December 1, 2019

Re: Case Series Analysis of Myopic Progression Control with a Unique Extended Depth of Focus Multifocal Contact Lens (Visioneering Technologies, Inc.'s NaturalVue Multifocal Lenses)

Dear Eye Care Professional:

Because we know that your time is valuable, we are pleased to provide you with an Executive Summary of a peer-reviewed scientific article entitled "Case Series Analysis of Myopic Progression Control with a Unique Extended Depth of Focus Multifocal Contact Lens," *as well as the article itself*.[1]

We believe that this study provides important scientific information that may assist you in making the best-informed treatment decisions for your patients who already wear contact lenses to correct myopia.

To ensure that we are providing this information to you responsibly, we would like you to be aware that:

- The study does not provide conclusive evidence that NaturalVue Multifocal contact lenses are safe and effective for controlling the progression of myopia. This article provides the results from a 32-patient retrospective case series. Although the results of the study suggest that extended depth of focus multifocal contact lenses may slow the progression of myopia, the study does not carry as much scientific weight as would a prospective, randomized controlled trial ("RCT") that included more patients.

- More robust studies are needed. Authors from FDA recently published a literature review cautioning that: "[a]lthough some contact lens clinical trials have demonstrated promising results in slowing the progression of myopia, many of these studies have significant limitations, including only short follow-up times, limited randomization, and incomplete masking."[2] Accordingly, more robust studies are needed.

- FDA has not cleared or approved NaturalVue Multifocal Lenses for controlling the progression of myopia. Like all disposable soft contact lenses, NaturalVue Multifocal Lenses have not specifically been cleared or approved for use in pediatric patients.

- NVMF's have been cleared by FDA for other uses. Those uses include: the correction of ametropia (myopia and hyperopia), and/or presbyopia in aphakic and/or non-aphakic persons in non-diseased eyes in powers from -20.00 to +20.00 diopters.

- Using contact lenses to control the progression of myopia presents known and unknown risks (risks such as vision-threatening corneal infections, i.e., corneal ulcers, particularly among children and adolescents). Problems with contact lenses, generally, can result in serious injury to the eye, and it is essential that patients follow their Eye Care Professional's directions and all labeling instructions for proper use of lenses. Additional warnings and precautions are in NaturalVue Multifocal Lenses labeling, at https://vtivision.com/wp-content/uploads/2018/02/NaturalVue-Package-Insert.pdf

  The literature review authored by employees from FDA, which was referenced above, cautions that "[b]ecause the slowing of the progression of myopia would likely be specific for a population of younger children, potentially with only minimal refractive error, and the risks associated with lens wear in this age group are not well-defined, FDA may regard [contact lenses worn for myopic control] as being higher

risk."[3] There are concerns related to "lens care, hygiene, and environmental factors (e.g., adult oversight and device user training)," including concerns about the potential for an increased incidence of microbial keratitis.[4]

- Visioneering Technologies, Inc. has affiliations with the study and some of its authors. The study summarized and appended hereto was funded in part by VTI. Several of the authors, J. Cooper, B. O'Connor and S. M. Dillehay are paid consultants to VTI.

Neither the Executive Summary, nor the copy of the peer-reviewed journal article itself, are intended to promote VTI's contact lenses, and therefore, they are not being distributed with any promotional materials for VTI products. If you have any questions regarding the use of center distance multifocal soft contact lenses to control myopia progression, or about the data within, please contact VTI Professional Services Department:

- Douglas P. Benoit, O.D., F.A.A.O., Executive Director, Professional Services, Visioneering Technologies, Inc. at 1-844-VTI-LENS (1-844-884-5367), extension 136, or email dbenoit@vtivision.com (cell: 603-545-9507).

- Peg Achenbach, O.D., F.A.A.O., Vice President of Professional Services and Clinical Science, Visioneering Technologies, Inc., at 1-844-VTI-LENS (1-844-884-5367), extension 102, or email pachenbach@vtivision.com, (cell: 201-981-2020).

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[1] VTI is committed to complying with the law and recognizes that FDA has effectively sanctioned the responsible distribution of peer-reviewed journal articles, like Cooper J, O'Connor B, Watanabe R, et al. Case series analysis of myopic progression control with a unique extended depth of focus multifocal contact lens. Eye Contact Lens. 2018 Sep;44(5):e16-e24. P<0.00000. See Revised Draft Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices (Feb. 2014), https://www.fda.gov/media/88031/download; FDA also has recognized that fair, balanced, truthful, and non-misleading summaries are appropriate. See Letter to Amarin Pharma, Inc, from Dr. Janet Woodcock, dated June 5, 2015, at 6, http://freepdfhosting.com/702316334b.pdf

[2] M. Robboy, O.D., et al., "Assessment of Clinical Trials for Devices Intended to Control Myopia Progression in Children," Eye & Contact Lens, Volume 44, Number 4, p. 212 (July 2018) ("Robboy Literature Review"). This article reviewed the following seven studies involving multifocal soft contact lenses: (1) Anstice NS, Phillips JR. Effect of dual-focus soft contact lens wear on axial myopia progression in children. Ophthalmology 2011;118:1152–1161; (2) Lam CS, Tang WC, Tse DYY, et al. Defocus incorporated soft contact (DISC) lens slows myopia progression in Hong Kong chinese schoolchildren: A 2-year randomised clinical trial. Br J Ophthalmol 2014;98:40–45; (3) Aller TA, Liu M, Wildsoet CF. Myopia control with bifocal contact lenses: A randomized clinical trial. Optom Vis Sci 2016;93:344–352; (4) Cheng X, Xu J, Chehab K, et al. Soft contact lenses with positive spherical aberration for myopia control. Optom Vis Sci 2016;93:353–366); (5) Paune J, Morales H, Armengol J, et al. Myopia control with a novel peripheral gradient soft lens and orthokeratology: A 2-year clinical trial. Biomed Res Int 2015:507512; (6) Walline JJ, Greiner KL, McVey ME, et al. Multifocal contact lens myopia control. Optom Vis Sci 2013;90:1207–1214; and (7) Sandkaridurg P, Holden B, Smith E, et al. Decrease in rate of myopia progression with a contact lens designed to reduce relative peripheral hyperopia: One-year results. Invest Ophthalmol Vis Sci 2011;52:9362–9367).

[3] Robby Literature Review, at 216.

[4] Robby Literature Review, at 217.

Case Series Analysis of Myopic Progression Control With a Unique Extended Depth of Focus Multifocal Contact Lens

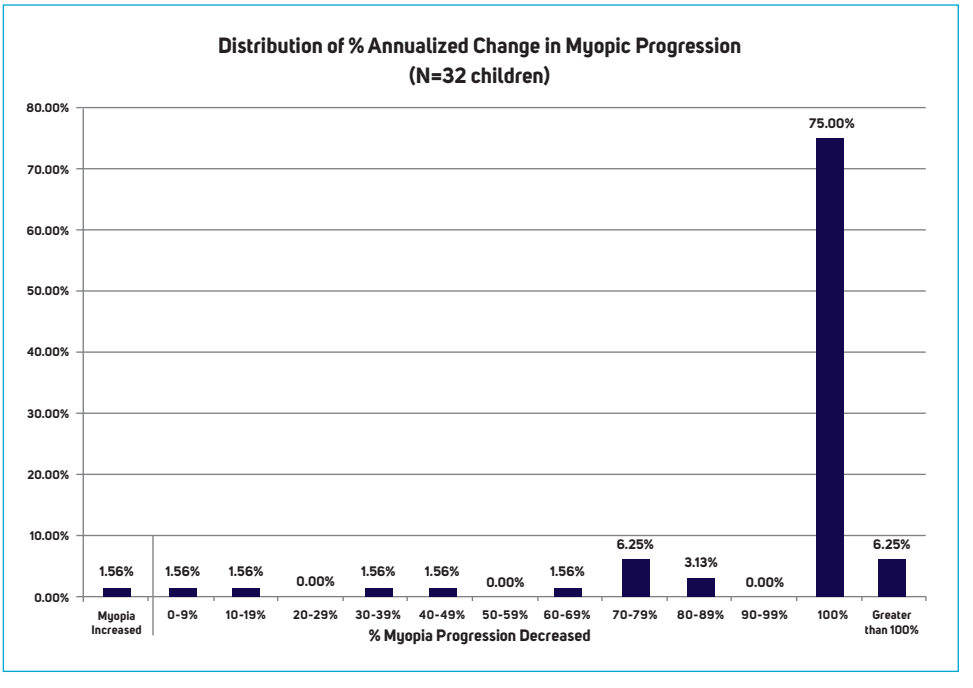
Objectives: To determine the rate of myopia progression in children fit with a commercially available extended depth of focus (center distance) multifocal soft contact lens with attributes theoretically expected to slow the progression of myopia.

Methods:

- A retrospective case series analysis of 32 patients (ages 6–19 years, mean 10.98±2.95) from 10 practice locations was performed. 2 additional children dropped out (lack of compliance/follow-up).
- Prior to the study, participants wore: spectacles (44%), spherical SCL's (37%), SMFCL's (15.6%), and Ortho K lens (3%).
- Clinical criterion:
  - At least –0.50 D of refractive progression since the previous examination.
  - Each child used as his/her own historical control.
  - Children were examined approx. every 6 months after initial fitting of the multifocal lenses.
    - At each follow-up visit, the amount of progression observed was divided by the number of months since the last examination. If a child was seen for more than one 6 month follow-up visit, the progression observed during the entire time that they had worn the contact lenses was analyzed. The monthly amount of progression was then annualized, before and after wearing the lenses.

Results:

- Annualized rate of myopic progression decreased for OD from –0.85 D per year (±0.43D) to –0.04 D per year (±0.18D) and for OS from –0.90 D per year (±0.57D) to –0.03 per year (±0.17D); Statistical significance: P<0.00000
- These data represent a reduction of 95.4% OD and 96.25% OS.
- Approximately 98.4% of the children showed reduction of annualized myopic progression; 91% showed a decrease of 70% or greater.
- Overall, 81.25% showed complete halting of myopic progression, including 6.25% demonstrating myopic regression.



Conclusions: This unique extended depth of focus (center distance) daily disposable multifocal contact lens was effective in slowing myopic progression in these children. Given the size, the retrospective nature of the study, and the limited controls, the study does not provide conclusive evidence that these lenses are safe and effective for myopic progression. More robust studies are needed.*

*This use has not been approved or cleared by FDA.

The peer-reviewed article, Cooper J, O'Connor B, Watanabe R, et al. Case series analysis of myopic progression control with a unique extended depth of focus multifocal contact lens. Eye Contact Lens. 2018 Sep;44(5):e16-e24, is attached.

Figures 2 and 3 illustrate the annualized amount of myopic progression before and after wearing the NVMF, for the right and left eyes, respectively. Individual variability can be seen in the data, with most children progressing fairly rapidly in their myopia before wearing the NVMF lenses. After wearing the NVMF lenses for 6 to 25 months, most of the children (81.25%) showed a halting of myopic progression (75%) or an actual regression (6.25%) in the amount of their myopia.

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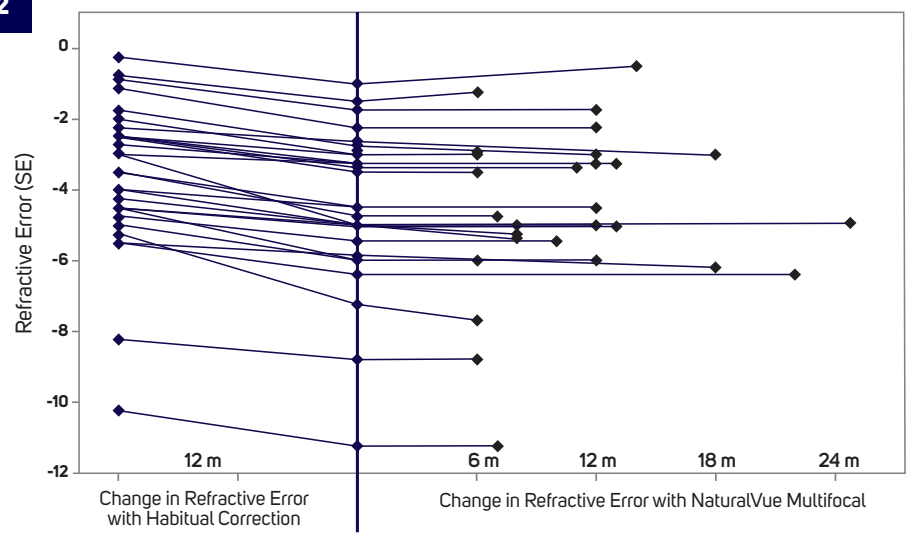

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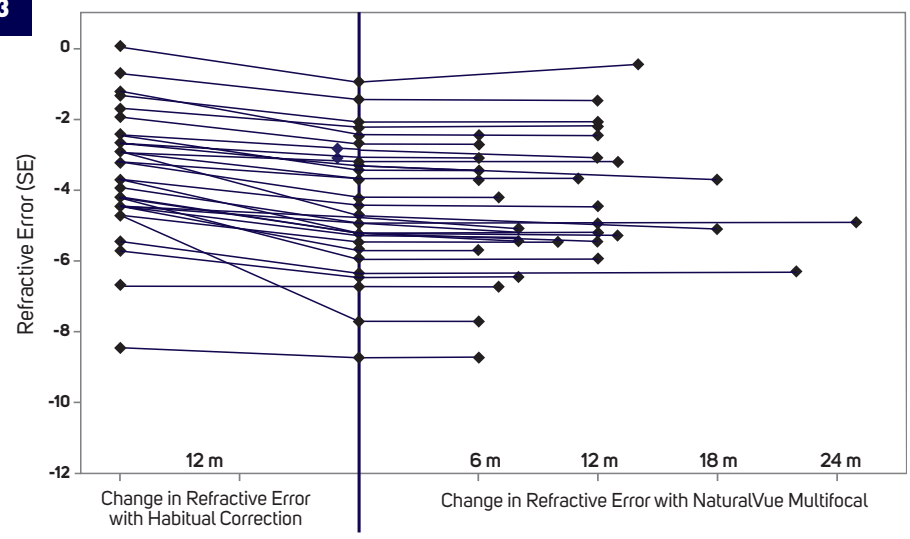

NaturalVue® Multifocal 1 Day Contact Lens Specifications

Full Power Range: +4.00 to -12.25 in 0.25D steps	**ADD:** One Universal Extended Depth of Focus design for an effective ADD up to +3.00
Design: Extended Depth of Focus (Center Distance)	**Material:** etalfilcon A (58% water)
Base Curve: 8.3	**Diameter:** 14.5
Visibility Tint: Light Blue	**Modality:** Single-Use Daily Wear
Pack Sizes: 90-pack Revenue, 30-pack Revenue, 10-pack Trial	**Replacement Schedule:** Daily Disposable
UV Protection: Class 2 UV Blocker The UV blocking averages 98% in the UVB range of 280nm to 315nm and 84% in the UVA range of 316nm to 380nm.*	

*UV absorbing contact lenses aren't substitutes for protective UV absorbing eye wear – for example, protective UV absorbing goggles or sunglasses – because they don't completely cover the eye and surrounding area. Patients should continue to use UV absorbing eye wear as directed. Note: Long term exposure to UV radiation is a part of risk factors associated with cataracts. Exposure is according to a number of factors, for instance environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV absorbing contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-absorbing contact lenses reduces the risk of developing cataracts or other eye disorders. Consult your Eye Care Professional for more information.

Indication for US:
NaturalVue® (etafilcon A) Multifocal 1 Day Contact Lens 510(k) US Indication for Use:
NaturalVue (etafilcon A) Multifocal Daily Disposable Soft (Hydrophilic) Contact Lenses are indicated for daily wear for the correction of refractive ametropia (myopia and hyperopia) and/or presbyopia in aphakic and/or non-aphakic persons with non-diseased eyes in powers from -20.00 to +20.00 diopters and with non-diseased eyes who may require a reading addition of up to +3.00D. The lenses may be worn by persons who exhibit astigmatism of 2.00 diopters or less that does not interfere with visual acuity.

Like other disposable, soft contact lenses for daily wear, NaturalVue Multifocal Lenses are not risk-free. Problems with contact lenses can result in serious injury to the eye, and it is essential that patients follow directions from Eye Care Professionals and labeling instructions for proper use of lenses. There may be increased risks for children (e.g., microbial keratitis), due for concerns about lens care and hygiene; user training and adult oversight is important. Additional risk information may be found in the product labeling at: at https://vtivision.com/wp-content/uploads/2018/02/NaturalVue-Package-Insert.pdf

OPEN

Case Series Analysis of Myopic Progression Control With a Unique Extended Depth of Focus Multifocal Contact Lens

Jeffrey Cooper, M.S., O.D., Brett O'Connor, O.D., Ronald Watanabe, O.D., Randall Fuerst, O.D., Sharon Berger, O.D., C.O.V.D., Nadine Eisenberg, O.D., and Sally M. Dillehay, Ed.D., O.D.

Objectives: To determine the rate of myopia progression in children fit with a commercially available extended depth of focus (center distance) multifocal soft contact lens with attributes theoretically expected to slow the progression of myopia.

Methods: A retrospective case series analysis of 32 patients (ages 6–19 years, mean 10.98±2.95) from 10 practice locations was performed. At initial presentation, 44% wore spectacles, 37.5% spherical soft contact lenses, 15.6% a different soft multifocal contact lens, and 3% orthokeratology lenses. All participants showed progression of at least −0.50 diopter with current corrections and were fit with an extended depth of focus (center distance) multifocal soft contact lens (NaturalVue Multifocal 1 Day Contact Lenses; Visioneering Technologies, Inc., Alpharetta, GA). Follow-up time was 6 to 25 months (mean: 10.94±4.76).

Results: Reductions in the annualized rate of myopic progression from −0.85 D per year ±0.43 D to −0.04 D per year ±0.18 D ($P<0.00000$) OD, −0.90 D per year ±0.57 D to −0.03 D per year ±0.17 D ($P<0.00000$) OS were observed. These data represent a reduction of 95.4% OD and 96.25% OS. Approximately 98.4% of the children showed reduction of annualized myopic progression; 91% showed a decrease of 70% or greater. Overall, 81.25% showed complete halting of myopic progression, including 6.25% demonstrating myopic regression.

Conclusions: This unique extended depth of focus (center distance) daily disposable multifocal contact lens was effective in slowing myopic progression in these children. These findings add to the growing evidence that center distance multifocal soft contact lenses may slow the progression of myopia.

Key Words: Myopia control—Myopic progression—Center distance multifocal—Myopic regression—Daily disposable soft contact lens.

(*Eye & Contact Lens* 2017;0: 1–9)

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J. Cooper: consultant to VTI, Treehouse Eyes, and Magic Leap; B. O'Connor: consultant to VTI; R. Watanabe: none declared; R. Fuerst: none declared; S. Berger: none declared; N. Eisenberg: none declared; and S. M. Dillehay: employee of VTI.

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Myopia is increasing in epidemic proportions, with its incidence reaching over 80% in a number of Asian countries.[1,2] In the United States, the incidence of myopia has been reported to be approximately 40%, which has doubled since the 1970s.[3] In addition to the incidence of myopia, its magnitude has also increased.[4] These factors have far-reaching implications because myopia has been identified as the sixth-leading cause of blindness, secondary to myopia-induced retinal detachment, macular degeneration, glaucoma, and cataract.[5–7] For this reason, there has been an increased desire to slow the progression of myopia.

Numerous animal studies have shown that altering visual stimuli can alter axial growth.[8,9] More specifically, various powered ophthalmic lenses (both plus and minus) can either shorten or lengthen eyes.[10,11] In addition, it has been shown that the peripheral portion of the eye is more important than the central portion of the eye for regulating eye growth.[12,13] These animal studies are paramount to current understanding of the progression of myopia.

When myopia is corrected with traditional contact lenses or glasses, the central retina is in focus, whereas the peripheral retina is out of focus, resulting in relative peripheral hyperopic defocus. From animal studies, it is believed that this peripheral hyperopic defocus may be the stimulus for the development of myopia.[12,13] Therefore, treatment of myopic progression must eliminate the peripheral relative hyperopic defocus created by spherically correcting ophthalmic lenses/contact lenses, or somehow block the biochemical process causing axial elongation.[5,14]

Orthokeratology corrects central vision while producing significant plus power in the midperiphery; it is presumed that this relationship slows the progression of myopia.[5,15–17] Meta-analysis has shown that orthokeratology slows the progression of myopia by 45% or a weighted mean difference of 0.13 mm per year in the axial length.[18,19] However, there is a concern by patients and doctors for microbial infection or possible long-term adverse effects with orthokeratology.[20,21] In addition, orthokeratology is not approved for refractive errors above 6.00 D of myopia and is reported to be less effective for lower amounts of myopia and in older patients.[22–25]

For these reasons, there has been interest in prescribing soft multifocal contact lenses, to slow the progression of myopia. Anstice and Phillips[26] evaluated a dual focus lens with a 3.36-mm zone of central distance vision correction and surrounding zones of 2.00 D of relative plus power; they reported that myopic progression was reduced by 37%. Holden et al.[27] evaluated a soft contact lens designed to slow the rate of myopia progression. After 6 months of wear, there was a 57% reduction in the progression of myopia. Lam et al.[28] evaluated contact lenses that incorporated +2.50/plano

Cooper, J., M.S., O.D., O'Connor, B., O.D., Watanabe, R., O.D., Fuerst, R., O.D., Berger, S., O.D. C.O.V.D., Eisenberg, N., O.D., & Dillehay, S. M., Ed. D., O.D. Case Series Analysis of Myopic Progression Control With a Unique Extended Depth of Focus Multifocal Contact Lens. Eye & Contact Lens. 2017. http://journals.lww.com/claojournal/Abstract/publishahead/Case_Series_Analysis_of_Myopic_Progression_Control.99309.aspx. Accessed November 01, 2017.

alternating concentric rings, whereby myopic progression was slowed by 25%. Unfortunately, none of the lenses used in the aforementioned studies are commercially available in the United States for practitioners to use in clinical practice.

There is only one study that used a contact lens that is currently commercially available in the United States. Walline et al.[29] used a Proclear (CooperVision, Pleasonton, CA) +2.00 add "D" multifocal; a 50% reduction in myopia after 2 years of wear as compared to an age-matched historical control group was reported. These results are encouraging, but many of the subjects in that study were not generally able to tolerate the higher add powers needed to provide a larger amount of relative plus in the periphery.

Visioneering Technologies, Incorporated (VTI, Alpharetta, GA) has recently introduced a daily disposable extended depth of focus (center distance) multifocal soft contact lens, NaturalVue Multifocal 1 Day Contact Lenses (NVMF), designed with approximately 8 to 11 D of relative plus power at the edge of the pupil (unpublished data), and approximately 20 D of relative plus power at the edge of the optic zone (US patents 6,474,814, 7,178,918). The smooth, gradual, continuous nature of the relative plus power increase creates an extended depth of focus and has been shown to provide visual acuity and stereoacuity similar to vision with the best-corrected spectacle refraction.[30] The lens design has been shown in animal (chick) studies both to inhibit the progression of up to −10.00 D of myopia[31] and to reverse it completely once myopia has developed.[32] In children, the lens design has been shown to move both meridians of the retinal image inside the retina.[33,34] In addition, the lens design has been shown to reduce the lag of accommodation and improve measured accommodative amplitudes in children, as compared to a single-vision contact lens.[30] The vision with the lens was also rated as highly as a single-vision contact lens,[30] using the Pediatric Refractive Error Profile developed by Walline et al.[35] to compare the vision-specific quality of life for children with refractive errors. Because this lens design has attributes theoretically expected to slow the progression of myopia and is commercially available, a retrospective case series analysis was undertaken to determine whether this multifocal lens design would slow the progression of myopia in clinical practice.

METHODS

A retrospective case series analysis of data from 32 consecutive patients that practitioners fit with the NVMF contact lenses within 10 practice locations between March 2015 and August 2016 was performed. All these patients completed at least one 6 month follow-up visit, with some patients being followed for up to 25 months. The lenses were prescribed within a clinical practice setting within their indicated use for the correction of myopia. Parents and children were advised that the lens design showed an appropriate design and animal data to support its use to slow myopic progression, but presently no long-term clinical data were available in that regard. Patients and parents provided assent and consent, respectively, for the use of these lenses, consistent with standard clinical practice, and with the Declaration of Helsinki for unproven interventions in clinical practice. Before the data were analyzed, they were deidentified and sent to one person for central analysis. Parental consent for use of the retrospective data was obtained before including it in this case series analysis. Because of the retrospective nature of the data review and the use of deidentified data, the study met the Exempt Criteria per 45 CFR 46.101 (b)(4). Therefore, written informed consent/assent was not required, and a waiver was obtained from the Southwest Independent Institutional Review Board, Inc (Reference SI-17-10).

Clinical Assessments

Each practitioner used his or her own clinical judgment as to the children whom needed to have their myopia progression addressed. As a clinical criterion, the child had to show at least −0.50 D of refractive progression since the previous examination before various options were presented to the patient and parents.

Various options for addressing the progression of myopia were discussed with the parents and children, including the use of low-dose atropine with or without progressive addition spectacle lenses (PALs), orthokeratology, soft multifocal contact lenses, and not doing anything other than continuing to monitor the child's myopic progression. The benefits and risks associated with each of these interventions were discussed with the patients and the parents. It was made clear to both the patients and the parents that each option showed published data available suggesting that it may slow myopic progression. Consistent with normal clinical practice, patients and parents gave verbal assent and consent to be fit with the NVMF contact lenses and were advised that they could refuse or discontinue treatment at any time. A few of the patients had previously been prescribed orthokeratology lenses and/or low-dose atropine, but these treatments were not successful in slowing the myopic progression. Normal fees were charged and collected for both the professional services and the contact lenses by each practice.

Assessing Efficacy of Treatment

The previous spectacle refraction and type of correction at the time of the initial visit, as well as the length of time since the previous examination was used as a starting point. The amount of progression observed at the initial visit as compared to the previous examination was then divided by the number of months since the previous examination. The monthly amount of progression was then annualized. In this way, each child served as his/her own historical control.

These children were examined approximately every 6 months after the initial fitting of the multifocal contact lenses. At each follow-up visit, the amount of progression observed was then divided by the number of months since the last examination. If a child was seen for more than one 6 month follow-up visit, the progression observed during the entire time that they had worn the NVMF contact lenses was analyzed. The monthly amount of progression was then annualized, before wearing the NVMF and after wearing the NVMF.

Statistical Analysis

Because there was variability in the amount of myopic progression between the two eyes of many of these children, data for each eye were analyzed separately. A Student's paired *t* test was used to compare the annualized historical refractive progression to the annualized refractive progression observed with the NVMF lenses, with a P value <0.05 denoted as statistically significant.

RESULTS

The children ranged in ages 6 to 19 years (mean: 10.98±2.95) at the time that they were fitted with NVMF lenses, with the most

frequent age (mode) being 11 years. Two children (6.3%) were older than 16 years, and 15 children (46.9%) were younger than 12 years. The percentage of females to males was 56% to 44%. Before wearing the NVMF contact lenses, the children were in various myopic corrections: 14 (44%) spectacles, 1 (3%) orthokeratology lenses, 12 (37.5%) single-vision spherical contact lenses, and 5 (15.6%) multifocal soft contact lenses (Biofinity Multifocal; CooperVision; iSight Myopia Controlens; GP Specialists, San Diego, CA; Acuvue 1 Day Moist Multifocal; Johnson & Johnson, Jacksonville, FL). The children had worn the NVMF contact lenses on average for 10.94±4.76 months, with a range of 6 to 25 months. Eight children (25%) had worn the lenses for 6 months, 17 (53%) for 7 to 12 months, 5 (15.6%) for 13 to 18 months, and 2 (6.2%) for 24 months or longer. The most frequent amount of time that the lenses were worn (mode) was 12 months with 12 children (37.5%); 19 children (59.4%) had worn the lenses for 12 months or longer.

Treatment Efficacy

The average annualized amount of myopic progression before wearing the NVMF contact lenses was −0.85 D per year ±0.43 D OD, which was reduced to −0.04 D per year ±0.18 D ($P<0.00000$) after wearing the NVMF lenses and −0.90 D per year ±0.57 D OS reduced to −0.03 D per year ±0.17D OS ($P<0.00000$). There were not any significant differences in the amount of myopic progression between OD and OS before ($P=0.48$) or after ($P=0.79$) wearing the NVMF lenses.

The decrease in the annualized myopic progression was 95.4% OD and 96.25% OS, with the most frequently observed decrease in myopic progression (mode) of 100% in each eye. The decrease in myopic progression ranged from −6.5%, indicating that the child's myopic refractive error had increased, to 167.7%, indicating that not only had no progression occurred, but also that the amount of the child's myopic refractive error had actually decreased, that is, regressed. There was not a significant difference in the percentage of decrease in myopia progression between the right and left eyes ($P=0.48$).

As shown in Figure 1, only 1.56% of the children continued to show an increase in myopia; 98.4% of all children demonstrated a decrease in the amount of myopic progression with the NVMF contact lenses. Almost 91% (90.6%) of the children showed a 70% decrease or greater in their amount of myopic progression. The distribution of these data shows a greater percentage of children exhibiting a decrease in myopic progression than would have been predicted based on previously published data for other myopic progression interventions.[26–29]

Figures 2 and 3 illustrate the annualized amount of myopic progression before and after wearing the NVMF, for the right and left eyes, respectively. Individual variability can be seen in the data, with most children progressing fairly rapidly in their myopia before wearing the NVMF lenses. After wearing the NVMF lenses for 6 to 25 months, most of the children (81.25%) showed a halting of myopic progression (75%) or an actual regression (6.25%) in the amount of their myopia.

Individual Case Examples

One of the younger children (age 8), who was progressing rapidly is shown in Figure 4. This child had progressed −0.75 D OD and −1.25 D OS over 12 months. After 12 months wearing the NVMF contact lenses, his myopia showed no progression, even though he was young.

Figure 5 depicts the myopic progression for a 14-year-old Asian male, who had been progressing in myopia at approximately 1.00 D per year. At age 13, he was fit with Biofinity "D" multifocal contact lenses with a +2.00 D add (CooperVision). This child demonstrated another 1.00 D of myopic progression after wearing those multifocal lenses for 9 months. This child was then fit in the NVMF contact lenses. For the next 25 months, the myopia did not progress in his right eye, whereas his left eye showed a 0.25 D regression in myopia.

Figure 6 shows a young female who had been followed by her practitioner for more than 7 years. At age 7, she was prescribed PALs with 0.025% atropine. At age 9, single-vision spectacles replaced her progressive addition spectacles because she was on a low dosage of atropine. However, her myopia began to progress, even with resumption of the use of the PAL lenses. At age 10, she

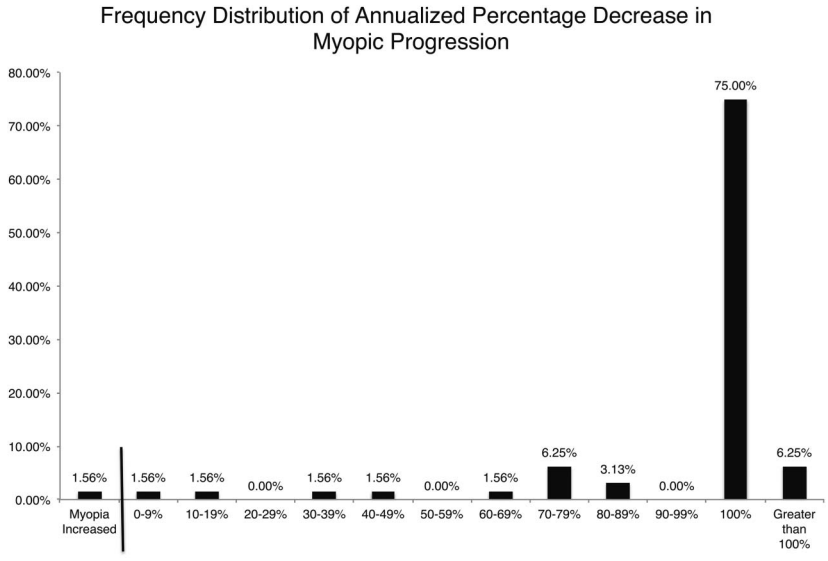

FIG. 1. Frequency distribution of the percentage change in the myopic progression after wearing NaturalVue Multifocal for 6 to 25 months. The percentage shown as greater than 100% decrease in myopia progression indicates that there was a regression in the amount of the refractive error observed in some subjects.

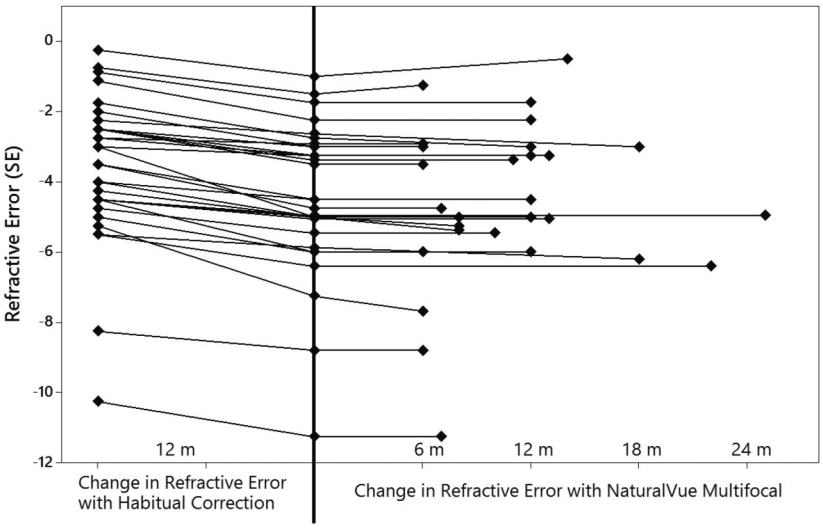

FIG. 2. Individual data plots of baseline refractive error (spherical equivalent [SE] in diopters) versus follow-up time (months), both before and after wearing NaturalVue Multifocal for 6 to 25 months (right eye). The change in the y-axis indicates the change in refraction, the change in the x-axis indicates the number of months that each treatment was followed, and the gradient of each line indicates the amount of myopic progression both before and after treatment.

was switched into the NVMF. After 18 months of wearing the NVMF lenses, her myopia has not progressed.

Figure 7 depicts the progressive refractive status of a 19-year-old female who had been followed by her practitioner since the age of 12. She wore spectacles and single-vision contact lenses for several years, and continued progressing approximately 0.50 D in her right eye and 0.25 D in her left eye each year for three consecutive years. At age 15, she was fit into a custom multifocal contact lens (iSight Myopia Controlens, GP Specialists) but continued progressing over the next 3 years: −1.00, −0.75, and −0.75 D in her right eye, and −0.50, −0.75, and −0.25 D in her left eye. Because this patient was now a high myope (−10.25 D spherical equivalent in her right eye and −6.75 D in her left eye), in college, and completing large amounts of near work, she was concerned that her myopia progression would continue possibly at an even faster rate. Her practitioner fit her into NVMF, and her myopia has not changed over the past 7 months. It remains to be seen if the myopia will not progress, as she continues to wear the lenses for a longer period. Because she is now 20 years old, it is unknown how her age may have impacted the observation of no progression for the past 7 months with NVMF.

In this pilot retrospective study, we have tried to portray representative historical progression of patients before and after intervention with NVMF. There were two children who showed little decrease in the amount of myopic progression or continued to increase in myopia. Figure 8 shows that there was no significant reduction in the rate of myopic progression for one 12-year-old child. This child, who is of Asian descent with both parents being myopic, is still wearing the NVMF contact lenses. In addition, low-dosage atropine was also prescribed. Figure 9 shows the myopic progression of the child with an increase in myopia. This 14-year-old female had previously used PAL spectacles in conjunction with 1.0% atropine. As a result of her failure to use atropine consistently, she discontinued the atropine and was treated with orthokeratology contact lenses. Similar to atropine, she was inconsistent in her treatment with the orthokeratology lenses. When she wore her orthokeratology lenses, her myopia was in abeyance. However, in high

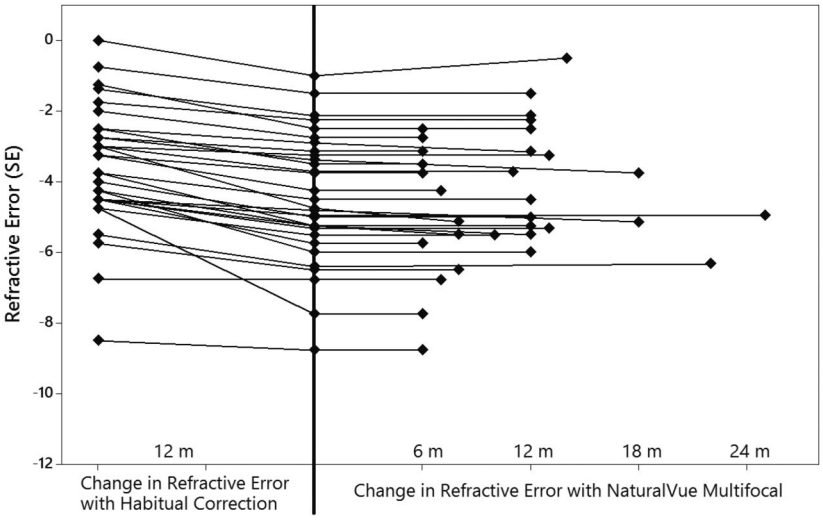

FIG. 3. Individual data plots of baseline refractive error (spherical equivalent [SE] in diopters) versus follow-up time (months), both before and after wearing NaturalVue Multifocal for 6 to 25 months (left eye). The change in the y-axis indicates the change in refraction, the change in the x-axis indicates the number of months that each treatment was followed, and the gradient of each line indicates the amount of myopic progression both before and after treatment.

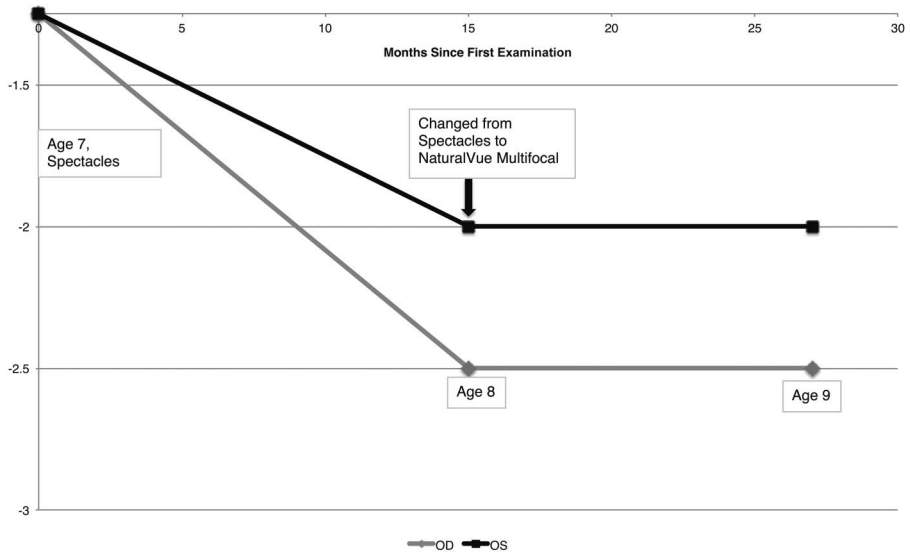

FIG. 4. Myopic progression is depicted by plotting individual patient refractive error (spherical equivalent in diopters) versus follow-up time (months), of myopic progression in an 8-year-old child who had been wearing spectacles, before and after wearing NaturalVue Multifocal for 12 months.

school, compliance again became an issue and she was refit into the NVMF contact lenses. After 2 months, both eyes showed an increase in myopia of −0.50 D. This increase might have been because she was fitted with her NVMF only a week after discontinuing orthokeratology. Since that time, her refractive error has not changed with the NVMF lenses over an 18-month period.

In addition to the 32 children included in this retrospective case series analysis, there were 2 additional children who discontinued wearing the NVMF contact lenses. One of the dropouts was a 7-year-old Asian child with two myopic parents who showed −0.75 D myopic progression OU before being fit with the NVMF lenses. The child did not consistently wear the contact lenses, and the decision was made to discontinue lens wear until the child was older. The second child who dropped out of wearing the lenses was 13 years old and did not return for her 6- or 12-month follow-up visits, so her results are unknown.

DISCUSSION

Both Cooper et al.[5] and a recent meta-analysis[36] of 16 different interventions for myopia have shown that there are currently 4 available treatment options that decrease the progression of myopia by approximately 50% or more: atropine 1%; low-dose atropine (generally concentrations of 0.01%); orthokeratology; and specific center distance multifocal contact lenses. The NVMF contact lens design has the largest amount of peripheral plus power compared with other commercially available center distance contact lenses. The NVMF is the only daily disposable center distance multifocal contact lens cleared by the FDA and commercially available in the United States.[37] Daily disposable contact lenses have been shown to have a 12.5 times lower risk of inflammatory events than soft contact lenses that are cleaned, reused, and replaced on a less frequent basis,[38] which is an important factor when considering contact lens selection in a young patient population.

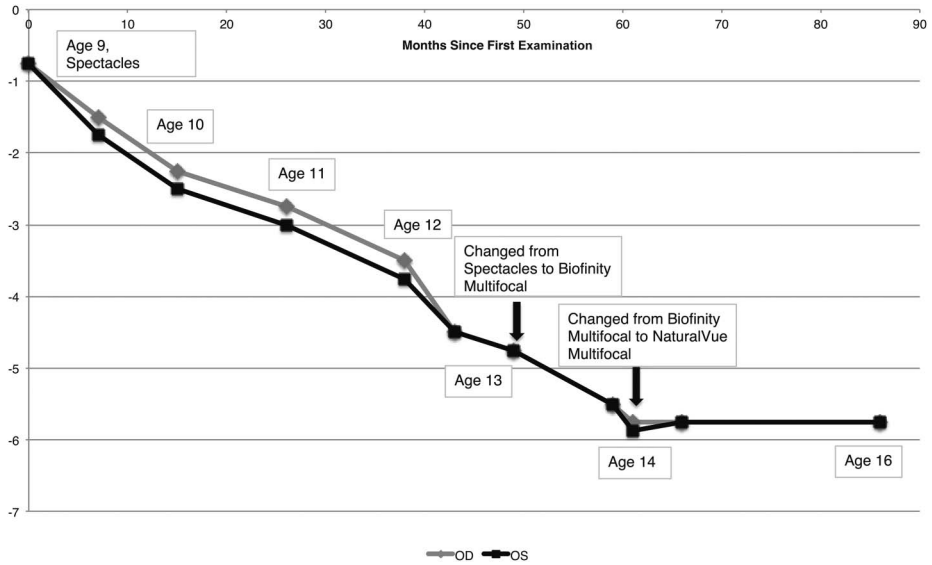

FIG. 5. Myopic progression is depicted by plotting individual patient refractive error (spherical equivalent in diopters) versus follow-up time (months), in a 14-year-old child who had been wearing a center distance multifocal contact lens initially, before and after wearing NaturalVue Multifocal for 25 months.

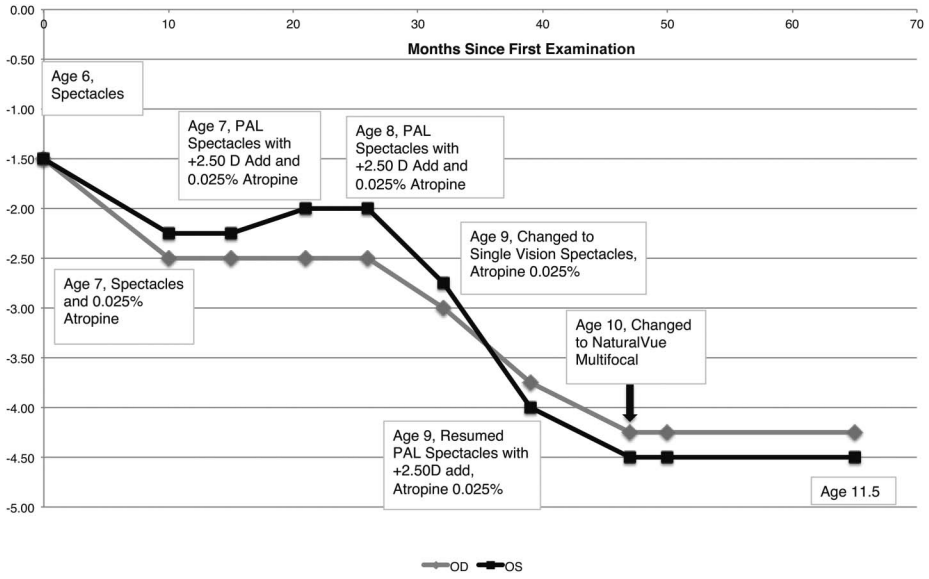

FIG. 6. Myopic progression is depicted by plotting individual patient refractive error (spherical equivalent in diopters) versus follow-up time (months), in a 10-year-old child who had used orthokeratology, spectacles, progressive addition spectacles, and atropine, before and after wearing NaturalVue Multifocal for 18 months.

Turnbull et al.[39] recently reported similar results to those found in this analysis also using a retrospective case series approach. They prescribed a dual focus soft contact lens for 32 children with an average age of 11.4±2.39 years (range not reported) and found a 91% decrease in the annualized myopia progression. However, in previous published data that same lens design only showed a decrease of 37%.[26] This discrepancy may be due to methodological differences. It also seems that at least 2 of the 32 participants were followed for a period of less than 6 months, which may have impacted the overall results. The lenses used by Turnbull et al.[39] are not currently commercially available in the United States.

Aller et al.[40] prescribed center distance bifocal contact lenses (Acuvue Bifocal, Johnson & Johnson) for myopic children ages 8 to 18 (average 13.0±2.5 years) with an eso fixation disparity at near and demonstrated a 72% reduction in myopia progression. Only patients with an eso fixation at near were included, which makes it inappropriate to draw conclusions for patients without such an eso fixation. The lenses used by Aller et al.[40] are not currently commercially available.[41]

A common criticism of retrospective case series analysis is that it does not provide the scrutiny found in double-masked, prospective, randomized controlled clinical trials. This pilot data analysis is the first step in planning a randomized clinical trial. We are aware that the results must be interpreted with limitations, including the fact that the exact mechanisms of the observed decreases in myopic progression are unknown for these children because both topography and axial length measurements were not taken. However, previous studies have shown that neither axial length nor keratometric findings change with soft spherical contact lenses.[42–44]

In our retrospective case series, as well as that of Turnbull et al.,[39] each child acted as his or her own historical control. From a clinical

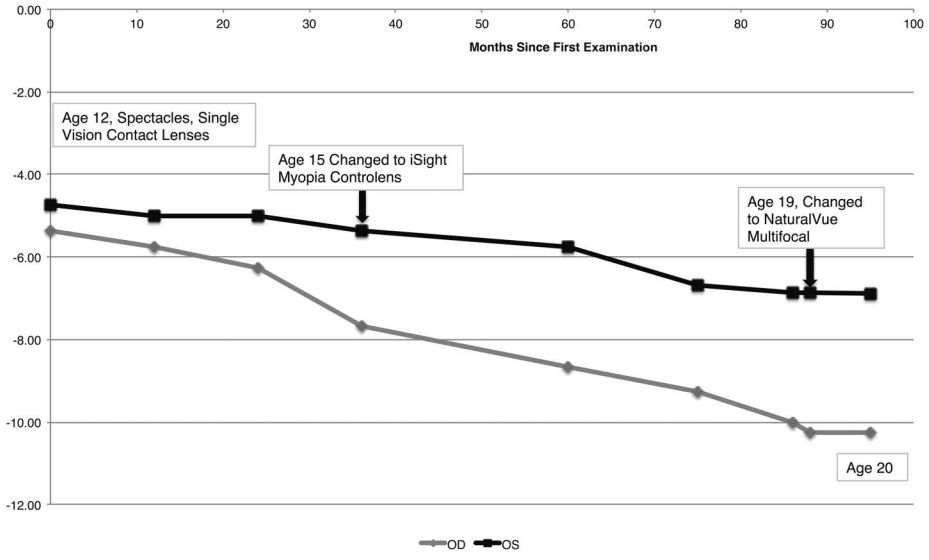

FIG. 7. Myopic progression is depicted by plotting individual patient refractive error (spherical equivalent in diopters) versus follow-up time (months), in a 19 year old who had used spectacles, single-vision contact lenses, and a center distance multifocal contact lens, before and after wearing NaturalVue Multifocal for 7 months.

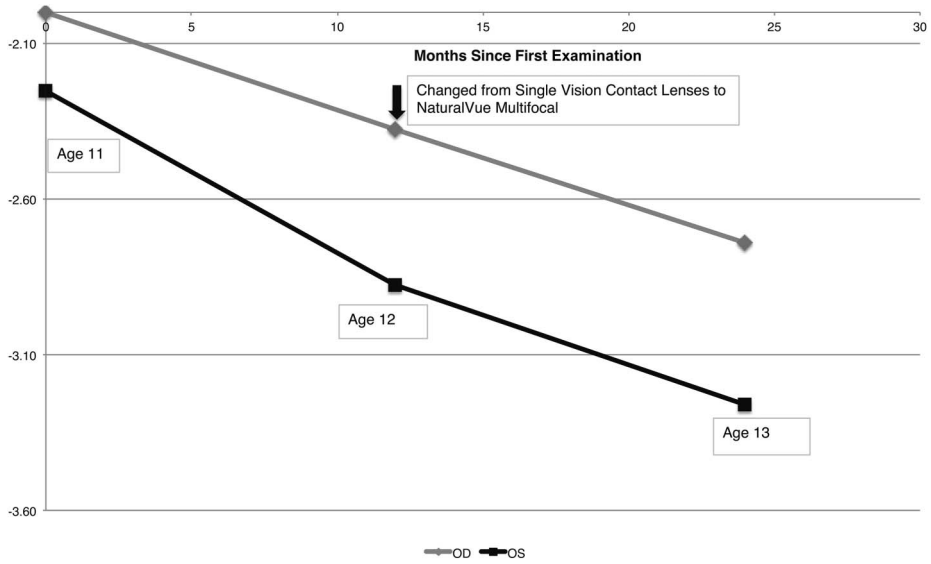

FIG. 8. Individual patient refractive error (spherical equivalent in diopters) versus follow-up time (months), showing a summary of myopic progression in a 12-year-old who exhibited little to no decrease in her myopic progression after wearing NaturalVue Multifocal for 12 months.

perspective, parents want to know the likelihood that an intervention will result in a decrease in myopic progression. Data from these case series in which each child serves as a historical control are thus useful in predicting outcomes for parents. It is possible that some of the children in this case series would have slowed or ceased myopia progression without intervention because of their age and/or genetic predisposition. However, the young age range, the refractive error range, and the refractive changes observed at baseline in the children included in these data, make this scenario less likely.

Normal progression of myopia has been generally considered to continue until about 18 years of age.[5] However, Irving et al.[45] showed that in a large clinical population of almost 6,400 people, progression of myopia continued until the early twenties. Fernandez-Montero et al.[46] showed that 10% of the work force after graduate school continued their progression of myopia well into their thirties. Bullimore et al.[47] showed in a retrospective study of 815 soft contact lens wearers that myopic progression was common in adults with 34.9% of 20 to 25 year olds, 19.6% of 25 to 30 year olds, 13.6% of 30 to 35 year olds, and 10% of 35 to 40 year olds still showing at least a 1.00 D myopic progression over a 5-year period. Likewise, the National Research Council Committee on Vision Working Group, which reviewed more than 500 articles on myopia published since 1950, concluded that up to 40% of low hyperopes and emmetropes entering college and military academies were likely to become myopic by the age of 25.[48]

Therefore, the children in this retrospective case series as a group would generally be expected to have continued to progress in their myopia without intervention. This, of course, does not negate individual observations of the clinician who notes that some children progress for a while and then stop or slow their progression pattern. Myopia progression patterns may vary widely among children and adolescents, some of whom will stop progressing at a younger age, whereas others will continue to progress into their twenties.

Gifford and Gifford[49] suggested that if a myopic child could be kept from progressing from −1.00 to −3.00 D, this would decrease the risk of myopic maculopathy by 4 to 5 times, retinal detachment

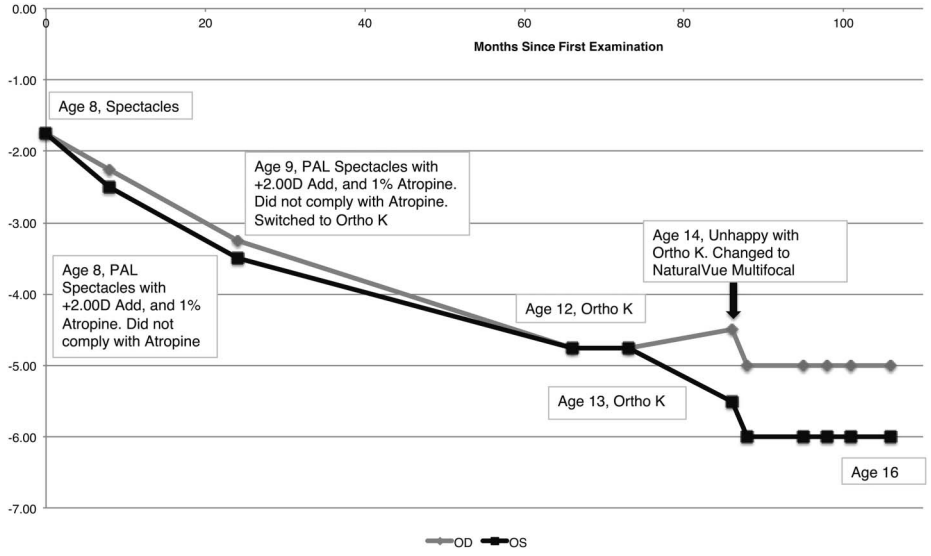

FIG. 9. Myopic progression is depicted by plotting individual patient refractive error (spherical equivalent in diopters) versus follow-up time (months), in a 14-year-old child who had exhibited an increase in myopic progression after using orthokeratology, spectacles, progressive addition spectacles, and atropine, before and after being fit with NaturalVue Multifocal. There was an increase in myopic progression observed during the first 2 months of wearing NVMF possibly because of the initial fit occurring only 1 week after ceasing ortho K lens wear, but no further progression was noted for the additional 18 months of the follow-up period.

by 3 times, and posterior subcapsular cataract by 1.5 times. If the data trends observed in this pilot retrospective case series were to hold, assuming a linear progression, a −1.00 D myope would become a −1.20 D myope after 5 years of wearing NVMF. On the other hand, if no myopia control occurred, the child would have progressed to −5.30 D. Although the results of this small sample population were followed for 6 to 25 months, one cannot predict what might happen over 5 years for any given child. Our data suggest that the amount of myopic progression would be reduced for children wearing the NVMF lenses.

CONCLUSIONS

This retrospective case series analysis strongly suggests that the unique extended depth of focus (center distance) design of the NVMF multifocal contact lens can slow the progression of myopia, with the percentage of reduction being higher than previously reported with other lens designs. The data also showed that the lens design demonstrated an actual regression in the amount of the myopic refractive error in some children.

We believe that the significant reduction of myopic progression observed in this study is due to the higher amount of plus in the periphery associated with the extended depth of focus optics in this unique lens design. Based on the theory that relative peripheral hyperopia is a factor in driving axial elongation, that is, myopia progression, the NVMF contact lens may be an effective treatment option for myopic progression control in children. Given the high risk of ocular complications with increased levels of myopia, practitioners should consider using multifocal contact lens designs that slow the progression of myopia in children as a proactive part of their clinical practice.

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