, inclusief de VS, en is momenteel niet in alle landen beschikbaar voor verkoop, inclusief de VS. MiYOSMART brillenglazen zijn mogelijk niet in staat om de aandoeningen van individuen aan te pakken als gevolg van natuurlijke tekortkomingen, ziekte, al bestaande medische aandoeningen en/of gevorderde leeftijd van de dragers. De hierin opgenomen informatie is algemene informatie en is niet bedoeld als medisch advies. De definitieve bepaling van de aanbeveling voor MiYOSMART brillenglazen tot 12 jaar moet worden gedaan door een oogarts/optometrist/orthoptist. Raadpleeg uw oogarts/optometrist/orthoptist voor meer informatie voordat u MiYOSMART brillenglazen gebruikt bij kinderen onder de 12 jaar.

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* In Nederland wordt deze aslengtegroei nog op leeftijd gespecificeerd. (zie MiYOSMART handboek punt 1.5D op pag. 11.

PLOS ONE

RESEARCH ARTICLE

A comparison of myopia control in European children and adolescents with defocus incorporated multiple segments (DIMS) spectacles, atropine, and combined DIMS/atropine

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Abstract

Purpose

To evaluate the efficacy of a myopia control spectacle lens (DIMS) at slowing the progression of myopia in a population of European children in comparison with 0.01% atropine and combined DIMS and atropine.

Methods

The study was a non-randomised experimenter-masked prospective controlled observational study of individuals aged 6–18 years with progressing myopia but no ocular pathology. Participants were allocated, according to patient/parent choice, to receive 0.01% atropine eyedrops, DIMS (Hoya® MiyoSmart®) spectacles, combined atropine+DIMS or single vision spectacle lenses (control group). The key outcome variables, cycloplegic autorefraction spherical equivalent refraction (SER) and axial length (AL), were measured at baseline and after three, six, and 12 months.

Results

Of the 146 participants (mean age 10.3y ±3.2), 53 received atropine, 30 DIMS spectacles, 31 atropine+DIMS, and 32 single vision control spectacles. Generalized linear mixed model analysis revealed for SER, whilst controlling for age and SER at baseline, at each stage all treatment groups had significantly reduced progression compared with the control group ($p<0.016$). For AL, whilst controlling for baseline age and AL, at 6 and 12 months all treatment groups had significantly less progression than the control group ($p<0.005$). For SER

manuscript. The specific roles of these authors are articulated in the 'author contributions' section.

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only, in pairwise comparisons at 12 months the atropine+DIMS group had significantly reduced progression compared with the DIMS only and Atropine only groups ($p<0.001$).

Conclusion

In a European population, DIMS and atropine are effective at reducing myopia progression and axial elongation in progressing myopia and are most successful at reducing myopia progression when used in combination.

Introduction

Approximately 30% of Europeans are myopic [1]. The prevalence of myopia is increasing worldwide and it is estimated that in 2050, 50% of the world population will be myopic [2]. Many factors are recognized, both genetic and environmental, that influence the development and progression of myopia, such as the education level and sunlight exposure [3, 4]. Myopia, especially high myopia, is associated with an increased risk of sight-threatening eye disease [5, 6], creating a long-term burden on public health [2, 7] and economies [8].

There is growing interest in methods that slow the progression of myopia [9], including atropine eye drops [10], dual focus contact lenses and spectacle lenses, and orthokeratology [11, 12]. Atropine has been widely used effectively for myopia control [13].

Defocus incorporated multiple segments (DIMS) spectacle lenses are designed to slow myopia progression in children, based on the principle of peripheral myopic defocus and simultaneous vision. They are a dual focus spectacle lens consisting of a central optical zone for correcting distance refractive error, and an annulus comprising several hundred circular segments, each ~1 mm in diameter with a relative positive power of 3.50D equally distributed throughout the mid-peripheral area in a honeycomb pattern [14]. DIMS spectacles reduce the progression of myopia and reduce axial elongation by 50–60% compared to single vision (SV) lenses [14–16]. The optical properties of DIMS spectacles [17] cause minimal [18] or no [16] adverse effects on vision.

The literature reveals no trials of DIMS in European populations and no studies comparing atropine with DIMS. It is believed that different mechanisms underly the benefit from atropine (non-accommodative, possibly via acting directly on receptors in the sclera) and optical approaches such as DIMS (reducing relative hyperopic defocus) [19]. Therefore, it is hypothesised that their combined use may create an additive effect, which to date has not been explored.

The goals of this study are to evaluate the efficacy of DIMS in slowing the progression of myopia in a population of European children in comparison with atropine and combined DIMS and atropine.

Materials and methods

Study design

The study was a prospective controlled observational study carried out in a paediatric ophthalmology clinic setting. The clinic has a reputation for myopia control and participants were highly motivated to pursue treatment, but often attended the clinic because of a preference for a specific intervention and therefore random allocation to study groups was not possible. Measurements of visual acuity (VA), cycloplegic autorefraction spherical equivalent refraction (SER), and axial length (AL) were taken by masked observers following a fixed protocol.

Potential participants underwent a full ophthalmological assessment including symptoms and history, presenting VA with pre-study spectacles, orthoptic testing, refraction (including cycloplegic autorefraction), and dilated fundoscopy. Suitable participants (see below) were provided with information on three options for myopia control: 0.01% atropine, DIMS spectacles, or combined 0.01% atropine+DIMS. These options were discussed with patients, parents, and clinicians (PN, AL) and participants and their parents were free to choose their preferred option, or to continue in single vision spectacles. Some families were hesitant to undertake a long-term pharmacological or novel optical treatment and therefore opted not to undertake myopia control at that time and instead to join the control group and wear single vision spectacles.

For all participants, written informed consent was obtained from parents/guardians. Participants were provided with their interventions and follow-up arranged after 3, 6, and 12 months. The outcome variables were assessed at each follow-up. The importance of attendance at follow-up was stressed to all participants, and telephone reminders were used together with rebooking of missed appointments to encourage attendance.

The study received approval from the Ethics Committee of the University of Milan and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Participants

The selection criteria are in Table 1. The target sample size was at least 30 participants in each group. Myopia milder than -0.50D (SER) was excluded to avoid potential difficulties persuading participants with minimal myopia to wear spectacles. Myopia higher than 4.00D was excluded to decrease the risk of any participants having syndromic myopia.

Interventions

DIMS spectacles (Hoya® MiyoSmart®) were prescribed and dispensed according to the manufacturer's fitting guide, with participants instructed to wear the spectacles as close to all waking hours as practical (e.g., not for bathing or swimming). For those receiving atropine, 0.01% drops (ATOM galenic formulation) [20] were used, with one drop being instilled in each eye every night, before sleeping. All participants throughout the study were free to ask for a re-evaluation of their myopic prescription.

Outcome variables

The outcome variables were always assessed in the same room with lighting set at 600 Lux by the same team of four orthoptists, all of whom were masked to the participants' interventions.

Table 1. Selection criteria.

Inclusion criteria	• Children/adolescents aged 6–18 years • Italian/European ethnicity • Myopia with SER from -0.50D to -4.00D • Astigmatism not more than 2.50DC • Anisometropia under 1.25D
Exclusion criteria	• Genetic syndromes suspected (e.g., Stickler, Marfan etc.) • Other eye diseases (such as glaucoma, juvenile cataracts or retinal abnormalities, any form of strabismus) • Myopia progression in the last year of less than 0.50D SER in either eye

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The primary outcome variables were the change in SER and in AL. Cycloplegic autorefraction was carried out after instillation of cyclopentolate (Allergan Ciclolux® 10mg/ml), with two drops in each eye instilled five minutes apart and refraction (Retinomax®) after 30 minutes (set to 0.25D, median of 3 readings for each measurement). AL was measured in each eye with a Zeiss IOLMaster® instrument.

To preserve masking, at each follow-up, VA testing was repeated with the refractive error determined at baseline worn in an optometric trial frame. An ETDRS LogMAR [21] chart was used in a computerised system that presented random letters. The clinical procedure was to use whole line scoring (criterion: 3/5 letters correctly read) in decimal units, with a test ceiling of 1.0 (0.0 LogMAR) acuity. The limitations for this secondary variable are considered further in the Discussion.

Statistical analysis

Continuous variables were summarized as mean with standard deviation and median with interquartile range. Categorical data were expressed with frequency and percentage. Differences across the groups in baseline characteristics were evaluated by the Kruskal-Wallis test.

A generalized linear mixed model (GLMM) was applied to evaluate the treatment effect on SER, AL and VA. The model included treatment and the interaction time by treatment as fixed effect, age and baseline value as fixed covariate; and subject and eye (right or left) as random effect. Multiple comparisons were adjusted using sequential Bonferroni. Two-sided p-values of less than 0.05 were considered statistically significant. IBM SPSS Statistics V.24.0 (IBM Corp. Released 2016, Armonk, New York, USA: IBM Corp), was used for statistical analysis.

Results

Study population

One hundred and forty-six participants with myopia and a mean age of 10.3 (± 3.21) years were enrolled and allocated to the four groups: DIMS (N = 30), atropine (N = 53), atropine +DIMS (N = 31), and single vision control (N = 32). Baseline characteristics are in Table 2. Since participants were not randomly allocated to groups, the groups differed significantly in some characteristics at baseline. Specifically, pairwise comparisons revealed the following statistically significant ($p<0.05$) differences: the DIMS group was older than other groups, atropine group was younger than the other groups; the control group and atropine group had lower values of SER than atropine+DIMS, and lower values than the DIMS group; and the atropine+DIMS group had higher values of AL compared to the control group and compared to the atropine group. However, the GLMM analyses were corrected for differences in these factors at baseline.

Limitations in the way visual acuity was assessed (whole line scoring and a test ceiling of 1.0 decimal) mean that at baseline, the mean, median, and limits of inter-quartile range of all groups were each 1.0 decimal. None of the participants had prior experience of myopia control.

All participants attended all three follow-up visits. Some appointments had to be rescheduled when participants failed to attend, but all appointments took place within 4 weeks of the due date. No adverse events were reported.

Primary outcomes: SER & AL

The results are illustrated in Figs 1 and 2 and the statistical analysis is summarised in Tables 3 and 4. For SER at 12 months (Fig 1 and Table 3), controlling for age and SER at baseline, the

Table 2. Participant characteristics at baseline[1].

	Total (N = 146)	Control (N = 32)	DIMS (N = 30)	Atropine (N = 53)	Atropine+DIMS (N = 31)	p
Age in years	10.28 ± 3.21	11.34 ± 3.96	13.37 ± 2.22	8.17 ± 1.84	9.81 ± 2.06	<0.001
	10 (7 to 13)	11 (8 to 15.5)	14 (12 to 15)	8 (7 to 9)	10 (8 to 11)	
Baseline SER (D), right	-1.77 ± 0.70	-1.54 ± 0.74	-1.97 ± 0.69	-1.56 ± 0.69	-2.16 ± 0.46	<0.001
	-2.00 (-2.25 to -1.25)	-1.62 (-2.00 to -0.87)	-2.00 (-2.25 to -1.75)	-1.75 (-2.00 to -1.00)	-2.00 (-2.25 to -1.75)	
Baseline SER (D), left	-1.77 ± 0.70	-1.54 ± 0.74	-1.97 ± 0.69	-1.56 ± 0.69	-2.16 ± 0.46	<0.001
	-2.00 (-2.25 to -1.25)	-1.62 (-2.00 to -0.87)	-2.00 (-2.25 to -1.75)	-1.75 (-2.00 to -1.00)	-2.00 (-2.25 to -1.75)	
Baseline AL (mm), right	24.79 ± 0.80	24.64 ± 0.79	24.87 ± 0.71	24.61 ± 0.87	25.16 ± 0.64	0.029
	25.01 (24.09 to 25.46)	24.46 (24.08 to 25.44)	24.91 (24.12–25.52)	24.33 (24.01–25.33)	25.12 (24.95 to 25.61)	
Baseline AL (mm), left	24.80 ± 0.80	24.64 ± 0.79	24.83 ± 0.71	24.66 ± 0.89	25.16 ± 0.63	0.05
	25.01 (24.11 to 2.52)	24.46 (24.08 to 25.44)	24.76 (24.11–25.52)	24.71 (23.89–25.33)	25.12 (24.95 to 25.56)	

[1]Results are expressed as mean and standard deviation (first line) and median and inter-quartile range (second line)

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key interaction (comparison with control group) was statistically significant ($p<0.001$) for all three treatment groups.

For AL at 12 months (Fig 2 and Table 4), controlling for age and AL at baseline, the results of each treatment group differed significantly from the control group ($p<0.001$). Figs 1 and 2 reveal the effects of each treatment is sustained over the year of the study, and indeed the AL appears more stable in the last six months than in the first six months. Considering Figs 1 and 2, the slowest progression occurred in the group receiving the combined atropine+DIMS intervention.

Secondary analysis: Changes in VA

When controlling for baseline age and VA, the deterioration in VA (measured with the refractive error found at baseline) at six months and 12 months was significantly less in each treatment group than in the control group ($p<0.001$).

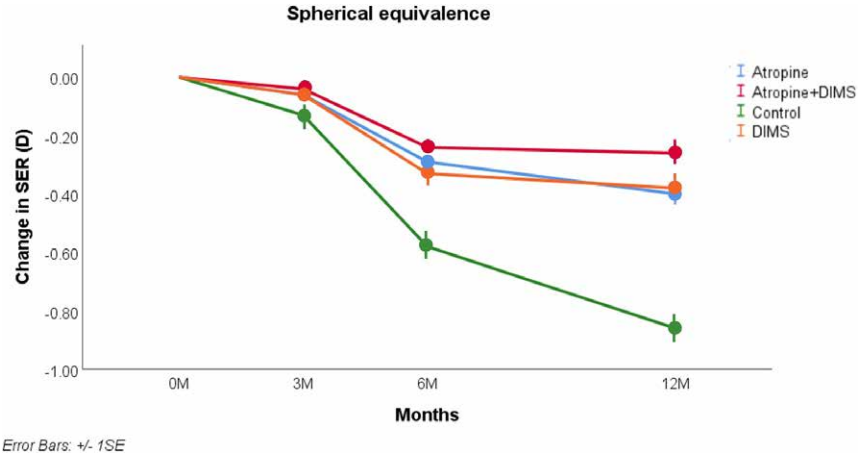

Fig 1. Model-adjusted mean and SE of myopia progression (SER) from baseline to 12 months.

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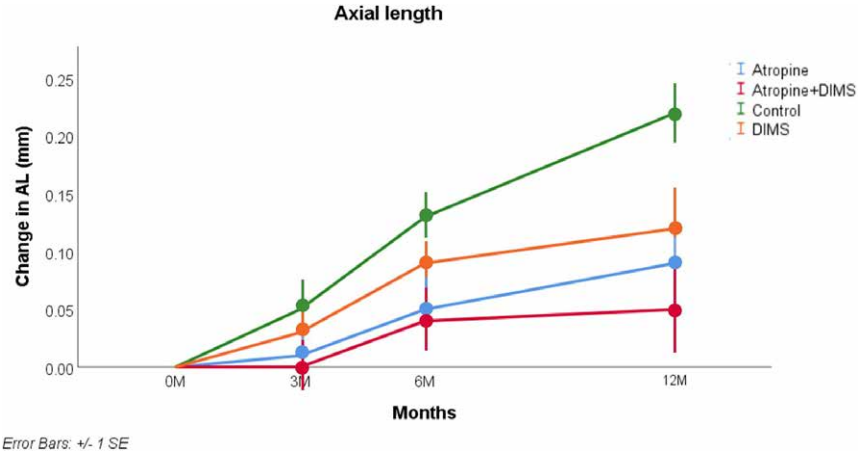

Fig 2. Model-adjusted mean and SE of change in axial length from baseline to 12 months.

Table 3. Treatment effect over time on SER.

Months	Control	Atropine	Atropine + DIMS	DIMS	P value
3M	-1.916 (0.017) (-1.949 to -1.882)	-1.821 (0.014) (-1.848 to -1.794)	-1.772 (0.017) (-1.806 to -1.738)	-1.845 (0.019) (-1.882 to -1.808)	Overall: p<0.001
					Control vs Atropine: <0.001
					Control vs Atropine + DIMS: <0.001
					Control vs DIMS: 0.015
					Atropine vs Atropine + DIMS: 0.05
					Atropine vs DIMS: 0.33
					Atropine + DIMS vs DIMS: 0.017
6M	-2.362 (0.018) (-2.397 to -2.326)	-2.070 (0.015) (-2.099 to -2.042)	-1.978 (0.019) (-2.014 to -1.941)	-2.087 (0.020) (-2.126 to -2.048)	Overall: p<0.001
					Control vs Atropine: <0.001
					Control vs Atropine + DIMS: <0.001
					Control vs DIMS: <0.001
					Atropine vs Atropine + DIMS: <0.001
					Atropine vs DIMS: 0.53
					Atropine + DIMS vs DIMS: <0.001
12M	-2.641 (0.028) (-2.696 to -2.587)	-2.165 (0.022) (-2.208 to -2.122)	-2.002 (0.028) (-2.058 to -1.946)	-2.153 (0.029) (-2.210 to -2.095)	Overall: p<0.001
					Control vs Atropine: <0.001
					Control vs Atropine + DIMS: <0.001
					Control vs DIMS: <0.001
					Atropine vs Atropine + DIMS: <0.001
					Atropine vs DIMS: 0.74
					Atropine + DIMS vs DIMS: 0.001

[1]Results are expressed as mean and standard error and 95%CI

Continuous predictors are fixed at the following values: Age = 10.281, Ser at baseline = -1.7671

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Table 4. Treatment effect over time on AL.

Months	Control	Atropine	Atropine + DIMS	DIMS	P value
3M	24.840 (0.007) (24.827 to 24.853)	24.797 (0.006) (24.786to 24.808)	24.802 (0.007) (24.789 to 24.815)	24.817 (0.008) (24.802 to 24.832)	Overall: p<0.001
					Control vs Atropine: <0.001
					Control vs Atropine + DIMS: <0.001
					Control vs DIMS: 0.06
					Atropine vs Atropine + DIMS: 0.56
					Atropine vs DIMS: 0.16
					Atropine + DIMS vs DIMS: 0.31
6M	24.916 (0.012) (24.892 to 24.939)	24.853 (0.009) (24.834 to 24.872)	24.843 (0.012) (24.819 to 24.867)	24.859 (0.013) (24.834 to 24.884)	Overall: p<0.001
					Control vs Atropine: <0.001
					Control vs Atropine + DIMS: <0.001
					Control vs DIMS: 0.004
					Atropine vs Atropine + DIMS: 0.99
					Atropine vs DIMS: 0.99
					Atropine + DIMS vs DIMS: 0.99
12M	25.010 (0.014) (24.982 to 25.037)	24.887 (0.011) (24.866 to 24.909)	24.851 (0.014) (24.824 to 24.879)	24.883 (0.015) (24.854 to 24.912)	Overall: p<0.001
					Control vs Atropine: <0.001
					Control vs Atropine + DIMS: <0.001
					Control vs DIMS: <0.001
					Atropine vs Atropine + DIMS: 0.13
					Atropine vs DIMS: 0.82
					Atropine + DIMS vs DIMS: 0.26

[1]Results are expressed as mean and standard error and 95%CI

Continuous predictors are fixed at the following values: Age = 10.281, Axial length at baseline = 24.7916

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Discussion

Although the present study is not a formal randomised controlled trial, the results are novel in reporting the effects of DIMS spectacle lenses and atropine, in isolation and combined, in a European population. The findings indicate that 0.01% atropine and DIMS are individually effective in this population, and even more effective when combined.

It has become commonplace in the literature on myopia control to use percentage reduction in progression as an index to describe treatment effect, but Brennan and colleagues cautioned that this can be misleading [22]. However, for comparison with previous literature, it is reassuring that after one year the percentage reduction in myopia progression (raw data, relative to the control group) in the atropine (57% in SER and 62% in AL) and DIMS (57% SER, 57% AL) groups is comparable to that quoted by other researchers, and is more marked in the combined atropine+DIMS group (70% SER, 77% AL).

The proportion of participants who showed, from baseline to 12 months, no increase in axial length was in the DIMS group 10%, in the atropine group 15%, and in the atropine +DIMS group 18%, compared with only 2% of the control group. Lam and colleagues reported that 14% of children wearing DIMS showed no axial elongation over 2 years [14],

and Bao et al with another lenslet design found no axial elongation in 28% of participants after one year [23].

Recent studies indicate a dose effect of atropine and suggest that 0.05% may be the optimum dose for balancing efficacy with side effects [24], although an age effect is evident with younger ages benefitting from higher doses [25]. However, this research, like most on myopia control, concentrates on Asian populations. The reduced pigmentation in populations of European racial origin raises the possibility that 0.01% may be more effective, although at present evidence is lacking. Joachimsen et al report more relevant side effects of 0.05% topical atropine in young Caucasian children, potentially compromising acceptance and compliance with this dosage [26].

Strengths and limitations

Most studies of atropine and all trials of DIMS have been on Asian populations and this study is an important extension of this work to a European population. Another strength of the study is the novel inclusion of a combined atropine+DIMS group.

A major weakness is that participants chose which intervention they received: there was no random allocation to groups. The clinic in which participants were examined had a reputation for myopia control with atropine and therefore more participants elected to be in this group. Although random allocation to groups is desirable to reduce the risk of bias, it has the disadvantage of making results less relevant to clinical practice. This is one reason why it has been argued that hierarchies of evidence should be replaced by an acceptance of the need for a diversity of approaches, including non-randomised observational studies [27].

Another limitation is that the study was single-masked, and participants were not masked to the treatment they received. In mitigation, it is helpful that the measurements of refractive error and AL were objective and taken by clinicians who were masked to the treatment that each participant was receiving. The method of measuring VA is suboptimal (whole line scoring and test ceiling of 1.0 decimal (0.0 LogMAR)).

The duration of the study of one year is similar to some other research in this field [23, 24], but does not address questions about long-term efficacy. Other research has addressed this issue [28]. Another question is about rebound effects when treatment is ceased. A rebound effect often occurs when atropine is withdrawn [28, 29], but may be avoided by tapering [30]. Many years ago it was hypothesised that optical interventions for myopia control work in a more natural way than atropine, through normalising the plane of the peripheral image shell nearer to the retina, and therefore are unlikely to cause a rebound effect on cessation of treatment [19]. Evidence from optical treatment using contact lenses supports this hypothesis [31], but this question has not yet been addressed with lenslet designs.

The study population represent individuals and families who are motivated to pursue myopia control and were attending a clinic that built a strong rapport with patients, which no doubt contributed to the high compliance rate. It is not known whether the findings will apply to less motivated populations. Similarly, it is not known whether the novel findings concerning combined atropine+DIMS apply to populations with other racial origins.

Conclusions

In conclusion, DIMS and 0.01% atropine appear to offer efficacious interventions for slowing myopic axial elongation and combining these two treatments seems most effective at slowing myopia progression. To the best of our knowledge, this is the first study of this type to be conducted on European participants.

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Validation: Paolo Nucci.

Writing – original draft: Rakhee Shah, David Francis Edgar, Bruce John William Evans.

Writing – review & editing: Paolo Nucci, Andrea Lembo, Irene Schiavetti, Rakhee Shah, David Francis Edgar, Bruce John William Evans.

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Review artikelen

Klinische methode voor myopie management

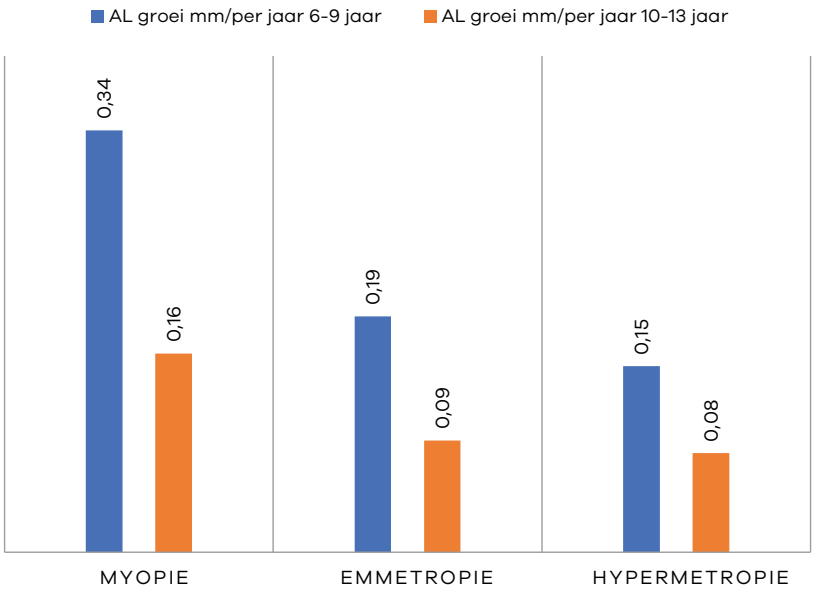
Myopie, ofwel bijziendheid, is een veelvoorkomende refractieafwijking. De prevalentie is alarmerend hoog in plaatsen zoals Hong Kong[1], Taiwan[2] en Singapore[3]. In Hong Kong worden kinderen steeds op een jongere leeftijd (5 of 6 jaar) myoop en tot 80% van de tieners is myoop.[1] Het probleem speelt echter niet alleen in Aziatische landen, maar wereldwijd en dus ook in Nederland. Uit de GenerationR studie van het Erasmus MC blijkt dat de prevalentie myopie onder 6-9 jarige kinderen 12% is. Indien myopie op deze leeftijd ontstaat is er een hoog risico op hoge myopie. Het aantal slechtzienden als gevolg van myopie zal naar verwachting verviervoudigen in 2050 en is daarmee de belangrijkste oorzaak van blindheid in Nederland.[70]

Hoog myopen hebben een vergroot risico op oogaandoeningen zoals maculopathie[4], retinale degeneratie, netvliesloslating,[5-6] cataract en glaucoom.[7] De lange termijn zorg en behandeling van deze myopie gerelateerde oogaandoeningen hebben een significante impact op de economie en op de zorgkosten.[8] Myopie is een dreigend probleem voor de volksgezondheid en effectieve controle (remming) van de aandoening zou helpen om dergelijke zorgen weg te nemen.

Mark Bullimore en Noel Brennan[78] hebben de data van vijf grote populatie studies geanalyseerd waaruit blijkt dat wanneer de myopie met 1D gereduceerd kan worden de kans op maculapathie met 40% verminderd. En de kans op maculapathie neemt met 67% toe bij iedere 1D toename van de myopie. Dit voordeel laat zich zowel bij laag als hoog myopen zien, ook al is de kans veel groter bij hoog myopen, de risico verlaging geldt voor alle myopen. Iedere dioptrie die tegengehouden kan worden is daarom winst.

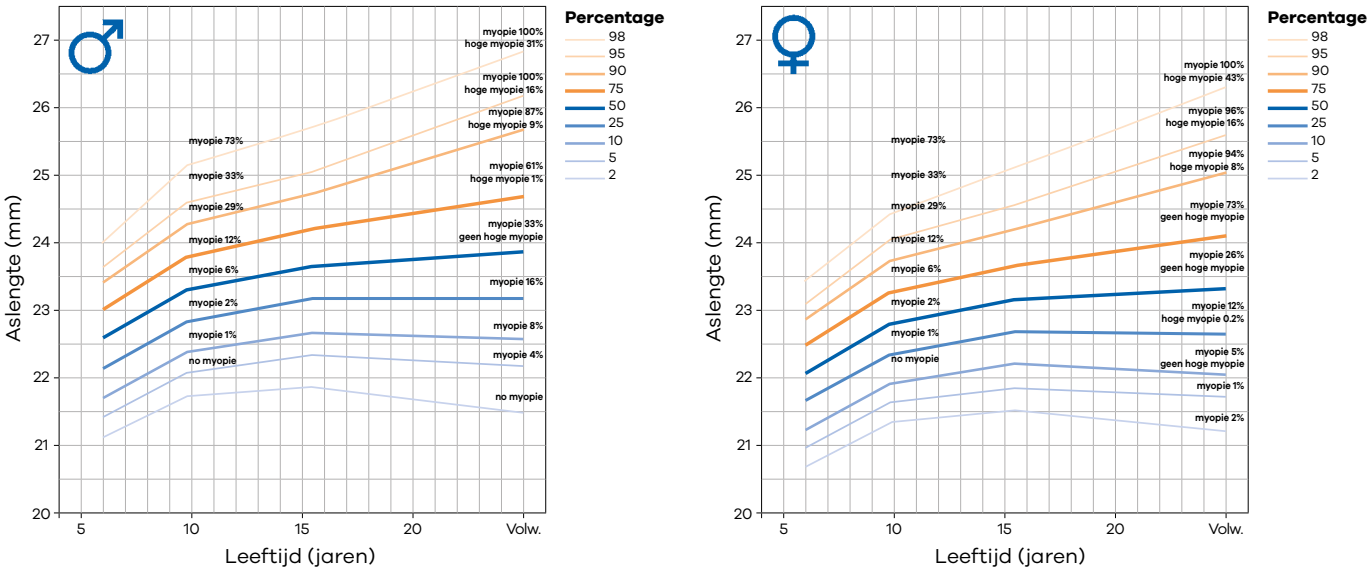
De belangrijkste oorzaak van myopie is toename van de oogaslengte, met name van de lengte van het achtersegment. De correlatie tussen sferisch equivalent en aslengte in een oog met myopie is hoog (>90%); een sferische equivalent van -6D of meer gaat doorgaans gepaard met een aslengte van 26mm of meer.[73] Door het meten van de aslengte kunnen we de groei van het oog vaststellen.

De aslengte is de afstand van het centrum van de cornea tot aan de fovea. De gemiddelde aslengte is bij de geboorte 17,5 mm en groeit tot gemiddeld 23,5 mm op volwassen leeftijd. Een hoog bijziend oog groeit door tot ten minste 26 mm lengte, maar dit kan oplopen tot > 30 mm.[78] Tijdens de eerste levensjaren is de groei het snelst en deze stopt doorgaans rond 13-jarige leeftijd, maar bij myopie kan de groei doorgaan tot zelfs 25-jarige leeftijd. Hoe vroeger de myopie ontstaat, hoe groter het risico op hoge myopie op latere leeftijd. Een myoop oog groeit sneller dan een emmetroop of hypermetroop oog, zie grafiek 1 (J.W.L. Tideman et al, 2020 ARVO abstract).



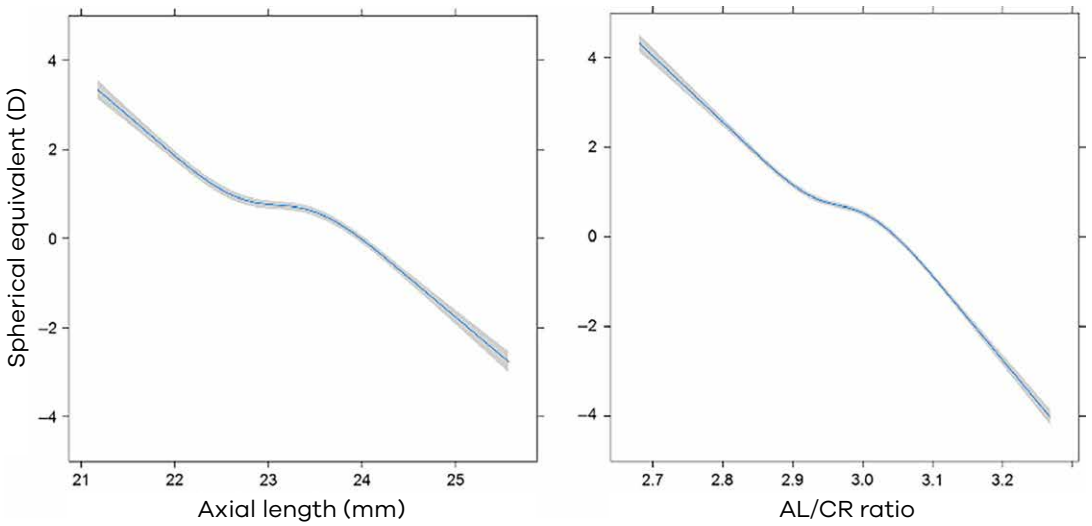
Grafiek 1. Gemiddelde aslengtegroei bij Europese kinderen naar refractie categorie

Aangezien myopie een aslengte probleem is, zou er ook op de aslengte gestuurd moeten worden. Tideman et al[70] heeft een aslengte curve gemaakt om het risico op hoge myopie vast te stellen. De aslengte van het oog kan gemeten worden met een biometer, waarbij het belangrijk is dat de metingen nauwkeurig en reproduceerbaar zijn.



Curve 1: Groeicurven met aslengte (mm) versus de leeftijd voor Europese proefpersonen, jongens (links) en meisjes (rechts), met het risico op myopie op volwassen leeftijd.

Indien de aslengte niet overeen komt met de gevonden sterkte , moet er verder onderzoek gedaan worden naar de oorzaak van de myopie, bijv topografie om keratoconus uit te sluiten.



Curve 2: links verhouding aslengte (mm) en sferisch equivalent (d), rechts AL/CR ratio[70]

Een aantal klinische behandelingen worden op dit moment toegepast om de myopie progressie bij kinderen af te remmen. Er is nog geen behandeling gevonden die de progressie helemaal stopt. De klinische behandeling voor myopie management kan verdeeld worden in farmatherapeutische behandeling en optische behandeling. Om te overwegen of een behandeling zinvol is, moet het de myopie progressie met minimaal 50% afremmen.[50-52] Daarnaast zijn ook levenstijladviezen belangrijk voor beide groepen.

Een behandeling is succesvol te noemen als de aslengte niet meer dan 0.25mm groeit in de leeftijd van 6-9 jaar, 0.15mm in de leeftijd 10-13 jaar en 0.1 in de leeftijd 14-18 jaar. Als er toch meer aslengte groei is, moet er overwogen worden om de therapie aan te passen. Bijvoorbeeld overstappen naar een hogere dosering atropine of een combinatietherapie instellen. (protocol Erasmus MC 2020)

Door de verschillende factoren die meespelen is het belangrijk dat we iedere myoop individueel beoordelen. Zijn er specifieke omgevingsfactoren, levenstijlfactoren en/of komt er myopie in de familie voor (genen). Dit stelt ons in staat een betere behandeling op ieder individu af te stemmen.

1. Farmatherapeutische behandeling

Atropine is het meest gebruikte medicijn voor myopie management, met name in Azie. Tabel 1 geeft een samenvatting van klinische onderzoeken van myopie management bij gebruik van atropine en pirenzepine. Atropine (1%) oogdruppels geven het meeste effect in het remmen van de myopie progressie[9-11], maar worden nauwelijks gebruikt in verband met bijwerkingen zoals fotofobie (lichtgevoeligheid) en wazig zien dichtbij. Recente onderzoeken laten zien dat lagere concentratie atropine (0.5% tot 0.01%)[12-18] ook een significant kan effect hebben op myopie progressie met minimale bijwerkingen.[14,15] Echter heeft atropine 0.01% weinig effect op de aslengte en wordt daarom in Nederland niet meer geadviseerd. Atropine 0.05% heeft een beter effect met weinig bijwerkingen en lijkt daarom de ideale dosis.[72] Bij gebruik van hoge dosis atropine is er een groter rebound effect meetbaar.[14] Het lange termijn gebruik van atropine is nog onzeker en moet verder onderzocht worden.

Tabel 1. Effect van atropine en pirenzepine op myopie progressie in vergelijking met een controle groep in de klinische onderzoeken.

References and years	Study design	Study duration (years)	Treatment methods	Control	Mean change in myopia progression (D)		Treatment effect, D
					Treatment	Control	Mean diff. (%)
Yen et al (1989)[9]	Randomised clinical trial	1	1% atropine, 1% cyclopentolate	Saline	Atropine: -0.22 Cyclopentolate: -0.58	-0.91	Atropine: 0.7 (77%) Cyclopentolate: 0.33 (36%)
Shih et al. (1999)[12]	Randomised clinical trial	2	0.5%, 0.25%, 0.1% atropine	0.5% tropicamide	0.5%: -0.04 0.25%:-0.45 0.1%: -0.47	-1.06	0.5%: 1.02 (96%) 0.25%: 0.61 (58%) 0.1%: 0.59 (56%)
Chau et al. (ATOM1) (2006)[10]	Randomised clinical trial	2	1% atropine	Placebo	+0.38	-1.20	1.58 (132%)
Fan et al. (2007)[11]	Interventiona control	1	1% atropine	No treatment	+0.06	-1.19	1.25 (105%)
Wu et al. (2011)[13]	Retrospective case–control	3	0.1% atropine	No treatment	-0.31	-0.90	0.59 (66%)
Chia et al. (ATOM2) (2012)[14]	Randomised clinical trial	2	0.5%, 0.1%, 0.01% atropine	placebo in ATOM1	0.5%: -0.30 0.1%: -0.38 0.01%: -0.49	-1.20	0.5%: 0.9 (75%) 0.1%: 0.82 (68%) 0.01%:0.71 (59%)
Clark et al. (2015)[15]	Retrospective case-control study	1	0.01% atropine	No treatment	0.0%: -0.10	-0.60	0.5 (83%)
Polling et al. (2016)[16]	Prospective and clini-cal-based study	1	0.5% atropine	Pre-treatment	0.5%: -0.10	-1.00	0.9 (90%)
Lee et al. (2016)[17]	Prospective	1	0.25%, 0.125% atropine	No treatment	0.25%: 0.00 0.125%: -0.05	-1.05	0.25%: 100% 0.125%: 95%
Wang et al. (2017)[18]	Randomised clinical trial	1	0.5% atropine	Placebo	0.5%: -0.80	-2.00	1.2 (60%)
Tan et al. (2005)[19]	Randomised double-masked	1	2% pirenzepine gel	Placebo	Pirenzepine -0.26	-0.53	0.27 (51%)
Siatkowski et al. (2008)[20]	Randomised double-masked	2	2% pirenzepine gel	Placebo	Pirenzepine -0.58	-0.99	0.41 (41%)

Pirenzepine is net zoals atropine, een muscarine antagonist, maar heeft minder cycloplegische en pupilverwijdende werking. Onderzoeken in de Verenigde Staten en Singapore laten zien dat myopie progressie wordt afgeremd met respectievelijk 51% en 77%.[19,20] Hoewel pirenzepine goede effecten laat zien op myopie management met weinig bijwerkingen van fotofobie en wazig zien dichtbij, is het niet goedgekeurd door de US Food and Drug Administration (FDA) voor myopie management en het is ook niet commercieel verkrijgbaar. In Nederland is pirenzepine ook niet toegestaan.

2. Optische middelen

2.1 Ondercorrectie

Gebaseerd op de hypothese dat verminderde accommodatie tijdens dichtbij werk, net als bifocale of multifocale glazen, is ondercorrectie overwogen als een oplossing voor myopie management. Maar uit onderzoek[21,22] blijkt dat ondercorrectie niet helpt tegen myopie progressie.

In een gerandomiseerd onderzoek werden kinderen gevraagd om een bril te dragen met een ondercorrectie die zorgde voor een visus van 6/12 op afstand. De ondercorrectie was 0.50 tot 0.75D.[21] Kinderen in de controle groep kregen volcorrectie.

Na 2 jaar had de groep met de ondercorrectie een grotere myopie progressie (-1.00D), dan de controle groep (-0.77D).

Uit een ander retrospectieve studie van 18 maanden, waarbij de data van een optometrie praktijk onderzocht is, blijkt ook dat ondercorrectie tot een grotere myopie progressie resulteert.[21]

2.2 Brillenglazen

2.2.1 multifocale en bifocale brillenglazen

Verschillende onderzoekers hebben het effect van multifocale glazen, bifocale glazen en bifocale glazen met prisma (PB), ook wel PAL's (Progressive Addition Lenses) genoemd op myopie progressie onderzocht. Ze verminderen de accommodatie voor dichtbij en er wordt gedacht dat dit de myopie progressie kan verminderen.

Het effect van PAL's op het remmen van de myopie progressie is niet klinisch significant onderbouwd (gemiddeld minder dan 0.2D per jaar) (Tabel 2).[23-28] Sommige kinderen met een esoforie en een accommodatie-lag lijken meer voordeel te hebben van PAL's[23-28], maar de resultaten zijn niet klinisch significant.

Echter, een clinical trial door Cheng et al.[29] laat zien dat in een selecte groep van snel progressieve myope kinderen, executive bifocale glazen met en zonder 3^basis nasaal een significant effect heeft vergeleken met enkelvoudige glazen. De myopie progressie kan in deze groep met 40%-50% afgeremd worden over een periode van 3 jaar en het effect is sterker wanneer er een accommodatie-lag aanwezig is.[29]

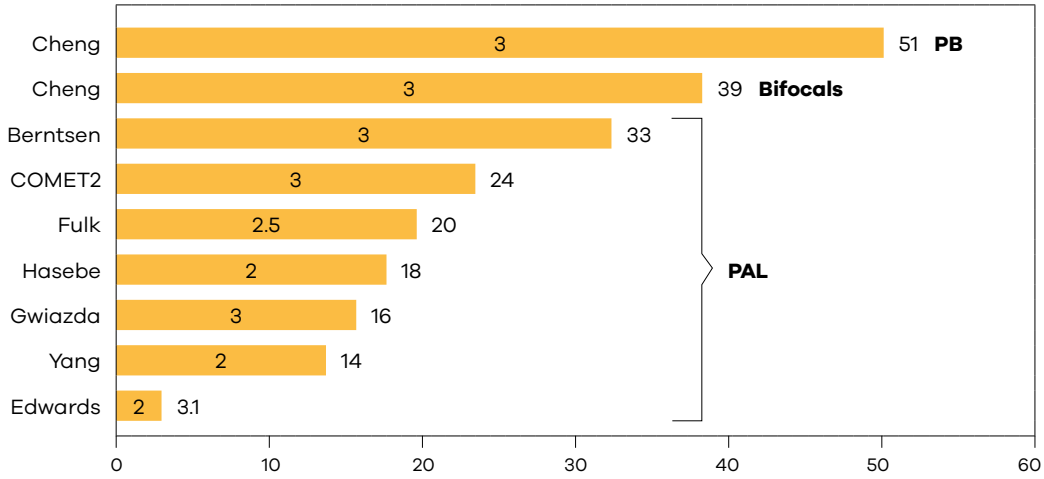
Het toevoegen van een prisma basis nasaal in de glazen was in het onderzoek een poging om de fusievergentie te verminderen om zo het effect van bifocale glazen te verbeteren. Het positieve effect hiervan is aangetoond bij verschil in sferisch equivalent. Echter, het effect van de bifocale glazen, gemeten bij verschil in aslengte, geeft geen verschil tussen wel en geen prisma. Daardoor zijn de mogelijke voordelen van prisma basis nasaal niet duidelijk genoeg. Vanwege het uiterlijk van het glas, zullen sommige kinderen deze optie niet kiezen.

Tabel 2. Myopiecontrole studies bij gebruik van PAL's

Authors and years	Study duration (years)	Design	Age (years), ethnicity	Inclusion Criteria of Rx (D)	Interventions and sample size (n)	Treatment effect in retarding myopia progression	
						Study period in D (%)	Per year in D
Edward et al. (2002)[23]	2	Randomised, double masked	7-10.5, Chinese	-1.25 to -4.5	- SV, n = 132 - PAL (1.5D Add), n = 121	0.14 (11%)	0.07
Gwiazda et al.(2003)[24]	3	Randomised, masked	6-11, diverse ethnicity	-1.25 to -4.5	- SV, n = 233; - PAL (2D Add), n= 229	0.20 (14%)	0.07
Yang et al.(2009)[25]	2	Randomised, masked	7-13, Chinese	-0.5 to -3	- SV, n=75 - PAL (1.5D Add), n=74	0.26 (17%)	0.13
COMET2 and PEDIG (2011)[26]	3	Randomised, masked, multi-centres	8 to12	-0.75 to -2.50	- SV, n =58 - PAL (2D Add), n= 52	0.28 (24%)	0.09
Berntsen et al.(2012)[27]	1	Randomised, masked, all worn SV in 2nd year	6 to11	-0.75 to -4.50	- SV, n =42 - PAL (2D Add), n= 41	0.18 (35%)	0.18
Hasbe et al.(2014)[28]	1.5	Randomised, masked, cross-over	6-12, Japanese	-1.25 to -6.	- SV, n=44; - PAL (1.5D Add), n= 42	1st period: 0.31 (18%) 2nd period: 0.02 (2%)	1st period: 0.2 2ndperiod: 0.01
Cheng et al.(2014)[29]	3	Randomised, masked	8-13, Chinese	-1 to -5.5	- SV, n=41; - BF (1.5D Add), n=48; - PBF (1.5D Add, 3ΔBI), n=46	BF: 0.81 (39%) PBF: 1.05 (51%)	BF: 0.27 PBF: 0.35
San-karidurg et al.(2011)[30]	1	Randomised	6-16, Chi-nese	-0.75 to -3.50	-type I, III lenses, SV, n = 50 each group -Type II, n =60	Type III lens: 0.29 (30% only in subgroup of children with myopic parents)	0.29 for subgroup of subjects
Lam et al. (2017)[32]	2	Randomised, masked	8-13, Chinese	-1.00 to -5.00	-SV = 90 -DIMS = 93	0.55 (59%)	0.28

COMET2 and PEDIG = Correction of Myopia Evaluation Trial 2 Study Group and the Paediatric Eye Disease Investigator Group, SV = single vision spectacle lens, PAL = progressive addition lens, BF = bifocal spectacle lens, PBF = prismatic bifocal lens, DIMS = Defocus Incorporated Multiple Segments spectacle lens

Figuur 1. Vergelijk van het effect van PAL's op de myopie progressie.[23-29] De duur van de studies is in jaren aangeduid in de balk.



Een ander voorgestelde hypothese was dat vermindering van relatieve perifere hypermetrope defocus myopie progressie kan verminderen.[30-31] Sankaridurg et al.[30] heeft een studie uitgevoerd om deze hypothese te testen door gebruik van drie glazen met een speciaal design (MyoVision™) dat de perifere hypermetrope defocus moet verminderen terwijl er centraal scherp zicht is.

Na 12 maanden werd er geen significante vermindering van myopie progressie gevonden in de behandelgroep ten opzichte van de controlegroep. Eén van de behandelglazen liet een reductie van 30% myopie progressie zien in een subgroep kinderen waarvan de ouders myoop waren. Een vergelijkbare studie met zachte contactlenzen[31] liet een beter significant effect zien en wordt beschreven onder het kopje zachte multifocale contactlenzen.

2.2.2 Nieuw type brillenglazen

Recentelijk is er een nieuwe techniek voor brillenglazen, genaamd Defocus Incorporated Mulitple Segments (D.I.M.S.) en ook Multi-Segment of Myopic Defocus (M.S.M.D.), gebruikt in een gerandomiseerde controle studie naar myopie management door Lam et al.[32]

De resultaten laten zien dat kinderen die D.I.M.S.-glazen dragen een reductie van 60% van de myopie progressie en aslengte hebben in vergelijking tot de kinderen die enkelvoudige glazen droegen.

Het D.I.M.S.-glas controleert de myopie door het principe van gelijktijdig scherp zicht en myope defocus. Het heeft centraal een optische zone voor correctie van de refractieafwijking met meerdere defocus segmentjes die voor constante myope defocus (3.50D) zorgen in de periferie. Het zorgt voor scherp zicht en myopie defocus in alle kijkrichtingen.[32]

2.3 Contactlenzen

2.3.1 Orthokeratologie

Orthokeratologie (Ortho-K) lenzen zijn harde zuurstofdoorlatende contactlenzen. Ze worden gedurende de nacht gedragen, vervormen (tijdelijk) de cornea en corrigeren lage tot matige myopie. Dit is de afgelopen decennia een veel populairdere manier geworden voor myopie management. Naast dat het overdag een scherp zicht biedt zonder hulpmiddel, heeft het ook een positief effect op myopie management. Het werkingsprincipe is dat het de myopie afremt doordat de lichtstralen in de periferie voor het netvlies vallen.[33]

Tabel 3 geeft een overzicht van de meest recente myopie management studies van Ortho-K.[34-40] De studies laten zien dat de groei van de aslengte significant vermindert met 31-63%.[34-40] Het gemiddelde behandeleffect is rond de 50% en kan het gevolg zijn van vermindering van de perifere hyperope defocus na corneavervorming.[41-42] Kinderen dragen 's nachts de lenzen terwijl ze slapen om de cornea kromming aan te passen voor een scherp zicht overdag. Echter brengt het dragen van deze lenzen een risico met zich mee. Hoewel de kans op een microbiele keratitis klein is, is de complicatie dermate ernstig dat het NOG (Nederlands Oogheelkundig Gezelschap) het dragen van deze lenzen afraadt onder de 12 jaar.[79]

Tabel 3. Overzicht van de meest recente myopie management studies van Ortho-K.

Authors and years	Study design	Study duration (years)	Control group	Mean change in AL (mm)		Treatment effect in retarding AL elongation
				Orthokeratology	Control	Mean difference (%)
Walline et al.(2009)[34]	prospective, historical controls	2	SVCL	0.25	0.57	0.32 (56%)
Kakita et al.(2011)[35]	self-selected retrospective	2	SV	0.39	0.61	0.22 (36%)
Cho et al. (2012)[36]	randomised clinical trial	2	SV	0.36	0.63	0.27 (43%)
Hiraoka et al.(2012)[37]	self-selected retrospective	5	SV	0.99	1.41	0.42 (30%)
Santodomingo-Rubido et al.(2012)[38]	self-selected prospective	2	SV	0.47	0.69	0.22 (32%)
Charm and Cho (2013)[39]	randomised clinical trial	2	SV	0.19	0.51	0.32 (63%)
Chen et al. (2013)[40]	self-selected prospective	2	SV	0.31	0.64	0.33 (52%)

SV = single vision spectacle lens, SVCL = single vision soft contact lens

2.3.2 Zachte bifocale en multifocale contactlenzen

Zachte bifocale contactlenzen met een center-distance design (worden in sommige studies dual power lenzen genoemd) kunnen ook de myopie progressie afremmen door myope defocus in de periferie te creëren.[43] De myope defocus moet ervoor zorgen dat de groei wordt afgeremd door gebruik te maken van natuurlijke optische signalen. Deze lenzen worden overdag gedragen.

Tabel 4 geeft een overzicht van klinische studies bij gebruik van zachte bifocale contactlenzen voor myopie management.[31, 44-48] Zachte bifocale contactlenzen geven een gemiddelde remming van ongeveer 50% van de myopie progressie, een vergelijkbaar resultaat met Ortho-K lenzen.

Het onderzoek door Aller et al.[47] geeft de meest belovende resultaten, een remming van de myopie progressie met 70%. Lam et al.[45] suggereert dat gebruik van DISC lenzen (Defocused Incorporated Soft Contact) bij gebruik van minimaal 6 uur per dag een groter effect op myopie management heeft, namelijk 50-60%.

Tabel 4. Klinische studies bij gebruik van zachte bifocale contactlenzen voor myopie management.

Authors and years	Study duration (months)	Study Design	Age (years old), ethnicity	Criteria of Rx (D)	Interventions and sample size (n)	Treatment effect in retarding myopia progression	
						Study period in D (%)	Per year in D
Anstice and Phillips (2011)[44]	10	Randomised, paired-eye control, cross-over	11-14, diverse ethnicity	-1.25 to -4.5	DF (Add+2D), n=40 SVCL, n=40	1st period: 0.25 (37%) 2nd period: 0.2 (54%)	1st period: 0.3 2nd period: 0.24
Sankaridurg et al. (2011)[31]	12	Randomised	7-14, Chinese	-0.75 to -3.5	RPH CL, n= 45 SV, n=40	0.29 (34%)	0.29
Lam et al.(2014)[45]	24	Randomised, masked	8-13, Chinese	-1 to -5	DISC (Add+2.5D), n=65 SVCL, n =63	0.21 (25%) 0.44 (50%) >6 hours 0.54 (58%) >7 hours 0.53 (60%) >8 hours	0.11
Paune et al.(2015)[46]	24	Prospective, nonran-domised	9 to 16, Cau-casian	-0.75 to -7	SRRG, n = 30 OK, n= 29 SV, n = 41	0.42 (43%)	0.21
Aller et al. (2016)[47]	12	Randomised, masked	8-18,	-0.50 to -6	BFSCL, n=39 SVCL, n=-40	0.57 (72%)	0.57
Cheng et al. (2016)[48]	24 (only 12 month data)	Randomised, masked	8-11	-0.75 to -4	+SA, n= 64 SVCL, n=63	6-month: 0.21 (56%) 12-month: 0.12 (20%)	0.16

DF = dual focus contact lens, SVCL = single vision contact lens, RPH CL = contact lens designed to reduce relative peripheral hyperopia, SV = single vision spectacle lens, DISC = Defocus Incorporated Soft Contact (DISC) lens, SRRG = soft radial refractive gradient contact lens, OK = orthokeratology, BFSCL = bifocal soft contact lens, +SA = soft contact lens with positive special aberration

3. Andere methodes voor myopie management en het afremmen van myopie progressie

3.1 Buitenactiviteiten

Recent epidemiologische studies hebben ontdekt dat kinderen die meer tijd buiten de deur besteden minder snel myoop worden of minder myopie progressie hebben, ongeacht de hoeveelheid dichtbijwerk en/of ouders die myoop zijn.[53-58] Er zijn ook aanwijzingen voor een positief effect van buitenactiviteiten bij jong volwassenen.[59]

Een longitudinaal onderzoek in Taiwan moedigde kinderen op een basisschool aan om tijdens de pauze naar buiten te gaan (behandelgroep), terwijl kinderen op andere scholen hun normale pauze routine hielden (controlegroep).[60]

De hoeveelheid myopie die na één jaar was ontstaan was significant hoger in de controlegroep (18%) dan in de behandelgroep (8%, $p<0.001$). De myopie was ook hoger in de groep die hun normale pauze-routine hielden (-0.38D/jaar) dan in de groep die werd aangemoedigd deel te nemen aan buiten activiteiten (-0.25D/jaar).

- Andere studies hebben ook aangetoond dat buitenspelen zorgt voor een remming van de aslengte groei bij zowel myope als niet myope kinderen.[75,76]

Hoe het mechanisme werkt dat bij buitenactiviteiten het oog beschermt tegen de ontwikkeling van myopie is nog onbekend. Echter, er zijn verschillende theorieën, zoals dat het ontspannen van de accommodatie bij het kijken op afstand in de buitenomgeving meer myope defocus geeft.

Een andere mogelijke factor is het duidelijke verschil in lichtintensiteit tussen buiten en binnenomgevingen.[61] Zonlicht heeft een veel hogere lichtintensiteit (15.000 lux) dan de meeste binnenverlichting (500 lux). Een ander alternatief is dat door pupilvernauwing bij hoge lichtintensiteit zorgt voor minder beeldverstrooiing op het netvlies, waardoor het signaal voor groei veroorzaakt door beeldvervaging op het netvlies wordt verminderd.

Tideman et al[73] heeft de relatie van vitamine D op aslenge en myopie onderzocht bij kinderen van 6 jaar oud. Lagere concentratie vitamine D waren geassocieerd met langere aslengte en een hoger risico op myopie.

- Dierstudies over myopie suggereren dat de hoge lichtintensiteit buiten mogelijk ook een beïnvloedende factor is.[61,62] Van natuurlijk daglicht is bekend dat het de afgifte van retinale dopamine stimuleert, wat een belangrijke neurotransmitter is bij de controle van de groei van het oog. In feite wordt myopie meestal veroorzaakt door een verhoogde aslengte op jongere leeftijd. De dierstudies tonen aan dat dopamine-agonisten de ontwikkeling van myopie remmen, terwijl dopamine-antagonisten het zicht korte periodes blokkeert om vormdeprivatie myopie te voorkomen.[63]

Naast de lichtintensiteit, kan ook de samenstelling van het zonlicht een rol spelen bij myopie management. Zonlicht is gekenmerkt door overvloedig zichtbaar licht met korte golflengte, zoals blauw in plaats van rood.[64] Dierstudies hebben aangetoond dat blauw licht een remmend effect heeft op myopie.[65,66] Onlangs stelden Torri et al.[67] voor dat violet licht (VL), dat niet aanwezig is in binnenruimtes, een rol kan spelen bij de ontwikkeling en het afremmen van de myopie progressie. Ze hebben aangetoond dat het VL een remming geeft van de myopie progressie en de aslengte bij kuikens.

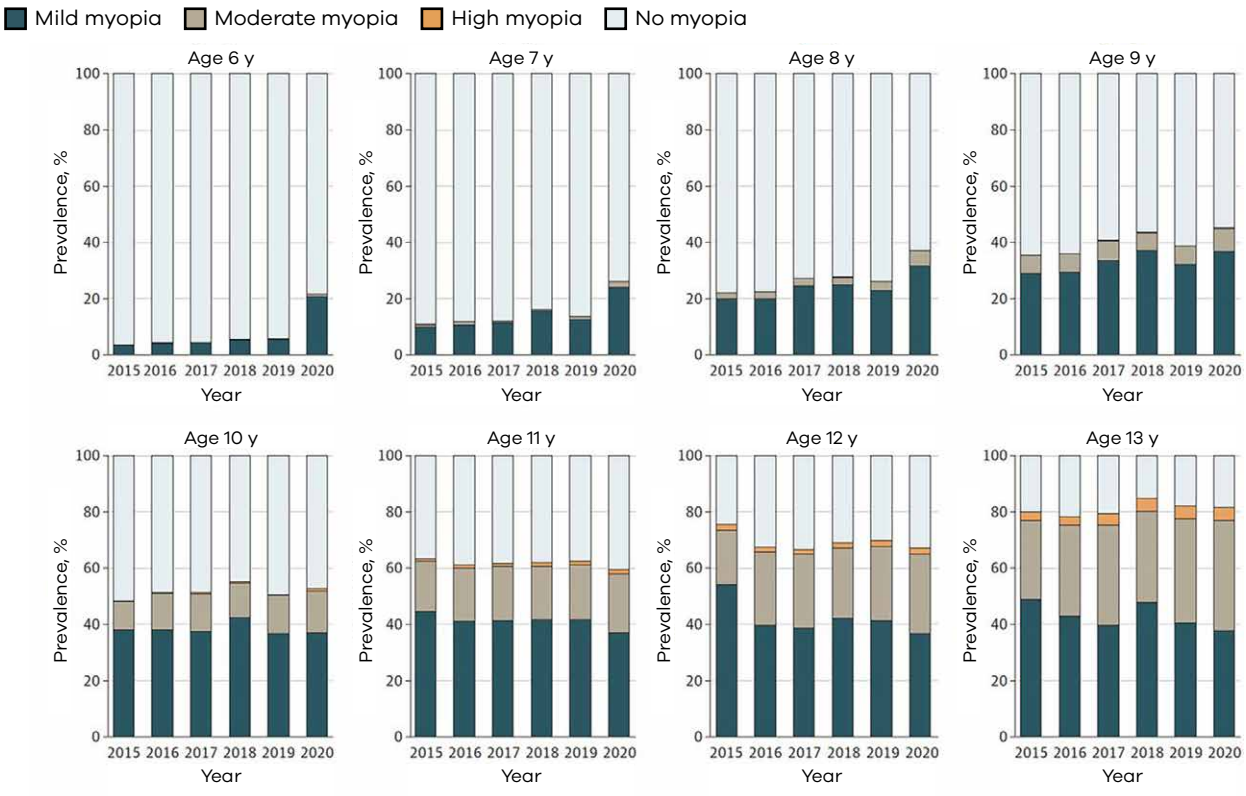
Op basis hiervan is een klinisch onderzoek uitgevoerd bij myope kinderen.

Een groep moest VL blokkerende glazen dragen, gedeeltelijk VL blokkerende contactlenzen of VL doorlaatbare contactlenzen. Verschil in aslengte werd na een jaar vergeleken. De resultaten laten zien dat kinderen die VL doorlaatbare contactlenzen hadden gedragen significant minder toename van de aslengte hadden in vergelijking met de andere groepen. Deze data bewijst dat VL kan bijdragen aan de bescherming van myopie progressie.

3.2 Binnenactiviteiten

Uit onderzoek van Tideman et al blijkt dat kinderen die meer dan 1 boek per week lezen een hoger risico hebben op myopie.

Uit een onderzoek naar het effect van Covid-19 blijkt dat de prevalentie myopie in de leeftijd 6-9 jarige sterk toegenomen is (zie afbeelding).[74] Het idee hierachter is dat we door Covid-19 minder buiten waren en de schermtijd toegenomen is. Huang et al heeft een meta-analyse uitgevoerd naar de relatie tussen dichtbij werk en myopie. Wanneer er meer tijd werd besteed aan dichtbij-activiteiten werd dit geassocieerd met een hogere kans op myopie en toename van myopie. Het verminderen van dichtbij-werk bij kinderen is belangrijk om myopie bij kinderen te voorkomen.



The prevalence of mild myopia increased in 2020 compared with previous years in children aged 6 to 8 years. Mild myopia: -3 diopters (D) < spherical equivalent refraction (SER) ≤ -0.5 D; moderate myopia: -6 D < SER ≤ -3 D; high myopia: SER ≤ -6 D; and no myopia: SER> -0.5 D.

3.3 Effectiviteit van myopie management

Verschillende studies hebben een meta-analyse uigevoerd over de effectiviteit van verschillende behandelingen en methodes voor myopie management.[50-52, 68]

Een review van negen gerandomiseerde controle onderzoeken waarin de effectiviteit van multifocale glazen en enkelvoudige glazen werden vergeleken, toonde aan dat multifocale glazen

met een additie van S+1.50 tot S+2.00D, geassocieerd zijn met een statisch significante afname van de myopie progressie bij schoolgaande kinderen.

Het effect is hoger bij kinderen waarvan de myopie bij aanvang van het onderzoek hoger was, het is gedurende een periode van 2 jaar of meer gevolgd.

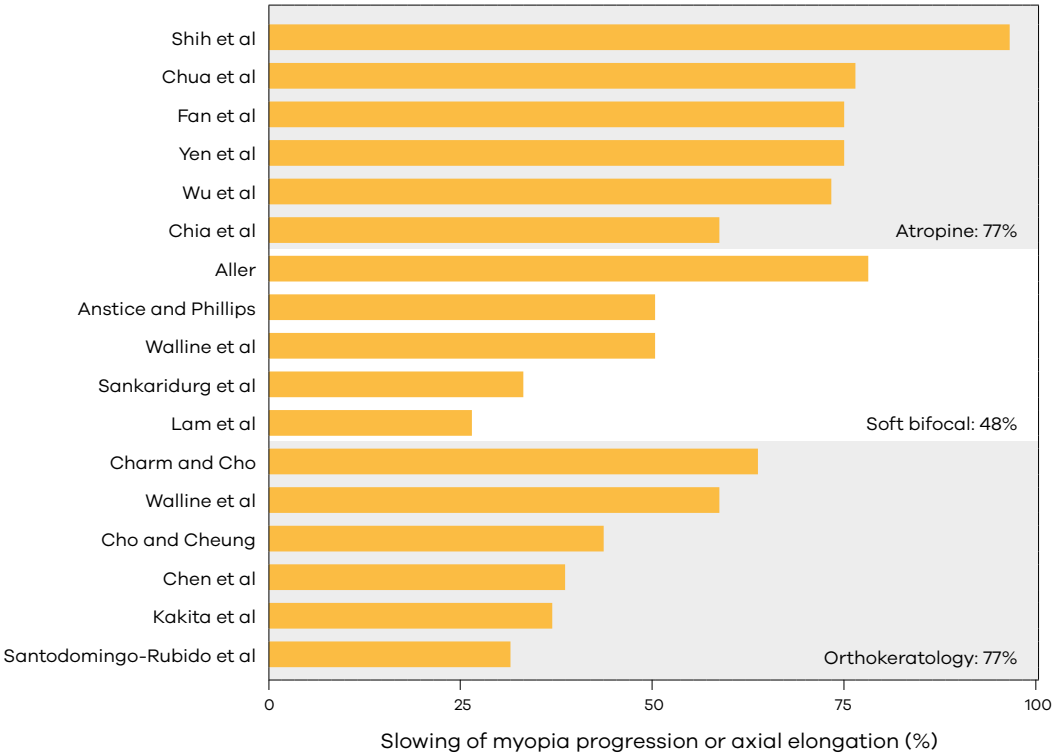
Een meta-analyse van 6 klinische studies naar de effecitiviteit van atropine op myopie management laat zien dat atropine myopie progressie afremt met 0.773D per jaar vergeleken met placebo behandelingen.[69] De analyse suggereerde ook dat er een dose-response relatie is tussen atropine en myopie, waarbij werd geconcludeerd dat 0.5% en 1% effectief blijken te zijn bij kinderen. Er zijn echter bijwerkingen geassocieerd met deze dosis zoals, lichtgevoeligheid, wazig zien dichtbij, glare en allergische blefaritis.

Een stude die de effectiviteit van atropine, zachte bifocale contactlenzen en ortho-K lenzen heeft vergeleken indiceert dat zowel zachte bifocale contactlenzen als ortho-K lenzen een effectiviteit van +/- 50% laat zien terwijl dat voor hoge dosis atropine >75% is. Figuur 2 toont de vergelijking tussen de verschillende behandeleffectiviteiten.[50]

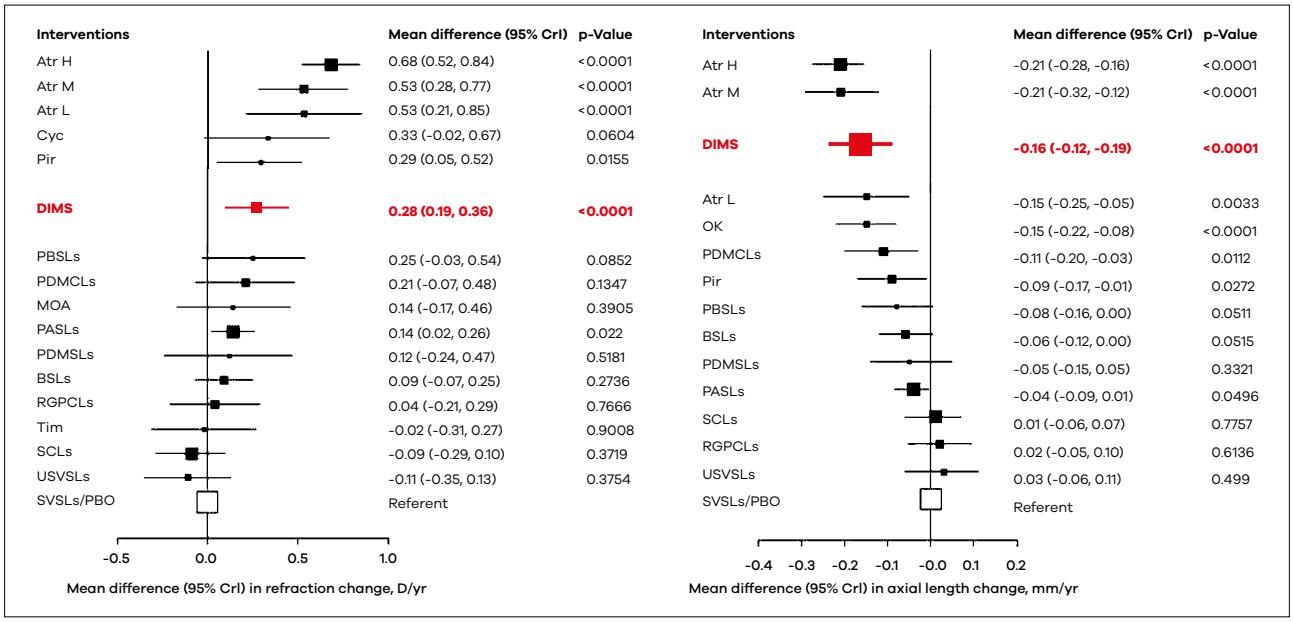
- Een andere recente studie (Figuur 3) vergelijkt de effectiviteit van farmatherapeutische en optische behandelingen voor myopie management bij kinderen. Het concludeert dat atropine, pirenzepine, ortho-K, zachte contactlenzen met myopie management kenmerken en multifocale glazen een effectieve en significante remming van de myopie progressie laten zien in refractie en/of aslengte.

De farmatherapeutische behandeling levert gemiddeld een behandeleffect op van ongeveer 50%. De behandeling met glazen levert een minimaal effect op voor mulitfocale glazen[25-27] en een matig effect voor executive bifocale glazen.[29] De onderzoekers hebben ook een random effects network meta-analyse uitgevoerd, waarbij het directe en indirecte bewijs werd gebruikt om de verschillende behandelingen te vergelijken met enkelvoudige glazen/placebo behandelingen.[52] Atropine als behandeling voor myopie management bleek het meest effectief te zijn en geeft een gemiddelde remming van 0.5 tot 0.6D per jaar.

Figuur 2. Vergelijking van behandeleffect met atropine, zachte bifocale contactlenzen en ortho-K lenzen bij myopie management extracted from Smith MJ, Walline JJ. Controlling myopia progression in children and adolescents. Adolesc Health Med Ther. 2015 Aug 13; 6:133-40.)

- 

Figuur 3. Vergelijking van effectiviteit van farmatherapeutische en optische behandelingen voor myopie management bij kinderen.



Huang J, Wen D, Wang Q, et al. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. Ophthalmology. 2016;123:697-708. D.I.M.S. data: Lam CSY, Tang WC, Tse DY, Lee RPK, Chun RKM, Hasegawa K, Qi H, Hatanaka T, To CH. Defocus Incorporated Multiple Segments (D.I.M.S.) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. British Journal of Ophthalmology. Published Online First: 29 May 2019. doi: 10.1136/bjophthalmol-2018-313739

Conclusie

Samenvattend zijn farmatherapeutische behandeling met hoge dosis atropine relatief meer effectief (>70%) dan optische behandelingen met contactlenzen of brillenglazen. Echter de bijwerkingen van atropine, zoals lichtgevoeligheid en wazig zien dichtbij, belemmeren de klinische toepassing. Lage concentatie atropine kan veelbelovend zijn voor myopie management met weinig bijwerkingen.

Voor optische behandelingen met PAL's en multifocale glazen zijn geen klinisch betekenisvolle effecten op het vertragen van de myopie progressie. Slechts één enkele studie bij gebruik van prismatische bifocale glazen laat een matig behandeleffect zien op de myopie progressie.

Ortho-K lenzen, zachte bifocale contactlenzen en de zeer recente D.I.M.S.-brillenglazen laten wel een klinisch significant behandeleffect zien (~50% to 60%). Deze methodes bevestigen dat myope defocus de ooggroei kan afremmen en myopie management door verschillende optische designs mogelijk is.

Hoewel er verschillende klinische methodes bestaan voor myopie management, variëren de effecten en geen van de methodes stopt de myopie progressie volledig. De meest geschikte behandelmethode moet worden bepaald door de oogzorgprofessional samen met het kind/ouders en zal gebaseerd zijn op leeftijd, myopie ouders ja/nee, snelheid van progressie, gezondheid van het hoornvlies en levensstijl van het kind.

Natuurlijk gaat de voorkeursoplossing naar het helemaal voorkomen van myopie bij kinderen. Grote studies hebben aangetoond dat de prevalentie van myopie bij kinderen die tijd besteden aan buitenactiviteiten aanzienlijk lager is dan bij kinderen die dat niet doen. Hoewel het onderliggende mechanisme van dit effect niet bekend is, is het een simpele manier om myopie te voorkomen door meer naar buiten te gaan, bijvoorbeeld tijdens schooltijd (in de pauze etc).

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Review artikel

Rol van accommodatie en binoculair zien

Het ontstaan van myopie en de progressie van myopie blijken gerelateerd te zijn aan een verhoogde accommodatie-convergentie/accommodatie (AC/A) verhouding welke kan worden waargenomen voordat myopie ontstaat. De theorie stelt dat een slechte of onnauwkeurige accommodatie met hoge accommodatielag, die als gevolg perifere hyperope defocus veroorzaakt tijdens kijken op korte afstand, een stimulans kan zijn voor axiale ooggroei. [1]

Een normale AC/A verhouding ligt tussen de 3:1 en 5:1. Een hoge AC/A verhouding is >5:1.[2]

Mutti en collega's ontdekten dat een verhoogde AC/A verhouding een risicofactor is voor het ontstaan van myopie en geassocieerd werd met een hogere accommodatie lag. Tijdens een 3-jarig follow up onderzoek onder myope kinderen was de accommodatie stimulus significant lager bij de snellere progressie (0.3D) dan bij de langzamere progressie (1.5D). De AC/A verhouding van de personen die myoop werden, begonnen 4 jaar voordat de diagnose myopie gesteld werd toe te nemen, en bleef aanhouden tot de diagnose gesteld werd, maar was niet van invloed op de verdere progressie.[1]

Accommodatielag van meer dan 1D komt vaker voor bij dichtbij kijken, zowel bij emmetropen als myopen. Een accommodatielag betekent niet meteen dat er ook een verminderde visus voor dichtbij is. De behoefte aan accommodatie hangt af van het bereik van scherp zicht dat wordt beïnvloed door monofocale en chromatische abberaties, pupilgrootte en neurale factoren.

Een hogere accommodatielag bij dichtbij kijken (welke hoger kan zijn bij myope kinderen als gevolg van de korte werkafstand) kan de (perifere) hyperope defocus vergroten bij myope ogen.

Binoculair zien is belangrijk bij het vormen van de afbeelding op het netvlies. Binoculair zien verbeterd de accommodatie respons op defocus en omgekeerd kan wazig zien als gevolg van defocus een nuttige aanwijzing zijn in het binoculair zien. Dit effect kan anders zijn bij myopen.

- Theoretisch gezien zorgt een hogere AC/A voor een verschuiving richting esoforie bij dichtbij-werk bij myope kinderen. De positieve fusionele vergenties zijn hoger bij progressieve myopen. Onderzoekers hebben nog geen duidelijk beeld van de rol van het accommodatiesyteem en de behandeling hiervan op dit gebied. Op basis van de huidige gegevens zouden oogzorgproffesionals moeten overwegen om het accommodatie-convergentie systeem te beoordelen bij jonge myopen en kinderen met het risico op het ontwikkelen van myopie, om ervoor te zorgen dat deze kinderen behandeld worden om een scherp zicht op het netvlies te geven.[3]

Kinderen en jong volwassenen met myopie vertonen ook verminderde accommodatiemogelijkheden en een hogere accomodatie convergentie vergeleken met emmetrope leeftijdsgenoten. Verminderde accommodatie bij myopie kan het functionele gevolg zijn van de anatomie door equatoriale vergroting in het oog. Sommige studies geven aan dat een hogere accommodatielag een voorspeller kan zijn voor myopieprogressie bij kinderen en jong volwassenen, terwijl anderen dat niet doen. Hoewel abnormale binocullariteit een risicofactor kan zijn voor myopieprogressie, heeft geen van de onderzoeken een extra effect op de risicobeoordeling laten zien in vergelijking met: brekingsfout en axiale lengte, erfelijkheid of omgevingsfactoren.[1]

Een pre-myoop is een persoon die op korte termijn kans heeft om een myopie te ontwikkelen. Bijvoorbeeld een hypermetropie van S+0.75 of minder op een leeftijd van 6 jaar indiceert dat myopie zich op korte termijn kan ontwikkelen.

Gegevens uit een onderzoek van McCullough et al. laat zien dat een aslengte groter dan 23.07 op 6-7 jarige leeftijd geasscocieerd is met een hoog risico op myopie in de toekomst. Kinderen met een hoog risico moet geadviseerd worden om meer tijd buiten door te brengen, aangezien dat het belangrijkste wetenschappelijk bewijs is dat effectief lijkt in het verminderen van de incidentie van myopie. 4

Leeftijd (jaren)	6	7-8	9-10	11
Refractie	S+0.75 of minder	S+0.5 of minder	S+0.25 of minder	S+0.00

Tabel 1: Leeftijdsgrenswaarden op basis van een etnisch divers Amerikaans onderzoek van meer dan 4.500 kinderen.4

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Review artikel

Optical modulations of refractive development in animal models of myopia

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Introduction

During development, our body parts actively regulate their size and shape. The eye, as the most important sensory organ, experiences a fundamental regulatory challenge that it must matches its axial length to the combined optical power of its refractory components. Intriguingly, the eye is not only the first organ responsible for forming vision perception; the eye itself is also being shaped by vision.

- The present literature review first describes how the use of animal models has contributed to understanding of the role of visual environment in controlling ocular growth. Secondly, it discusses the various scientific evidences for the existence of an active feedback mechanism that constantly align the position of retina to the focal plane of the eye. Lastly, the review specifically examines the experiments which collectively suggested that visual experience can be manipulated for inhibiting excessive eye growth by introducing defocused optical image anterior to the retina through the use of dual-power lenses. Such optics, named "myopic defocus", provides a basis for the subsequent development of contact lenses and spectacle lenses designed for the purpose of controlling myopia progression in children and teenagers.

Earlier literatures on the induction of refractive error

In more than 150 years ago, *Cohn* stated that "myopia is a result of too much close work".[1] However, there was no scientific evidence to prove myopia is a result of controllable environmental conditions. Therefore, for many years, the consensus was that myopia was by-and-large genetically determined.

- The earliest experimental evidence about the influence of visual environment on myopia development can be traced back to the 1960s. *Young* reported that monkey raised in restricted visual space developed myopia.[2] In late 1970s, scientists designed experiments to assess the consequences of visual form deprivation on the cellular receptive-field properties in the central visual pathway.[3,4] Originated from unintended findings, chicks[5], cats[6], tree shrews[4], and rhesus monkeys[7] were subsequently developed as experimental models of myopia (fig. 1). Such visual form deprivation was mostly carried out by suture of eye lids, or placement of translucent diffusers over eyes (fig. 2). Chicken, for example, developed over 20 dioptres of myopia within two weeks with ocular elongation of >2mm following form deprivation. A-scan ultrasonography revealed that elongation of the vitreous chamber is the common major structural change among the animal models. Similar to the myopia in human, thinning of the choroid and fibrous sclera were also observed.[8-11] The key lesson from the experimental myopia following visual form deprivation is that visual exposure during the early stage of development provides critical information for the eye to reach their normal near-emmetropic state.

Emmetropization: the active regulatory mechanism

Generally speaking, naturally occurring refractive errors are scarce and small in magnitude among both wild and domesticated animals including pigeon[12], chick[13], tree shrew[14], rhesus monkey[15], fish[16], marmoset[17], and guinea pig.[18] The early natural refractive development in most animal models happens to be similar to human refractive development in terms of refractive distribution. Refractive error generally showed a board distribution at birth in monkeys, at eye opening in tree shrews, and at hatching in chicks. But with time, their refractive errors approaches emmetropia from hyperopia with a reduced variability between animals.[19,20] This findings were similar to the narrowing of dispersion of refractive errors (fig. 3) with age in children.[21,22] Such phenomenon coined the term "emmetropization", which implies that axial elongation and/or the optical components are regulated to match the focal plan with the retina. Initially, it was controversial whether emmetropization was a passive result of development or was a result of actively feedback mechanism. The increasing number of studies using animal models have provided the definitive evidences that the process is active, and that a visual feedback mechanism regulates the axial dimension primarily through modulating the vitreous chamber depth.

Compensation for hyperopic and myopic defocuses

Interventions that move the image plane behind the retina (hyperopic defocus) promote axial elongation. In contrast, interventions that shift the image plane in front of the retina (myopic defocus) cause inhibition of axial eye growth. These indicated that the eye has the capability to detect the relative positions of image plane, and accordingly alter its rate of axial growth to re-approach the state of emmetropia. The fact that compensations can be quite accurate over a range of induced defocus[23-25] strongly suggests the existence of an active and precise regulation of the axial dimensions by visual inputs.

When a negative lens is fitted over a developing eye (fig. 4), the eye responds and compensate rapidly with an accelerated rate of growth until the imposed defocus is being neutralized.[23,26] In other words, the experimented eye approached emmetropia under the lens and became intrinsically myopic after removal of the lens. Therefore, it is commonly known as lens-induced myopia (LIM). Conversely, when a positive lens is fitted over a developing eye, the eye responds by compensating with an inhibited rate of axial growth until the imposed defocus is being neutralized. The experimented eye developed relative emmetropia under the lens but became intrinsically hyperopic after removal of the lens. This manipulation is therefore called lens-induced hyperopia (LIH). Both LIM and LIH are closed loop system as the processes terminate when the adjusted rates of growth have fully compensated for the imposed lens power. It is generally accepted that the compensatory growth responses are stimulated by the sign or the magnitude of defocus, which is detected by the retina, although the exact underlying mechanisms are not completely clear.

The compensation for lower powered positive lenses (LIH) was found to be qualitatively consistent across animal species. It slowed axial elongation in chicks[27], tree shrews[28] and macaque monkeys.[25] When the power of the positive lenses was higher, different species demonstrates different responses. For lens powers of +10D to +15D, chick eyes still underwent hyperopic growth.[27] Rhesus monkeys showed insignificant refractive changes when exposed to binocular treatment of high powered positive lens.[15] Tree shrews, however, developed relative myopia when exposed to high powered positive lens as if they were under visual form deprivation.[28] Further experiment has shown that monkey[15] was also capable to compensate for stronger lenses when the power was increased stepwise. These results suggested that different species have different operative range of emmetropization towards imposed myopic defocus.[29] Apparently, chicken has a wider range. It may be due to their smaller body size, shorter viewing distance or the presence of a stronger choroidal compensatory mechanism.

The range of operation towards imposed hyperopic defocus (LIM) in higher primate is not so limited in comparison, because the eyes are usually fitted with lenses with powers within their accommodative capacity of the eye. And that the animals may exert accommodation to partly neutralize the imposed hyperopic defocus to produce focused images at least for part of the time.

Role of Accommodation

Based mainly on clinical observations, one of the earlier hypotheses for the cause of myopia was that myopia is caused by increased accommodation during protracted near work.[30] Such notion was supported by the finding that atropine (one of the common cycloplegics) inhibited myopia in monkeys.[31] Nevertheless, subsequent animal studies showed that atropine also blocked experimental myopia in an avian model in which it cannot block accommodation[32], suggesting that the effect of atropine was mediated via a non-accommodative mechanism. Furthermore, compensation to imposed defocus has been shown to persist when accommodation is surgically or pharmacologically eliminated.[33-35] These evidences strongly suggest that accommodation is not crucial for emmetropization. However, the accuracy (lead/lag) of accommodation may still indirectly influence the development of myopia as it determines the magnitude and amplitude of defocus imposed on the retina.

Dimensional changes in ocular structures

Sclera forms the outer coat of the eye, defining its shape and size. In vertebrates, sclera generally comprises an inner cartilaginous layer and an outer fibrous layer. In primates, only the outer fibrous layer is present. It composed primarily of collagen fibrils, elastin fibrils and associated proteoglycans. In experimental myopia, there is an upregulation of degradative process, downregulation of synthesis process and consequently a loss of material in the fibrous sclera.[9, 36-40] As a result of the active remodelling of the sclera, the fibrous sclera becomes thinner[9-11,41] and more extensible[42], rendering it more readily expanded by the physiological intraocular pressure.

Choroid is the vascular layer of structure that metabolically support the sensory retina from behind. Animal studies showed that the choroid expands and thickens in volume in response to myopic defocus, pushing the photoreceptor layer forward towards the image plane. It also thins and shrinks in volume in response to hyperopic defocus, pulling the photoreceptor layer posteriorly towards the image plane. In chicks, choroidal thickness is much more obvious than the choroidal thinning percentage-wise.[8] Similar dimensional changes of choroid, but much less marked, have also been found in other species such as guinea pigs[43], marmosets[17], tree shrews[44] and rhesus monkeys.[45] With the recent advance in optical coherence tomography, similar changes has been observed in human as well.[46]

One unique feature of dimensional choroidal changes is that it compensates the imposed defocus in a relatively short amount of time, by moving the retina towards the focal plane in minutes to hours following the introduction of defocus.[47] In large mammalian species with a relatively thin choroid, dimensional changes in choroid have a smaller optical effect compared to that of smaller animals. E.g. chicks.

Local control and spatial localization

One of the most interesting aspects of emmetropization is that the feedback loop is independent of the central nervous system but is entirely within the eye. Compensation to diffuser and lens induced defocuses still occurred (with some quantitative differences) when the optic nerve had been surgically sectioned or when the action potential of ganglion cell had been pharmacologically blocked.[48-51]

Another important aspect is that emmetropization is spatially localized so that a region of the posterior globe may elongate independently. Studies have found that naturally occurring lower field myopia existed among several species including pigeon[52], toad and chicken.[53] It was proposed that this is an adaptive feature to the visual environment, allowing the animals to see various objects below and above the horizon simultaneously with little accommodative effort. Experimental study supported this notion by showing that upper field myopia was induced from housing chicks in enclosure having a low ceiling.[54] Similarly, it have been shown that compensatory changes took place in hemifields of the eye where visual form deprivation was induced through diffusers covering the corresponding halves of visual field in chicken[55], guinea pigs[56], tree shrews[57] and rhesus monkey.[58] Further evidence comes from the findings that ocular growth was retarded or accelerated regionally on the posterior eye where myopic defocus or hyperopic defocus were respectively applied using powered lenses in the conjugate visual field (fig. 5). This localized feedback have been shown in chicken[59] and tree shrews[28] and rhesus monkey.[60,61]

These localized aspects of emmetropization indicate that the major underlying signaling pathways for regulating ocular growth and myopia development lie within the eye, spanning from the retina to choroid and sclera. A detailed review of literature on the signaling pathways may be found in a previous paper.[62]

Spatial-temporal integration of emmetropization

From animal studies, it is now clear that the retina is able to detect the sign of defocus and elicit compensatory mechanical changes in choroid and sclera. It is also clear that myopic defocus is a major optical STOP signals while hyperopic defocus is a major optical GO signals. Because the natural visual environment usually comprises a combination of optical signals that changes from one occasion to another occasion (fig. 6), studying the sign of defocus experienced by the retina and their spatial-temporal interactions are critical in understanding refractive development.

In general, effects of the GO and STOP optical signals increase with the duration of the stimulation. The GO signal requires essentially constant stimulation to be effective, while the STOP signal is effective even when imposed as short periods of stimulation. Visual form deprivation was decreased by interruptions as short as 15min in chicks[63] and 1hr in monkeys.[64] Normal vision was less effective in reducing hyperopia induced by myopic defocus than reducing myopia induced by hyperopic defocus.[65] In chicks, myopic defocus tended to dominate hyperopic defocus when the eye experienced alternating defocuses of opposite directions.[66]

Animal studies has shown that emmetropization was modulated by the ratio of myopic and hyperopic defocus present in the visual space. Interestingly, myopic defocus was also found to be more potent.[67,68] Myopic defocus occupying percentages of 25% and 33% of the tested visual field were able to substantially inhibit myopia and produced hyperopia, respectively. The potential influence of the interplay of defocuses in space on myopia development was extensively discussed in a previous review.[69]

Using myopic defocus against myopia development

Although the exact mechanisms of emmetropization remains elusive, evidences from animal studies have accumulated with time and increasingly suggested that myopic eye growth could be inhibited by manipulating myopic defocus. Unlike animal experiments, it is impractical to imposed myopic defocus simply through positive lenses or by under-correcting pre-existing myopia. To translate the use of myopic defocus for controlling myopia clinically, one must satisfy the need to simultaneously provide good vision through correcting existing refractive errors. The situation becomes even more complicated as human often exert a lag of accommodation during near work, and that the STOP effect of any imposed myopic defocus would only materialize if the eye can differentiate it from the hyperopic defocus resulted from lag of accommodation.

This question was tested in our experimental animal models using concentric dual-powers lenses having multiple annuli of alternating powers, which refract incoming rays into two longitudinally distinct image shells (fig. 7). Our first trial using chicks as model has shown that refractive development of the animals was determined by the positions of both image shells in a dose-dependent manner.[67] The eye apparently can integrate information of the competing defocus stimuli and use them to modulate its growth. For example, chicks fitted with a +10D/-10D dual-power lens (with 50:50 area ratio) developed an intermediate refractive set-point slightly biased towards hyperopia. The resultant set-points were found to change with the powers of the applied competing defocuses but were always intermediates with respect to the elementary lens powers. In our second trial using guinea pigs as model, it was found that incorporating a plano (-5D/0D) or positive power (-5D/+5D) in a similar dual-power lens design induced an inhibited ocular growth and a smaller amount of myopia compare with animals that wore single vision lens (-5D) having the same negative power.[70]

In a different study on marmosets, dual-power multi-zone contact lenses of alternating powers (-5/+5D, 50:50 area) produced relative hyperopia in the treated eyes equivalent to that produced by a +5D single vision contact lenses.[71] In a recent trial on infant rhesus monkeys, the effects of dual-power spectacle lenses with alternating powers of +3D and plano (+3D/pl) or -3D and plano (-3D/pl) were tested. The +3D/pl lens induced relative hyperopia similar to that produced by a +3D single vision lens. Moreover, the -3D/pl lens induced a refractive status more hyperopic than that resulted from wearing a -3D lens.[72] To summarize, myopic defocus imposed under a dual image shell paradigm appeared to be effective in slowing axial eye growth.

Conclusion

The eye is not only the first organ for forming visual perception, the eye itself is also being shaped by vision. The present manuscript reviewed the key scientific discoveries about the optical regulation of refractive eye growth since 1960s. Many animal studies have provided solid evidences for the existence of an active feedback mechanism that constantly align the position of retina to the focal plane of the eye. Such process is now commonly known as emmetropization. The major GO optical signal of emmetropization is hyperopic defocus which is the result when optical image is formed posterior to the photoreceptor layer. The major STOP optical signal is myopic defocus, which is the result when optical image is formed anterior to the photoreceptor layer. Experiments using dual-power lens on chicks, guinea pig, marmosets and rhesus monkeys collectively suggested that myopic eye growth can be inhibited by incorporating myopic defocus on ophthalmic lenses. This forms the scientific basis for controlling myopia progression in children through incorporation of myopic defocus into corrective lenses.

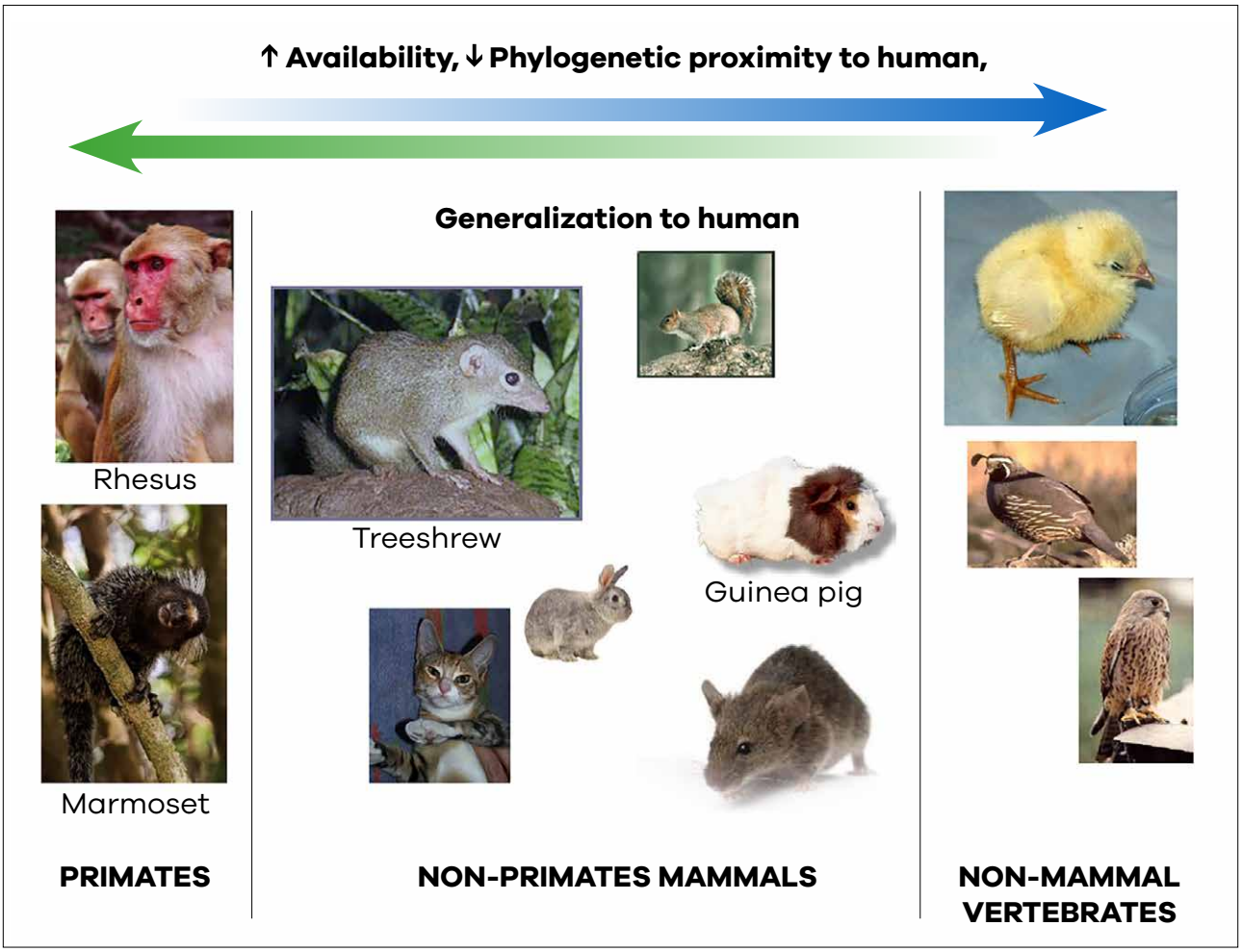

Figure 1. Animal models of myopia

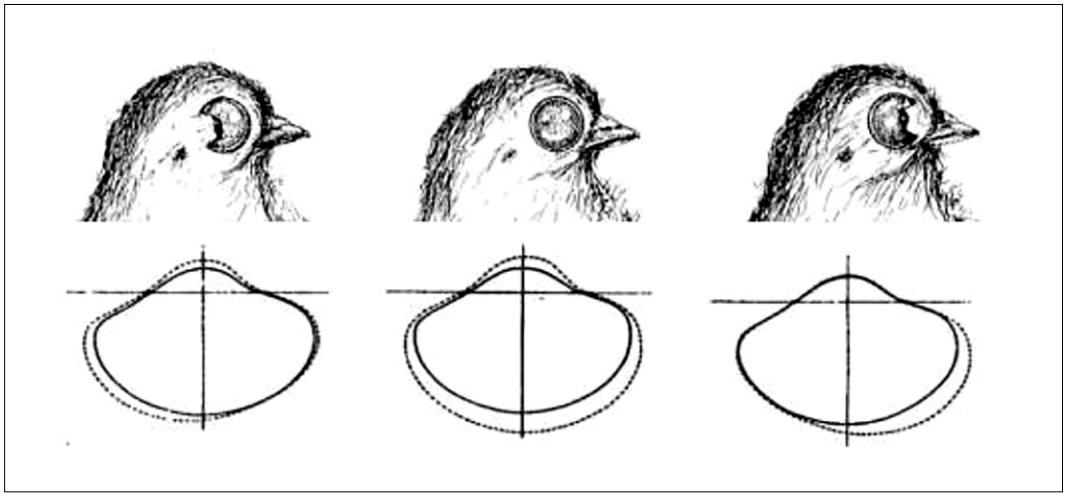

Figure 2. Visual form deprivation of chicks eyes. When chicks were raised with white translucent occluders covering their eyes so that either the nasal half, the temporal half, or all of the retina was visually deprived, the resulting ocular enlargement was limited to the deprived part of the retina, regardless of which half of the retina was visually deprived; the nondeprived part remained nearly emmetropic.

(Taken from Wallman, J, et al, *Science, 1987. 237(4810): p. 73-7.)*

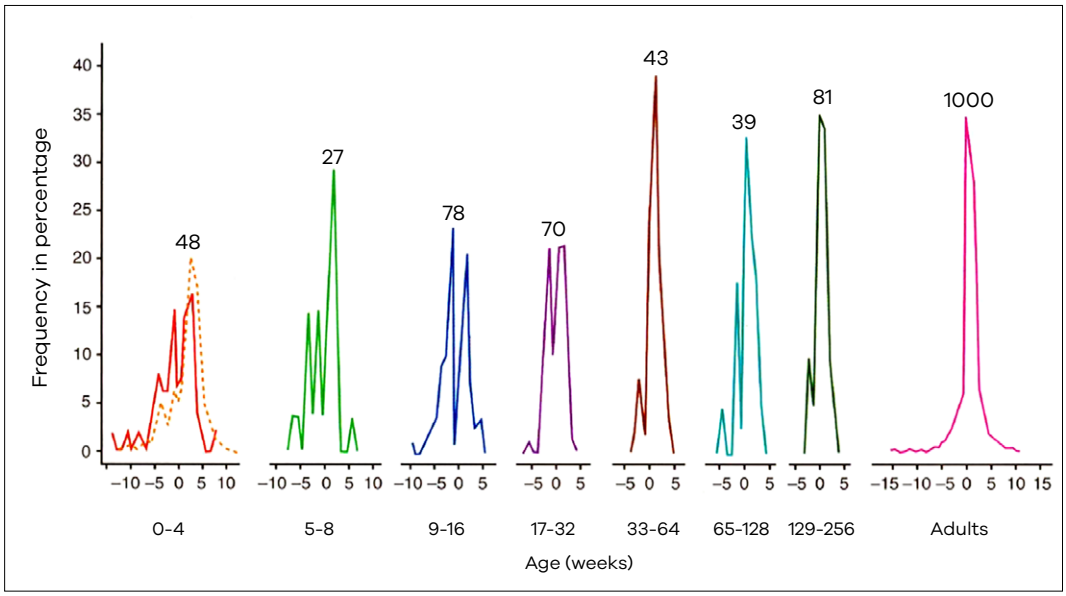

Figure 3. Narrowing of distribution of refraction during the first 5 years of life.
(Taken from Grosvenor T, Chapter 2 in Primary Care Optometry 5th edition. Butterworth-Heinemann St. Louis)

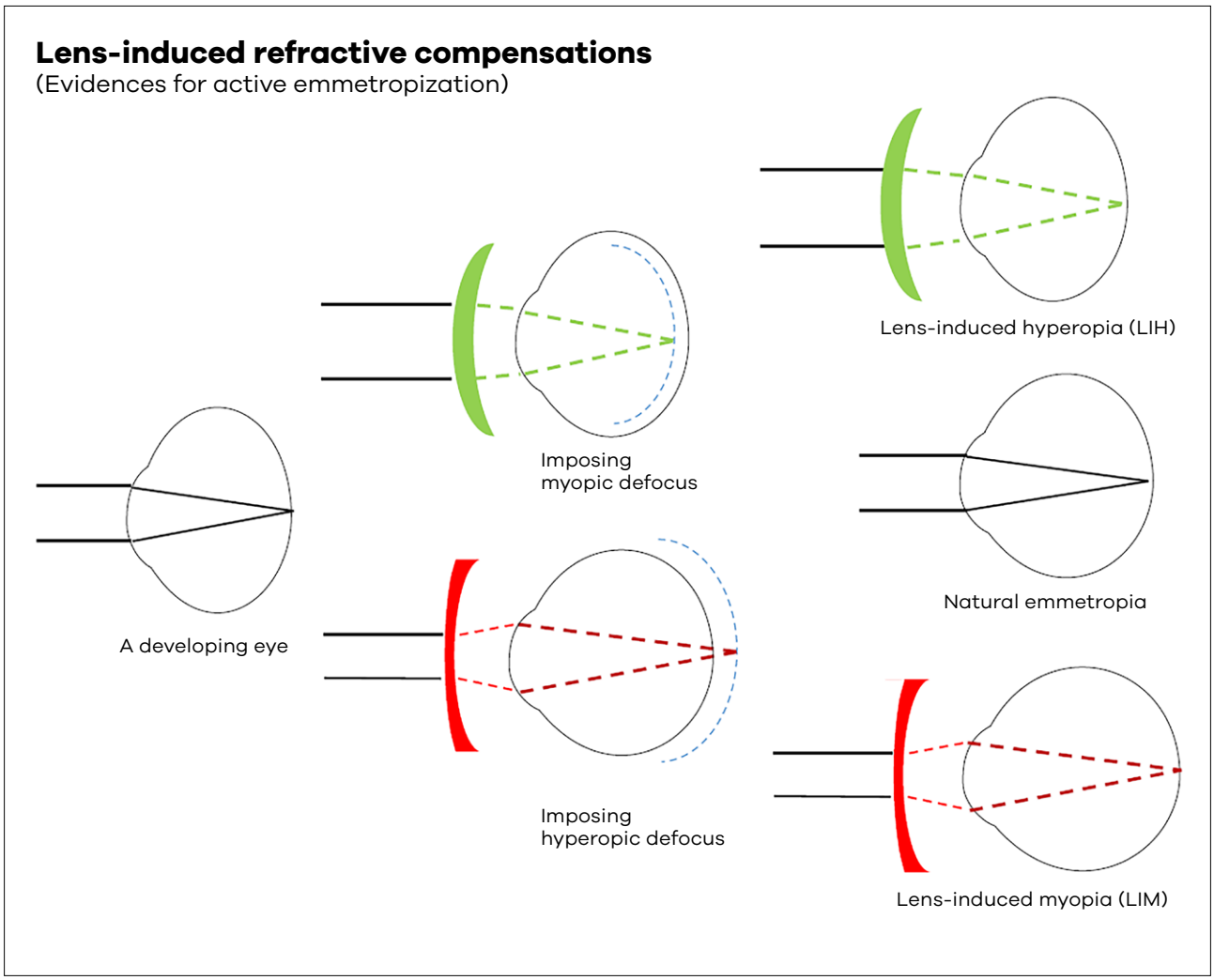

Figure 4. Schematic diagrams of lens-induced compensations (Figures drawn by Dennis Tse).

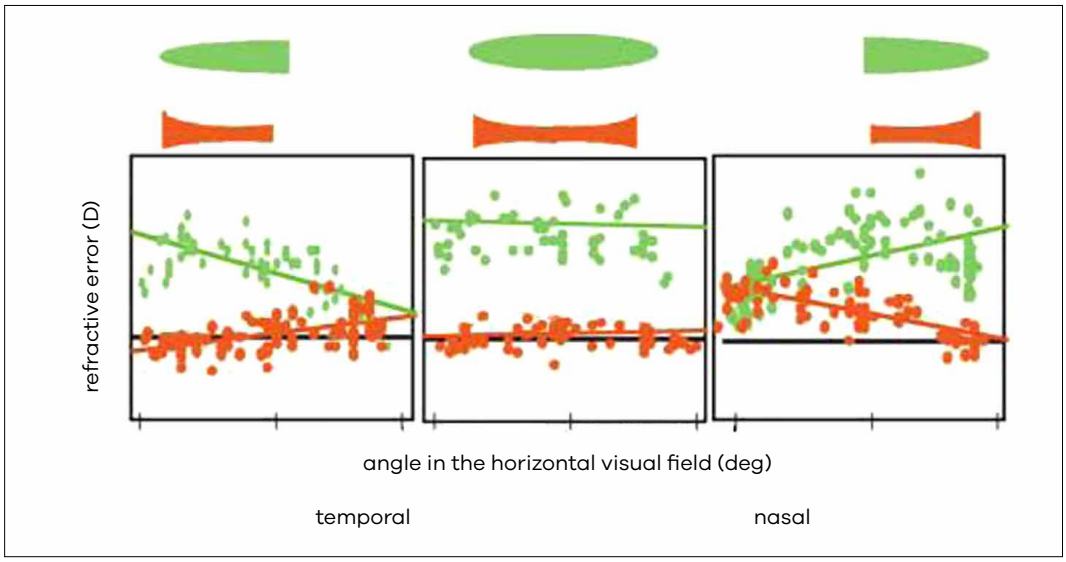

Figure 5. Refractions measured across the horizontal visual field of chicks following application of fullfield negative lenses (middle) or lens segments (left and right panel). Compensatory refractive changes were localized to the defocused half of visual field. (Taken from Diether, S and Schaeffel F, *Vision Res, 1997. 37(6): p. 659-68)*

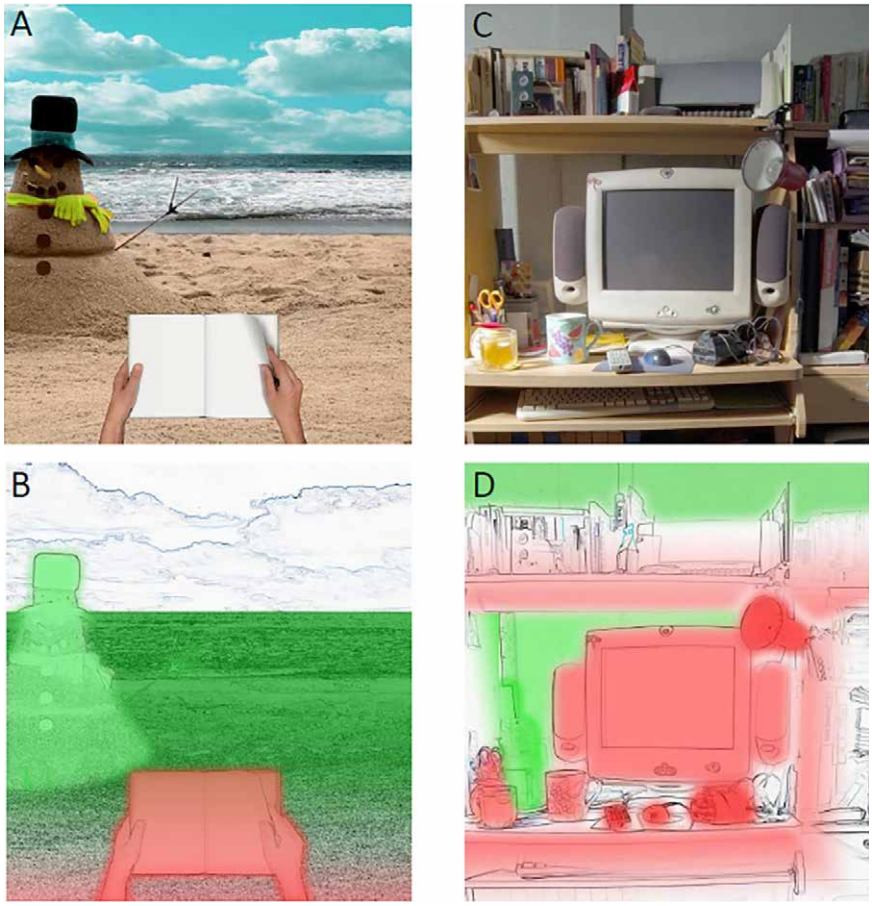

Figure 6. Examples of visual environments characterizing different profiles of simultaneous defocus. **(A)** A spacious outdoor reading environment. The subject adopts a frontal reading posture. **(B)** Map of optical defocus distribution for (A). Saturation of the colors represents relative strength of defocus. **(C)** Example of a confined indoor working environment. **(D)** Map of optical defocus distribution for (C). Saturation of the colors represents relative strength of defocus. (B, D) Green: myopie defocus; Pink: hyperopic defocus. (Taken from Tse DY, Lam CS et al. IOVS, *Vision Res, 2007. 48(12): p.5352-9)*

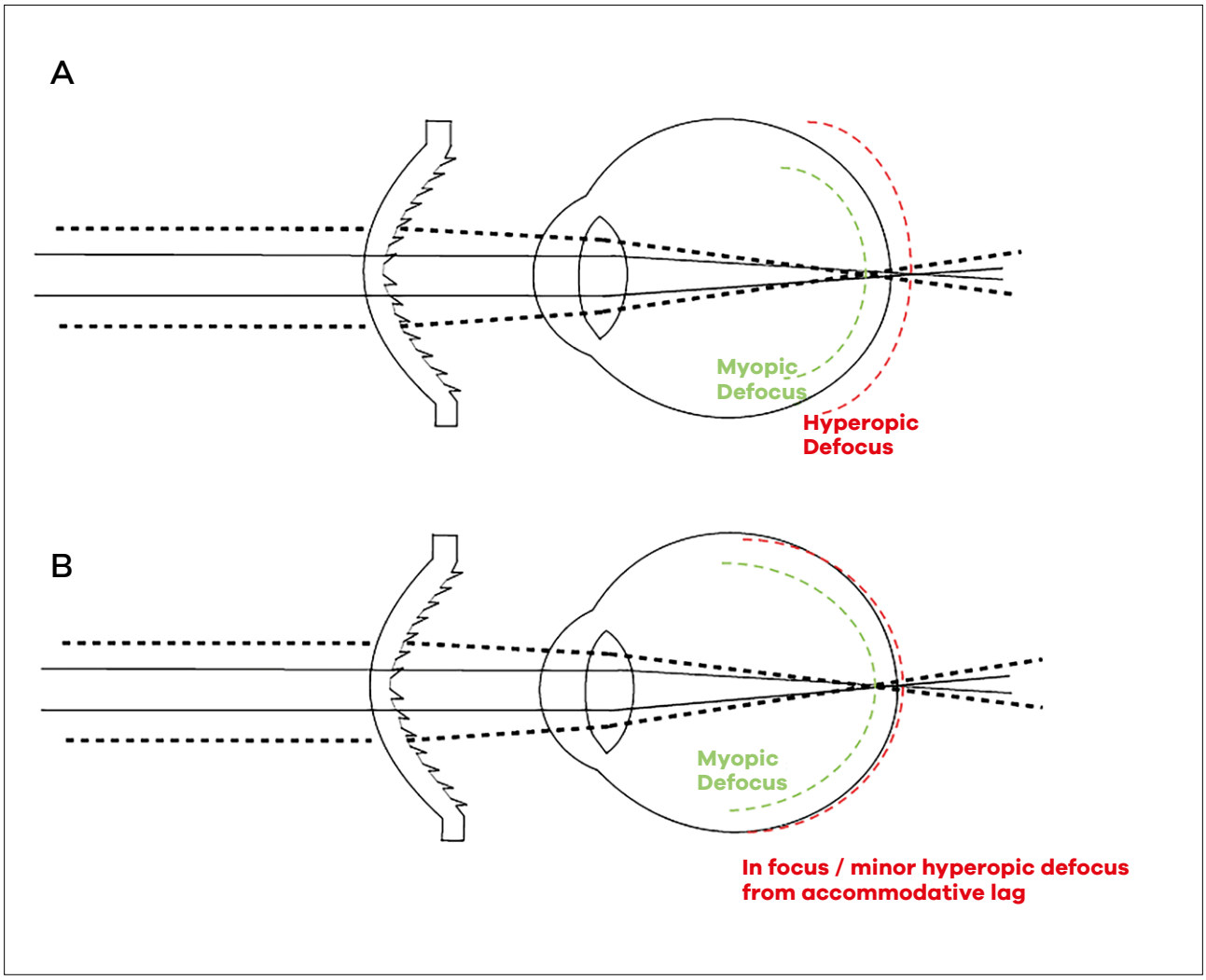

Figure 7. The optic powers of concentric dual-power lens produce two distinct image shells. **A)** A dual-power lens configurated to simultaneously impose myopic defocus and hyperopic defocus in animal models. **B)** A dual-lens lens configurated to correct existing refractive error and impose myopic defocus simultaneously for myopia control (Figures drawn by Dennis Tse).

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