〈Review〉

# Challenge for Myopia-Progression Control using Spectacles

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**ABSTRACT** An overview of myopia control studies using spectacles performed over the past 25 years is provided herein. To address defocus behind the retina (a key factor triggering excessive elongation of the eye), progressive addition lenses (PALs) or peripheral-aspherized PALs have been used in a number of randomized clinical trials (RCTs). While RCTs reported statistically significant inhibitory effects, they were not clinically meaningful. In response, multiple segments lenses based on the defocus incorporated theory (DIMS) were developed and evaluated in RCTs. DIMS lenses achieved superior effects, showing an inhibitory ratio > 50%. By controlling excessive axial elongation during childhood, the spectacles may reduce the risk of severe eye diseases associated with high myopia in adulthood.

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Key words：Myopia control, Children, Randomized clinical trial, Progressive addition lens, Multiple segments lens, Axial length

## INTRODUCTION

To summarize my final lecture about retiring from Kawasaki Medical School, I will provide an overview of myopia control research using spectacles that has progressed over the past 25 years. I will also introduce the findings of the randomized clinical trials (RCTs) we have conducted at Okayama University Medical School and Kawasaki Medical School and explain how our research activity has contributed to this scientific progress.

## WHY ARE TREATMENTS TO PREVENT MYOPIA PROGRESSION NECESSARY?

Statistics on visual acuity reported annually by the Ministry of Education, Culture, Sports, Science, and Technology indicate a constantly increasing number of schoolchildren with low visual acuity (Fig.1). This finding is considered to be primarily due to the growing population of children with myopia. While environmental factors such as the widespread use of smartphones and the Global and Innovation Gateway for All (GIGA) School Program have been suggested as contributing factors, the exact reasons for this increase remain unclear.

According to predictions by Holden[1], the global myopic population was 1.3 billion in 2000, but is projected to surge to 4.9 billion by 2050, with a 5.8-fold increase in the population of individuals with high myopia. High myopia is typically associated

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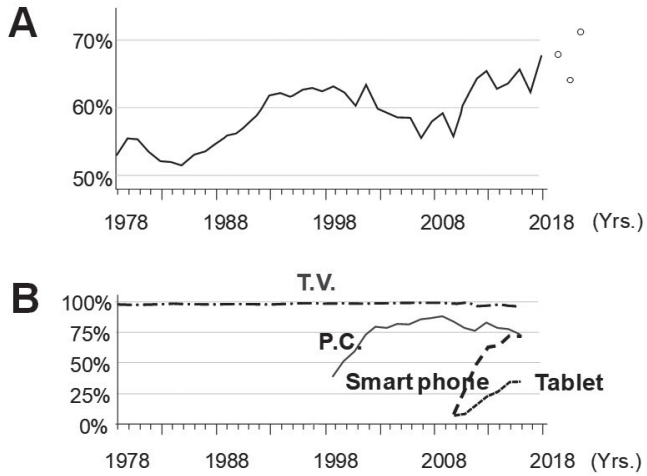


Fig. 1. Changes in the percentage of high school students with unaided visual acuity < 1.0 (A) and the penetration ratio of smartphones and other digital devices (B). Over the past 50 years, this percentage has increased, with a slight acceleration after the introduction of smartphones in 2010. Open circles highlight percentages in the past three years.

Table 1. Odds ratios for the onset of myopia-associated complications in different refractive groups[2].

| Refraction, strength of myopia | -2 D | -6 D | -8 D |
|---|---|---|---|
| macular degeneration | 2 | 41 | 127 |
| retinal detachment | 3 | 9 | 22 |
| cataract | 2 | 3 | 6 |
| glaucoma | 2 | 3 | - |

with excessive elongation of the axial length of the eye, which leads to pathological changes in the retina and choroid. These changes significantly increase the risk of developing serious diseases, such as macular degeneration, retinal detachment, and glaucoma, as shown in Table 1[2]. The rise in these intractable ocular diseases is expected to impose significant social and economic burdens on healthcare systems. Therefore, comprehensive measures to control myopia progression and excessive axial elongation during childhood are a pressing societal imperative.

## THE PRINCIPLE UNDERLYING SPECTACLE TREATMENT

When I was a resident (around 1985), the concept of treatment to prevent myopia was often regarded as something like an occult science, and there was a prevailing attitude in Japan that serious researchers should avoid engaging in it. However, an analysis of PubMed statistics reveals that scientific papers on myopia prevention have increased exponentially in recent years.

A pivotal moment in this field was the animal experiments Smith and his colleagues at Houston University conducted[3, 4]. Their 30-year study involved more than 800 rhesus monkeys and provided a critical finding: during the developmental period, the eye adjusts its axial length in response to a given visual environment. This mechanism, called "the visual regulation of axial length", became a cornerstone in understanding myopia progression and developing strategies for its prevention.

In brief, the developing eye has a form of homeostasis that adjusts the axial length to the visual environment. A clear retinal image acts as a stop signal for axial elongation, while hyperopic defocus (behind the retina) triggers excessive axial length elongation. Figs. 2 and 3 show some of their

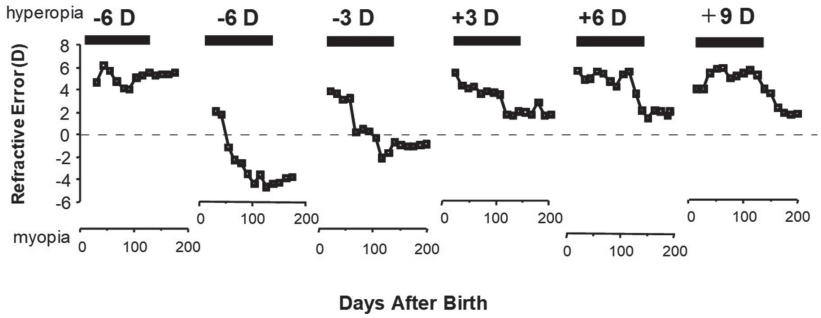


Fig. 2. Smith's experiment on lens-induced myopia (modified from Ref. 3). Six infant monkeys wore spectacle lenses of different powers, and subsequent refractive changes were followed up. A rapid decrease in hyperopia followed by myopia development was noted in concave- lens-wearing monkeys (except for an atypical case in the first column). In convex-lens-wearing monkeys, hyperopia persisted during the lens-wearing period (indicated by the bold bars).

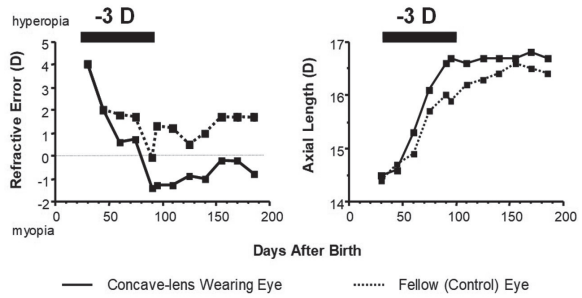


Fig. 3. Synchronous changes were observed in myopia progression and excessive axial length (modified from Ref. 3). Excessive elongation of the eye explains myopia induced by concave lenses.

findings[3, 4]. Six infant monkeys were fitted with spectacle lenses of different powers, and subsequent refractive changes were examined. Although individual differences in refractive error were noted, monkeys generally exhibited mild hyperopia just after birth. In concave- lens-wearing monkeys, hyperopia was rapidly reduced and was followed by the development of myopia. In contrast, in convex-lens-wearing monkeys, hyperopia persisted during the lens-wearing period and gradually decreased after the lenses were removed. Additionally, simultaneous axial-length measurements revealed that myopia induced by concave lenses was caused by excessive axial elongation.

The findings of this study appeared to revolutionize ophthalmic practice. Until then, Japanese ophthalmologists, including the author, explained to children and their parents that "myopia will progress regardless of whether glasses are worn". However, these findings revealed that the spectacle power prescribed may attenuate the future strength of myopia. This discovery placed greater responsibility on ophthalmologists to prescribe glasses for children and acted as a catalyst for active research into treatments that control the progression of myopia.

In the past century, many researchers primarily attributed myopia progression to an increase in the refractive power of the crystalline lens due to excessive accommodation, based on the empirically

observed correlation between myopia and near work. However, with advances in biometric techniques, such as laser interferometry to measure the axial length of the eye, a strong correlation was found between the rates of myopia progression and axial elongation. The primary cause of myopia progression was subsequently identified as excessive axial elongation, which has become a consensus among researchers.

## CAUSE OF DEFOCUS BEHIND THE RETINA

If the visual control of axial lengths works, why does hyperopic defocus behind the retina, which serves as the trigger, occur in children's everyday lives? The initial hypothesis was the lag-of-accommodation theory by Gwiazda[5, 6]. In brief, accommodation is the autofocus function of the eyes, a type of feedback control that strives to maintain a clear retinal image in response to changes in the viewing distance. However, when accommodation responses are objectively measured, a specific amount of error occurs due to the nature of the neurological function. Starting from tonic accommodation (generally 1-1.5 D near the far point), the accommodation response gets smaller as the viewing distance decreases, resulting in increased defocus behind the retina (or the lag of accommodation). If accommodation lag triggers the visual regulation of axial length, this may explain the previously unexplained causal relationship between axial elongation and near work. Accommodation lag is a physiological phenomenon that typically stays within the depth of focus of the eye. Due to sensory adaptation, children rarely notice the blurring of an image. However, in today's information-driven society, smartphones and gaming machines need to display much information in a limited space. These conditions may lead to shorter viewing distances, greater accommodation, and increasing lag of accommodation. If the accommodative lag hypothesis is correct and children do not view anything closer than the tonic accommodation (100 cm and closer), myopia progression and excessive axial elongation do not occur. However, this guidance is unrealistic for children nowadays. An alternative that attracted wide attention is progressive addition lenses (PALs)[7].

## THE FIRST RCT AIMING FOR MYOPIA CONTROL IN JAPAN

PALs are typically prescribed for the treatment of presbyopia to compensate for the age-related reduction in accommodation. By wearing PALs, children reduce the amount of accommodation by the near addition power. For example, at a viewing distance of 33 cm, the required accommodation for clear vision is +3 D and exceeds the tonic accommodation, causing accommodative lag. When PALs with a near addition of +1.5 D are used for the same condition, the required accommodation decreases to the level of tonic accommodation (+1.5 D), removing the accommodative lag. Therefore, PALs are expected to prevent excessive axial elongation and myopia progression.

The author conducted an RCT in 2008 that evaluated the effects of PALs on myopia progression[8]. Considering the strong effects of family history on myopia progression, this study employed a crossover design. Ninety-two elementary school children with mild to moderate myopia and wearing glasses at enrollment, were recruited, randomly divided into two treatment groups, and followed up for 36 months (Fig. 4). During the first half of the trial (0-18 months), Group 1, which used PALs, showed an average treatment effect of 0.31 D (slowing myopia by 26%) relative to Group 2, which used conventional single vision lenses (SVLs). In the second half of the trial (18-36 months), after switching the type of glasses, Group 2, now using PALs, showed only a 0.02 D treatment effect (slowing myopia progression by 2%) relative to Group 1, using SVLs. An analysis

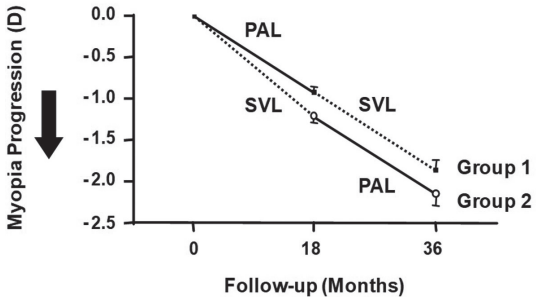


Fig. 4. Findings of our RCT on Japanese schoolchildren using PALs (modified from Ref. 8). In the first half, myopia progression was slower in Group 1, wearing PALs, than in control Group 2, wearing SVLs. In the second half, the difference between the two groups was negligible. The overall inhibitory effect over 18 months was 0.17 D ($p = 0.004$). Mean values with SEs are shown.

of the entire dataset using a mixed-model ANOVA yielded the following conclusions:

1. The mean inhibitory effect was 0.17 D/18 months ($p = 0.004$). When converting the effect size into the inhibitory ratio (change in the control group - change in the treated group) × 100%), it was 15%.

2. The mean inhibitory effect was greater in Group 1 (which began treatment earlier), indicating no rebound after the discontinuation of PALs ($p < 0.05$).

## THE SECOND RCT AIMING FOR MYOPIA CONTROL IN JAPAN

The peripheral retinal defocus theory attracted wide attention following the accommodative lag hypothesis. In brief, some animal experiments showed that, when concave lenses or light-diffusing filters were applied to specific portions of the visual field, axial elongation occurred in the corresponding areas of the retina[9, 10]. These findings suggested that the visual regulation of axial length was not limited to the fovea, but functioned across the entire retina and operated locally. Even in emmetropic eyes, individual differences in eye shape exist. In prolate eyes with a smaller radius of retinal curvature, focusing on the fovea often results in hyperopic defocus on the peripheral retina due to discrepancies between the retinal curvature and the image shell constructed by the cornea and crystalline lens. Moreover, corrective glasses for myopia exacerbate this issue because light rays from the peripheral visual field pass obliquely through the lenses, leading to increased minus power and astigmatic aberrations, causing hyperopic defocus on the peripheral retina.

To address hyperopic defocus on the peripheral retina (i.e., another trigger for axial elongation), radial refractive gradient (RRG) lenses were developed[11]. Unlike PALs, which increase plus power in the lower part of the lens, RRG lenses feature a near-concentric design where plus power increases gradually as the distance from the center increases. When wearing these lenses, light rays from the peripheral visual field pass through lens regions with added plus power, shifting the focus forward and reducing the hyperopic defocus. This optical effect was also expected to retard myopia progression. Our positively- aspherized PALs (Fig. 5) were also specially designed lenses to reduce hyperopic defocus on the peripheral retina. Similar to traditional PALs, they have a near-addition segment in the lower part of the lens (addition power: +1 D or +1.5 D) with minimal astigmatic aberration. Additionally, in the three

other quadrants, the lens gradually increases plus power from the center towards the periphery. This hybrid lens combines the advantages of PALs, which reduce accommodative lag during near work, and RRG lenses, which alleviate hyperopic defocus on the peripheral retina. As a collaborative study with Zeiss and Wenzhou University in China, the author conducted the second RCT to evaluate their efficacy[12].

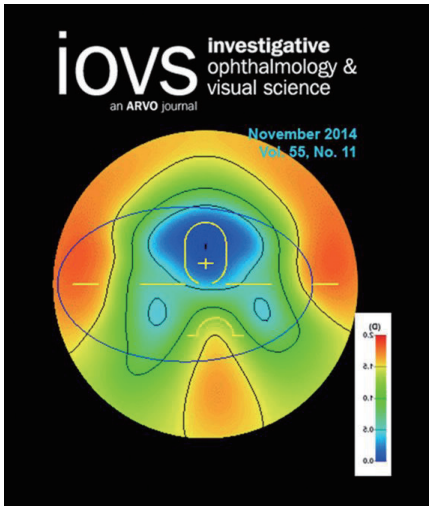


Fig. 5. The mean addition power map of PA-PAL with +1.50 D near addition (Carl Zeiss) appeared on the front page of IOVS (modified from Ref. 12). Lens diameter = 60 mm.

The study design was a two-year, parallel-group RCT. Participants were elementary school students with mild or moderate myopia, and 169 children completed the entire follow-up period. Myopia progression and axial elongation were compared among the lenses in Fig. 6. The findings obtained revealed the following:

1. The inhibitory effects on both myopia progression and axial elongation of PA-PALs with +1.5 D near addition were greater than those of PA-PALs with +1.0 D near addition.

2. PA-PALs with +1.5 D near addition exerted a mean inhibitory effect of 0.24 D at the end of the first year and 0.27 D at the end of the second year ($p < 0.05$).

3. Regarding axial elongation, the mean inhibitory

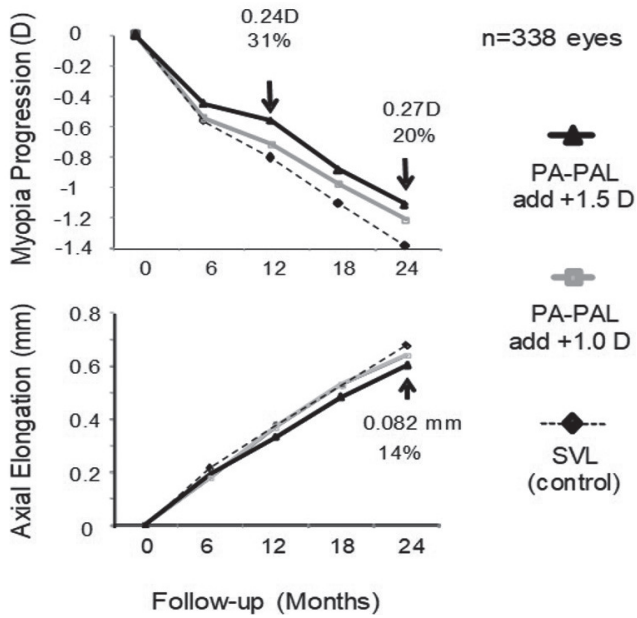


Fig. 6. Findings of our RCT using PA-PALs (modified from Ref. 12). Mean values with SE were plotted. The effect sizes (D) and inhibitory ratios (%) of PA-PALs with +1.5 D near addition were noted at particular points in time.

effect was 0.082 mm at the end of the second year ($p < 0.05$).

4. The effects of the treatment changed over time. When converting 2-year effect sizes into inhibitory ratios, they were 20% for myopia progression and 14% for axial elongation. These ratios were slightly higher than those in our RCT using PALs; however, PA-PALs were not commercialized.

## COMPREHENSIVE PERSPECTIVE ON PALS

RCTs using PALs, including those conducted by the authors, have been performed at least seven times worldwide (Table 2). Even when we include target studies that limited participants, the range of the mean inhibitory effects on refractive error and axial length were 11-33% and 2-16%, respectively. Large-scale epidemiological studies reported that eye diseases previously recognized as complications of high myopia, such as macular degeneration and retinal detachment, showed a parallel increase in risk from mild to high myopia as myopia progressed[13]. For example, the risk of developing macular degeneration is estimated to decrease by 40% if the progression of myopia may be suppressed by 1 D, regardless of the degree of myopia. Therefore, the International Myopia Institute[14] and Food and Drug Administration[15] have claimed ≥ 40% and ≥ 30%, respectively, as clinically meaningful inhibitory ratio. Therefore, although the treatment effects of PALs were statistically significant, they were considered to be too small clinically. PALs cannot be recommended for schoolchildren as a preventive treatment for myopia.

Flitcroft[16] explained the reason for poor treatment effects using accommodation error maps. The defocus on the peripheral retina is affected by the viewing distance, viewing direction, and three-dimensional space structure and, thus, changes dynamically. Therefore, fixed optical systems, such as spectacle lenses, do not sufficiently remove a fluctuating defocus. At this point (around 2010), myopia-control research with spectacles appeared to come to an end. However, the collective findings of RCTs indicated that controlling myopia progression, which once appeared to be impossible, was indisputably achievable, leading to the paradigm shift described in the next chapter.

Table 2. Findings of control trials using PALs（No. 1 - 8）and specially aspherized lenses（No. 9 - 11）.

| No. | Author | Year | Lens | Design | n | inhibitory ratio in myopia progression (%) | inhibitory ratio in axial elongation (%) |
|---|---|---|---|---|---|---|---|
| 1 | Leung | 1999 | PAL | 2yrs CT | 46 | 46 | 50 |
| 2 | Shih | 2001 | PAL | 2yrs RCT | 188 | 15（$p < 0.001$） | 2（n.s.） |
| 3 | Edwards | 2002 | PAL | 1.5yrs RCT | 298 | 11（n.s） | 3（n.s.） |
| 4 | COMET | 2004 | PAL | 3yrs RCT | 469 | 14（$p < 0.001$） | 15（$p < 0.001$） |
| 5 | Hasebe | 2008 | PAL | 3yrs RCT | 92 | 15（$p = 0.004$） | n.a. |
| 6 | Yang | 2009 | PAL | 2yrs RCT | 178 | 21（$p = 0.01$ | 16（$p = 0.04$） |
| 7 | COMET2 | 2011 | PAL | 1.5yrs RCT | 118 | 24（$p < 0.05$） | n.a. |
| 8 | Berntsen | 2012 | PAL | 1yrs TRCT | 85 | 33（$P = 0.01$） | n.a. |
| 9 | Sankaridurg | 2010 | RRG | 1yrs CT | 100 | 30（$p < 0.05$） | n.a. |
| 10 | Hasebe | 2014 | PA-PAL | 2yrs RCT | 169 | 20（$p < 0.02$） | 12（n.s.） |
| 11 | Kanda | 2018 | RRG | 2yrs TRCT | 207 | n.s. | n.s. |

RRG = Radial Refractive Gradient design lens, PA-PAL = Positively-Aspherized PALs. CT = non-randomized Clinical Trial, T-RCT = Targeted RCT with selected children, n.a. = not available.

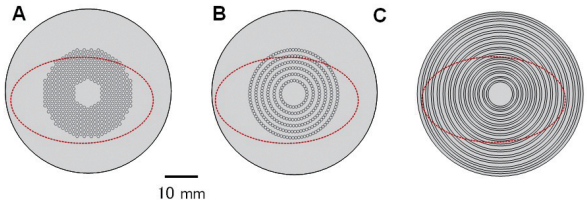


Fig. 7. Design of commercially available DIMS lenses A: MiyoSmart (HOYA), B: Stellest (ESSILOR), C: MyoCare (ZEISS). The red ovals indicate the typical area of spectacle frames.

## PARADIGM SHIFT IN RESEARCH USING SPECTACLES

In the early 2010s, research teams from U.C. Berkeley[17], Hong Kong Polytechnic University[18], and Houston University[19] independently conducted experiments with animal models using chicks and macaque monkeys, and reported that the provision of a second and relatively large defocus in front of the retina may stop the extensive elongation of axial length. This finding marked a breakthrough in myopia progression control research and is widely known as the defocus incorporated theory. Until then, our aim had solely been to remove the hyperopic defocus (i.e., the trigger for axial elongation). However, it was now known that the visual regulation of the axial length system may be suppressed by creating an optically conflicting condition. Defocus Incorporated Multiple Segments (DIMS) lenses were designed based on this theory, and RCTs have all reported good outcomes.

The first DIMS lens to appear in the market was MiyoSmart, developed through joint research between Hong Kong Polytechnic University and HOYA[20]. This lens features approximately 400 micro-lenses (lenslets) with a diameter of 1 mm and a refractive power of +3.5 D, arranged in a honeycomb pattern, excluding the central clear area (Fig. 7A). In the primary gaze position, incident light passes through the central clear zone and no vision degradation occurs. Fifty percent of the light from the peripheral field passes through the lenslets, creating a secondary focus +3.5 D before the retina, separate from the primary focus of the lens carrier. When the gaze direction shifts, several lenslets are always included within the pupil area, maintaining compliance. Since the secondary focus is blurred due to diffraction, and multiple images are created, children cannot use it during near work, ensuring that the accommodation response remains normal.

The next lens developed was Stellest (Fig. 7B) by ESSILOR[21]. The lenslets are arranged around the central clear zone in six concentric circles. Unlike MiyoSmart, the lenslets in Stellest are aspheric, with a refractive power ranging between +3.1 D and +5.6 D. A previous study reported that visual acuity and contrast sensitivity when looking through the lenses were similar to those of SVLs, with no significant difference from MiyoSmart[20].

The last DIMS lens to emerge from the three major lens manufacturers was MyoCare by Zeiss (Fig. 7C). They feature a ring structure surrounding the central clear zone, and each ring works as a tiny cylindrical lens. Light passing through the rings creates a secondary focus in front of the retina with astigmatic aberration. The refractive power of the cylindrical lenses is available in two variants: +4.6 D for MyoCare and +3.8 D for MyoCare S in spherical equivalent. While Stellest uses aspheric aberration (HALT technology), MyoCare utilizes astigmatic aberration (CARE technology) to expect more potent outcomes by axially elongating the secondary focus and producing some volume. This

approach is expected to yield more potent treatment outcomes[21].

## OUTCOMES OF RCTS USING DIMS LENSES

The findings of an RCT using MiyoSmart were reported in 2020. A total of 183 myopic schoolchildren were followed up for two years. Average inhibitory ratios were 52% for myopia progression and 62% for axial elongation (Table 3) [20]. This effect was 2- to 3-fold more potent than that of PALs. A study from the third year of wear confirmed that treatment effects continued[22]. During the follow-up period, changes were observed in the pattern of defocus on the peripheral retina, providing supportive evidence for the treatment mechanism of DIMS lenses. Furthermore, a study from the sixth year, although based on a small sample, investigated the continuity of effects after the cessation of DIMS wearing and found no rebound[23]. The long-term safety of the treatment in terms of visual function was examined and showed no changes in eye position or accommodation amplitude[24]. In Europe, a controlled trial, although non-randomized, was conducted, and similar inhibitory effects to those reported in the study above were reported[25]. This study also examined the synergistic effects of combining DIMS lenses with low-concentration atropine eye drops.

Stellest lenses were reported in 2022. A two-year follow-up study on 157 myopic schoolchildren revealed average inhibitory ratios of 55% for myopia progression and 51% for axial elongation[21]. Outcomes from the third year of wearing were also reported, demonstrating constant treatment effects[26]. Additionally, comparisons of these lenses with highly aspheric lenslets and those with weakly aspherized lenslets showed that the former exerted a more potent inhibitory effect. This finding supports the HALT technology claimed by ESSIROL. In Europe, post-market follow-up studies and RCTs investigating combination therapy with low-concentration atropine are underway. The RCT on MiyoSmart was conducted in Hong Kong, while the RCT on Stellest was performed in Wenzhou. Although both studies were performed in China, significant differences were observed in the rates of myopia progression and axial elongation in the control groups. Therefore, caution is required when comparing treatment effects between these lenses, whereas differences in their inhibitory ratios were

Table 3. Inhibitory ratio and optical characteristics of DIMS lenses*

| Product name | MiyoSmart | Stellest | MyoCare | MyoCare S |
|---|---|---|---|---|
| Company | HOYA | ESSILOR | ZEISS | |
| 2-year inhibitory ratio | | | | |
| myopia progression | 52% | 67% | n.a. | n.a. |
| axial elongation | 62% | 64% | n.a. | n.a. |
| range of lens power. | 0.00 to -10.00 D ≤ cyl-4.00 D | 0.00 to -10.00 D ≤ cyl-4.00 D | 0.00 to -9.00 D ≤ cyl-6.00 D | |
| applicable age (yrs) | 8 - 16 | 8 - 16 | < 10 | ≥ 10 |
| size of the central clear zone | 9.4 mm | 9 mm | 7 mm | 9 mm |
| diameter of lenslets | 1.0 mm | 1.12 mm | 0.8 mm* | 0.8 mm* |
| refractive power of lenslets | + 3.5 D | + 3.1 to + 5.6 D | + 4.6 D | + 3.8 D |
| lenslets/carrier ratio | 1 | | | |
| characteristic of lenslets | spherical lens | aspherized lens | cylindrical lens | |
| lens material | polycarbonate | | | |

Diameter in the meridional direction. n.a. = not available.

negligible (Table 3).

Regarding MyoCare, different RCTs (with 1,700 children) are ongoing in China and Europe. An interim report from a two-year RCT conducted in Wenzhou introduced a newly proposed treatment efficacy metric, i.e., the Emmetropic Progression Ratio (EPR = ((axial elongation in control eyes - axial elongation in treated eyes) / (axial elongation in control eyes - axial elongation in emmetropic eyes) × 100%)) and reported an average EPR of 63% in children aged 9 years and younger and 86% in those aged 10-12 years.

## THE COMPREHENSIVE PERSPECTIVE OF THE DIMS LENS

RCTs using DIMS lenses have consistently demonstrated a strong inhibitory effect. The effect size exceeds the clinically meaningful level (30-40% and higher[14, 15] for all three lenses. On the other hand, epidemiological studies have already demonstrated that genetic and environmental factors both contribute to myopia progression. Therefore, it's not surprising if differences in inhibitory effects would exist among countries with different ethnic and societal backgrounds. In this case, the Pharmaceuticals and Medical Devices Agency (PMDA) typically imposes RCTs conducted in Japan as a condition for approval; however, this typically takes 3-6 years, including planning, participant recruitment, and data analyses. This issue of device lag now poses serious issues for healthcare administration, regardless of the medical field; if Japanese children cannot benefit from advances in science simply because of their location, it is unfortunate.

Low-dose atropine eye drops, one of the other potential myopia control treatments, are used off-label, and myopia-control contact lenses, including Ortho-K, are classified as Class III medical devices, requiring RCTs in Japan. On the other hand, spectacle lenses are classified as Class I devices in developed countries, and international practice approves a Class I device based solely on the application without a review of treatment and adverse effects. Therefore, MiyoSmart is sold in 32 countries worldwide, based on the findings of only one RCT in Hong Kong. Regarding MyoCare, before the RCT was completed, more than one million pairs had been sold in China, Australia, New Zealand, and Canada. If the PMDA classifies the DIMS spectacle lens as a Class I device and follows international practices, the device lag will be instantly solved.

## ADVANTAGES OF MYOPIA CONTROL SPECTACLES

Spectacles are empirically safe. Furthermore, since spectacle correction for refractive errors also serves as a preventive treatment, this minimizes the time, psychological, and financial burdens on a child and their guardians, making the treatment easier to undergo over the long term. Moreover, spectacles may be used with low-concentration atropine eye drops. Preliminary studies demonstrated that this combination enhanced the treatment effect[25].

## CONCLUSIONS

When I reflect on the journey over the past 25 years, numerous pieces of evidence regarding myopia control have emerged in rapid succession both from basic and clinical research. Consequently, what was once considered an occult science has become a true science, and what was once a mere fantasy is becoming a reality today. It is a great joy for me to have witnessed such dramatic changes in this research field and also to have made some contributions by conducting RCTs. I want to take this opportunity to thank my colleagues and friends at Kawasaki Medical School, Okayama University Medical School, Houston University, and Carl Zeiss Vision for their guidance and support, as well as the participants of the RCTs who provided a kind

understanding of and cooperation to my endeavors.

## REFERENCES


1) Holden BA, Fricke TR, Wilson DA, *et al.*: Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology 123: 1036-1042, 2016.

2) Ueda E, Yasuda M, Fujiwara K, *et al.*: Trends in the Prevalence of myopia and myopic maculopathy in a Japanese population: The Hisayama Study. Invest Ophthalmol Vis Sci 60: 2781-2786, 2019.

3) Hung LF1, Crawford ML, Smith EL: Spectacle lenses alter eye growth and the refractive status of young monkeys. Nat Med 1: 761-765, 1995.

4) Smith EL 3rd: Environmentally induced refractive errors in animal (In Myopia and near worked: Rosenfield M, Gilmartin B): 57-90, Buttweworth Heinemenn, Oxford, 1998.

5) Gwiazda J, Thorn F, Bauer J, *et al.*: Myopic children show insufficient accommodative response to blur. Invest Ophthalmol Vis Sci 34: 690-694, 1993.

6) Gwiazda J, Hyman L, Hussein M, *et al.*: A randomized clinical trial of progressive addition lenses versus single vision lenses on myopia progression in children. Invest Ophthalmol Vis Sci 44: 1492-1500, 2003.

7) Lung JTM, Brown B: Progression of myopia in Hong Kong Chinese schoolchildren is slowed by progressive lenses. Optom Vis Sci 76: 346-354, 1999.

8) Hasebe S, Ohtsuki H, Nonaka T, *et al.*: Effect of progressive addition lenses on myopia progression in Japanese children: a prospective, randomized, double-masked, crossover trial. Invest Ophthalmol Vis Sci 49: 2781-2789, 2008.

9) Diether S, Schaeffel F: Local changes in eye growth induced by imposed local refractive error despite active accommodation. Vision Res 37: 659-668, 1997.

10) Smith EL 3rd, Kee CS, Ramamirtham R, *et al.*: Peripheral vision can influence eye growth and refractive development in infant monkeys. Invest Ophthalmol Vis Sci 46: 3965–3972, 2005.

11) Sankaridurg P, Donovan L, Varnas S, *et al.*: Spectacle lenses designed to reduce the progression of myopia: 12-month results. Optom Vis Sci 87, 631-641, 2010.

12) Hasebe S, Jun J, Varnas SR: Myopia control with positively aspherized progressive addition lenses: a 2-year, multicenter, randomized, controlled trial. Invest Ophthalmol Vis Sci 55: 7177-7188, 2014.

13) Bullimore MA, Brennan, NA: Myopia control: Why each diopter matters? Optom Vis Sci 96, 463-465, 2019.

14) Wolffsohn JS, Kollbaum PS, Berntsen DA, *et al.*: IMI Clinical myopia control trials and instrumentation report. Invest Ophthalmol Vis Sci 60: M132-M160, 2019.

15) Walline JJ, RobboyMW, Hilmantel G, *et al.*: Food and Drug Administration, American Academy of Ophthalmology, American Academy of Optometry, American Association for Pediatric Ophthalmology and Strabismus, American Optometric Association, American Society of Cataract and Refractive Surgery, and Contact Lens Association of Ophthalmologists co-sponsored workshop: controlling the progression of myopia: Contact lenses and future medical devices. Eye Contact Lens 44: 205-211, 2018.

16) Flitcroft D: The complex interactions of retinal, optical and environmental factors in myopia aetiology. Prog Retin Eye Res 6: 622-660, 2012.

17) Liu Y, Wildsoet C: The effect of two-zone concentric bifocal spectacle lenses on refractive error development and eye growth in young chicks. Invest Ophthalmol Vis Sci 22: 1078–1086, 2011.

18) Tse DY, To CH: Graded competing regional myopic and hyperopic defocus produce summated emmetropization set points in chick. Invest Ophthalmol Vis Sci 52: 8056-8062, 2011.

19) Arumugam B, Hung LF, To CH, *et al.*: The effects of simultaneous dual focus lenses on refractive development in infant monkeys. Invest Ophthalmol Vis Sci 55: 7423-7432, 2014.

20) Lam CSY, Tang WC, Tse DY, *et al.*: Defocus incorporated multiple segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol 104: 363-368, 2020.

21) Bao J, Huang Y, Li X, *et al.*: Spectacle lenses with aspherical lenslets for myopia control vs single-vision spectacle lenses: A randomized clinical trial. JAMA Ophthalmol 140: 472-478, 2022.

22) Lam CS, Tang WC, Lee PH, *et al.*: Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: results of a 3-year follow-up study. Br J Ophthalmol 106: 1110-1114, 20220.

23) Li X, Huang Y, Yin Z, *et al.*: Myopia control efficacy of spectacle lenses with aspherical lenslets: Results of a

3-year follow-up study. Am J Ophthalmol 253: 160-168, 2023.

24) Lam CSY, Tang WC, Zhang HY, *et al.*: Long-term myopia control effect and safety in children wearing DIMS spectacle lenses for 6 years. Sci Rep 13: 5475, 2023.

25) Nucci P, Lembo A, Schiavetti I, *et al.*: A comparison of myopia control in European children and adolescents with Defocus Incorporated Multiple Segments (DIMS) spectacles, atropine, and combined DIMS/atropine. PLoS One 18: e0281816, 2023.

26) Li X, Huang Y, Yin Z, *et al.*: Myopia control efficacy of spectacle lenses with aspherical lenslets: Results of a 3-year follow-up study. Am J Ophthalmol 253: 160-168, 2023.