Agreement and Repeatability of Noncycloplegic and Cycloplegic Wavefront-based Autorefraction in Children

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SIGNIFICANCE: Increasing prevalence of refractive error requires assessment of ametropia as a screening tool in children. If cycloplegia is not an option, knowledge about the increase in uncertainty for wavefront-based autorefraction is needed. The cycloplegic agent as the principal variant presents cross-reference and allows for extraction of the influence of accommodation.

PURPOSE: The purpose of this study was to determine the repeatability, agreement, and propensity to accommodate of cycloplegic (ARc) and noncycloplegic (ARnc) wavefront-based autorefraction (ZEISS i.Profiler plus; Carl Zeiss Vision, Aalen, Germany) in children aged 2 to 15 years.

METHODS: In a clinical setting, three consecutive measurements were feasible for 145 eyes (OD) under both conditions. Data are described by spherical equivalent (M), horizontal or vertical astigmatic component (J0), and oblique astigmatic component (J45). In the case of M, the most positive value of the three measurements was chosen, whereas the mean was applied for astigmatic components.

RESULTS: Regarding agreement, differences for ARc minus ARnc were statistically significant: for M, 0.55 (0.55 D; mean [SD]; P < .001), that is, more hyperopic in cycloplegia; for J0, −0.03 (0.11 D; P = .002); and for J45, −0.03 D (SD, 0.09 D; P < .001). Regarding repeatability, astigmatic components showed excellent repeatability: SD < 0.11 D (ARnc) and SD < 0.09 D (ARc). The repeatability of M was SD = 0.57 D with a 95% interval of 1.49 D (ARc). Under cycloplegia, this decreased to SD = 0.17 D (ARc) with a 95% interval of 0.50 D. The mean propensity to accommodate was 0.44 D from repeated measurements; in cycloplegia, this was reduced to 0.19 D.

CONCLUSIONS: Wavefront-based refraction measurement results are highly repeatable and precise for astigmatic components. Noncycloplegic measurements of M show a systematic bias of 0.55 D. Cycloplegia reduces the propensity to accommodate by a factor of 2.4; for noncycloplegic repeated measurements, accommodation is controlled to a total interval of 1.49 D (95%). Without cycloplegia, results improve drastically when measurements are repeated.

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The measurement of wavefront aberrations has become a widely used and applicable technology in ophthalmology and vision science over the last decade. Therefore, it is essential to know about the metrological details of these devices used to determine the objective refraction. The focus of the article is measurements in children.

It has been suggested to use wavefront-based autorefraction to determine central refractive errors in pre-school and schoolchildren.1 Therefore, because screening studies increasingly use such devices,2–4 it is important to establish repeatability and accuracy of wavefront-based devices.

For data from a typical clinical setting, the feasibility of wavefront-based autorefraction in children is examined first. Second, the agreement between cycloplegic measurements and results under natural conditions are investigated. Noncycloplegic refractions in children, despite their obvious disadvantages, become more frequently used. In most countries of Europe, the application of cycloplegic drops is considered an invasive method. Therefore, ethics councils sometimes refrain from giving permission to more general orientated studies in children to include cycloplegic screening of refractive error. Third, to estimate the short-term repeatability of refraction data under both conditions, repeated measurements in both cases are obtained. From these data, the propensity to accommodate is investigated.

Agreement of noncycloplegic and cycloplegic measurements of autorefraction (abbreviated as ARnc and ARc hereinafter) within one instrument was established only in a few studies; none of them are wavefront-based devices.5–11 Some method comparison studies of ARc or ARnc measured with wavefront-based devices exist with regard to subjective refraction or retinoscopy.12–15 including one study on a handheld wavefront-based device in 40 children (age, 5 to 17 years).12 Therefore, the only data for ARc and ARnc in the same wavefront-based instrument were obtained for a handheld device.

Research studies examining different objective methods investigating repeatability of autorefractor measurements in children have used handheld autorefactors and eccentric photorefactors.6,16–18 More recently, wavefront-based autorefactors were investigated for repeatability in adults,13,14,19–23 children,12,24 and infants.25 The three studies investigating repeatability for wavefront-based measurements in children are not sufficient to estimate repeatability for a larger age range nor can their data be used as cross-reference for
examinations with the tabletop ZEISS i.Profiler plus (Carl Zeiss Vision GmbH, Aalen, Germany) in children: cycloplegic repeatability data were presented for the COAS G200 system, a wavefront-based tabletop design (Wavefront Sciences, Albuquerque, NM), by Martinez et al. in 81 subjects around 12 years of age. Noncycloplegic repeatability in 74 infants was studied for handheld wavefront-based SureSight (Welch Allyn, Skaneateles Falls, NY) by Adams et al. Rosenfield and investigated repeatability of cycloplegic and noncycloplegic wavefront-based autorefraction for a handheld device in a small group of five subjects (age, 5 to 17 years) for the SVOne (Smart Vision Labs, New York, NY).

Very few data on noncycloplegic and cycloplegic measurements of autorefraction in children within one instrument based on wavefront-based technology exist. Our study expands these data regarding the range of age, range of refractive errors, and the number of participants.

METHODS

This study was approved by the institutional ethics board of the Medical Faculty of Leipzig University. Informed written consent from at least one parent or legal guardian and verbal assent from each child were obtained. The child then was invited to participate in the wavefront-based autorefraction and had the opportunity to opt out at any point in time. Clinical refraction data were examined for all children as part of their routine visit between May and November 2013 at the Paediatric Ophthalmology Section of the Department of Ophthalmology at the University Hospital Leipzig. Routine examination included the assessment of refractive errors by cycloplegic retinoscopy and by using wavefront-based autorefraction before and after application of cycloplegia. The individual performing retinoscopy was not aware of wavefront-based autorefraction results. Cycloplegia was induced by applying 0.5% tropicamide (Mydram, Bausch & Lomb GmbH, Berlin, Germany) as part of the clinical routine eye examination. Yazdani et al. showed that differences between tropicamide and cyclopentolate are not significant for a 1% solution. Furthermore, the percentage concentration of 0.5% was used successfully in previous studies. Nevertheless, this may be considered to be a weak cycloplegic agent. To this end, each eye was checked by the leading ophthalmologist during retinoscopy for absence of fluctuations of the neutral retinoscopic reflex and absence of a light-induced change of pupil diameter. If it were judged that cycloplegia was incomplete, one more dose would be necessary. However, such a case was not observed.

Data were obtained in the following sequence. The measurement protocol prescribed three repeated measurements of noncycloplegic wavefront-based autorefraction. The autorefraction measurement process per eye takes less than 1 minute once the child is situated in front of the machine. Then, one drop of the aforementioned cycloplegic agent was administered into each eye, and after an interval of 10 minutes, a second drop was inserted into each eye. Twenty minutes after the second drop was administered, cycloplegia was examined as described previously. Then, three repeated measurements with wavefront-based autorefraction in cycloplegia were obtained.

One optometrist (HL) performed both autorefractions with the wavefront-based device (ZEISS i.Profiler plus, Carl Zeiss Vision GmbH). In total, 201 children (106 male and 95 female, aged 2 to 15 years) were examined in the given time frame. Children with a pathological chief complaint and/or abnormalities/diseases of the retina, lens, or cornea were excluded from this clinic-based data set before the current analysis. However, data of subjects with strabismus (if fixation for single-eye measurements was adequate), amblyopia, nystagmus, or anisometropia were allowed to be included into the analysis. Children who had fewer than three measurements under either measurement condition were excluded from the presented analyses. Both eyes were analyzed separately, and according to current practice, only data on one eye (right eyes) are presented in text and tables.

A wavefront aberrometer based on a Hartmann-Shack sensor, the ZEISS i.Profiler plus, was used to measure the outcome wavefront for each eye of the participant three times. A chin and head rest was used to stabilize the subject's head. The alignment with reference to the measurement instrument was achieved automatically by detecting the pupil center. A fixation target is used to reduce the eye's movement. In case of blinking or a larger decentration of the eye, the measurement is repeated automatically after a few seconds. During the measurement, the subject looks through the optics of the instrument at a projected target (hot air balloon with colored stripes), which undergoes a fogging process to relax accommodation. Then, a series of images are taken with the Hartmann-Shack sensor and combined into one result. This entire process is called one measurement.

The process of presenting the target is divided into three parts: (1) a fogged target is shown in the beginning; (2) the far point of the eye is measured, and the optical distance of the projected target is adjusted accordingly to produce a sharp image; and (3) as a last step, the image of the target is slowly fogged during 3 seconds to deaccommodate the eye. During this deaccommodation process, three internal measurements are obtained. This procedure is considered to minimize accommodation.

The eye's wavefront is measured over the complete pupil, which is detected automatically by the instrument. However, to determine autorefraction data, the internal software reduces the evaluated pupil size to a diameter of 3 mm. In this central region, the second-order Zernike coefficients of the wavefront are determined and converted to equivalent sphere (M) and two astigmatic components, J0 (horizontal/vertical astigmatism) and J45 (oblique astigmatism), as described previously.

To minimize the influence of accommodation, the most positive value of the spherical equivalent (M) is chosen. To emphasize this fact, instead of a mean value, the least negative (myopic) result of the three measurements is applied. The three results for the astigmatic components (J0 and J45), however, are represented by their ordinary mean value.

Statistical Assessment of Repeatability and Agreement

Agreement

For the comparison of noncycloplegic and cycloplegic wavefront-based autorefraction, the method comparison approach by Bland and Altman is applied. Agreement between measurement conditions was assessed by computing the difference between measurements in both conditions, ARc minus ARnc for each subject. These differences are averaged across the group to give the mean difference, termed bias. A positive value for the bias signalizes a more myopic result for ARnc, that is, potential accommodation.

Repeatability

The measurements are repeated by the same operator in a time interval of a few minutes. This could be referred to as short-term
repeatability; however, the common wording of repeatability is applied.

Two different statistical approaches are used to determine the repeatability for the astigmatic components and the spherical equivalent. The three measurements for astigmatic components J0 and J45 are represented by their mean value and their spread by the standard deviation. The representative variability of all subjects is then described by the pooled variance (arithmetic mean of individual variances):

$$S_p^2 = \frac{1}{N} \sum_{n=1}^{N} S_n^2$$

This quantity is also known as “within-subject variability” from an analysis of variance, where each subject is treated as a group. By taking the square root of pooled variance, a pooled standard deviation $S_p$ is calculated. The 95% reference interval is estimated by $\pm 1.96 \cdot S_p$.

In case of the spherical equivalent $M$, the method to evaluate the results is different. Here, the most positive value of the set of three measurements is chosen. The rationale behind this approach is the following. If the status of the eye with the lowest refractive power is considered as zero accommodation, the process of accommodation can change the results only in one direction, namely, increasing the refractive power, leading to more myopic values of the spherical equivalent. In other words, accommodation cannot be negative. Hence, we elect the most positive value of $M$, or the one with the lowest accommodation. The elected value will be denoted by a tilde, $\tilde{M}$.

The variance of this elected value has to be estimated to access its repeatability. It is assumed that the elected value will deviate from the true one, denoted $M$, by an unknown amount of accommodation $A$. Hence,

$$\tilde{M} = M - A$$

where the accommodation $A$ is positive or zero. Only if the accommodation is zero, the desired value $M$ is measured.

An estimate for the probability distribution for the occurrence of accommodation can be extracted from presented repeated measurements in the following way. From the most positive value, the remaining two measurement results are subtracted for each eye:

$$\Delta M_k = \tilde{M} - M_k \quad k = 1, 2$$

They represent the propensity to change the accommodation. These remaining values are pooled for all eyes, and their distribution is taken as an empirical proxy to the propensity to accommodate.

The mean of this distribution describes the offset from zero accommodation (bias). The standard deviation is taken as an estimate for the repeatability.

In addition, an exponential distribution ($\lambda \exp(-\lambda x)$), with only one parameter $\lambda$, is fitted to the data. Both the mean and the standard deviation are given by the inverse of the fitting parameter $\lambda$. Simplicity and the reasonable shape motivated the heuristic choice of the exponential distribution.

Under cycloplegia, such argument applies to a much lesser extent for measurements as well, where a remaining tonic accommodation does not necessarily guarantee zero accommodation. Having this caveat in mind, information on accommodation behavior during the measurement process presents valuable empirical information, which is available only from repeated measurements.

RESULTS

First, the aspects of feasibility are presented. Noncycloplegic wavefront-based autorefraction was termed ARnc, and cycloplegic measurements are referred to as ARc. All children in the said time frame were examined. After exclusion of children with aforementioned pathologies, 187 children entered the investigation. Here, nystagmus was present in three subjects with minor severity; amблиopia was present in 16 eyes.

As a first finding, wavefront-based autorefraction was not successfully obtained in 11 young children for the initial ARnc measurement (ages, 1 to 4 years plus a 12-year-old); here the main reasons were anxiousness or an excess of body/head movements during measurement. In these children, ARc was not attempted. In addition, further 15 children have no ARc measurements, as they declined to be examined by cycloplegic autorefraction at the end of their visit; their ages were 3 to 12 years.

Because the wavefront-based measurement was part of the children’s routine visit at the Department of Ophthalmology, three measurements were encouraged but not mandatory. For the presented article, children who had fewer than three autorefractor measurements under either measurement condition were excluded from the respective repeatability and agreement analyses. Depending on the attention and cooperation of each child during measurement, for ARnc, fewer than three measurements were obtained in 10 children (ages, 2 years [one child], 3 years [five children], 6 years [two children]), and for ARc, fewer than three measurements were obtained in 16 children (ages, 3 years [three children], 4 years [one child], 5 years [four children], 6 years [three children], 7 years [one child], 8 years [one child], 9 years [one child], 10 years [two children]).

Based on three measurements per eye and measurement technique, the intersection formed the analyzed data set, which consisted of 145 children (ARc: 73 pre-school children; mean [standard deviation] age, 4.9 [1.0] years) and 72 schoolchildren (mean [standard deviation] age, 9.3 [2.2] years). The descriptive results of the mean across the groups are presented in Table 1. The spans of refractive errors are greater than 16 D for M, 3.9 D for J0, and 1.8 D for J45.

Agreement of Wavefront-based Autorefraction

Agreement: Astigmatic Components (J0, J45)

For the comparison of wavefront-based autorefraction without cycloplegia and with cycloplegia, data for the astigmatic components are shown in a Bland-Altman plot; see Fig. 1, where the difference of data for the two conditions along the ordinate is plotted against the mean along the abscissa. The abscissae are scaled identically for both components, rendering a visual impression of the much smaller span of the oblique component J45 in comparison with J0.

A clinically irrelevant bias of $–0.026$ D (J0) and $0.025$ D (J45) was found. The total width of the 95% reference interval is $0.40$ D (J0) and $0.33$ D (J45). Hence, 95% of all differences for measurements under the two conditions are smaller than 0.4 D. All data points including probable outliers that present the typical clinical situation are shown in Fig. 1; see Table 2 for full results.
Most of the differences do not follow from the dissimilarity between measurement conditions (ARc or ARnc) but reflect the repeatability of each method itself. This can be seen from the coefficients of repeatability (√2 · 1.96 · SD) for each condition. The results are the following: 0.24 D for J0 and 0.21 D for J45 in cycloplegia and slightly higher values of 0.30 D for J0 and 0.29 D for J45 without cycloplegia; see Table 3 for full results. All differences (less than tenths of a diopter) are clinically irrelevant. Therefore, statistics are omitted.

The results of the analysis of left eye data (not presented) agree with the results obtained for the right eye.

The statistical comparison of agreement (J0, J45) between ARnc and ARc for pre-school (younger than 7 years) children versus schoolchildren showed no statistically significant difference.

**Agreement: Spherical Equivalent (M)**

The agreement for the spherical equivalent (M) can be estimated from the Bland-Altman plot in Fig. 2. As stated previously, the values for the spherical equivalent are determined from the most positive value of three measurements. The ARnc minus ARc difference results in a bias of +0.55 D (P < .001). Hence, measurements without cycloplegia are more myopic, as can be expected from the remaining accommodation. The limits of agreement for the differences span an interval of total width of 2.21 D, or 1.10 D to either side of the bias value (bias, 0.55; −0.55 to +1.65); for full results, see Table 2.

Although the Bland-Altman plot focuses on the agreement of final results, the scatterplot in Fig. 3 illustrates the variability as available from repeated measurements. Data points show the most positive measurement result. The bars, extending in negative direction (to the left or downward), represent the range of accommodation with reference to the data point. The inset expands the densely populated region between −1.5 and 2.5 D. Most of the data lie above the bisecting line (not shown), as expected from results being more myopic in the ARnc condition.

Analyses for pre-school versus schoolchildren resulted in no statistically significant differences. As before, results for the left eye (not shown) are nearly identical.

**Repeatability of Wavefront-based Autorefraction**

**Repeatability: Astigmatic Components (J0, J45)**

The distributions of the centered coordinates for both astigmatic components J0 and J45 are shown in Fig. 4. The distributions are too leptokurtic to represent a normal distribution. The Jarque-Bera test rejects the null hypothesis that a normal distribution is present, at a level of P < .001 for all distributions. This is a typical result for data from a clinical environment because far-lying outliers distort the otherwise normal distribution.

The spreads of the distributions, as described by the pooled standard deviation, are 0.11 D (J0) and 0.08 D (J45) under the ARnc condition and 0.09 D (J0) and 0.08 D (J45) under the ARc condition; see Table 3 for full results. The Ansari-Bradley test rejects the null hypothesis that variances are different at P < .001. Hence, measurements without cycloplegia are more astigmatic, as expected from the remaining accommodation. The limits of agreement for the differences span an interval of total width of 0.49 D, or 0.24 D to either side of the bias value (bias, 0.49; −0.24 to +0.24); for full results, see Table 2.

**Repeatability: Equivalent Sphere (M)**

To evaluate the repeatability of the spherical equivalent M, the standard deviation of the empirical distribution of accommodation

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**TABLE 1. Overview of descriptive statistics regarding noncycloplegic (ARnc) and cycloplegic (ARc) wavefront-based autorefraction**

| Measurement error data (D) | ARnc | ARc |
|----------------------------|------|-----|
| **Refractive error data (D)** |      |     |
| All children (n = 145)     | Mean | 1.38| 1.92|
|                           | SD   | 2.21| 2.34|
|                           | Min  | −8.02| −8.60|
|                           | Max  | 8.44| 8.78|
| ARnc compared with ARc     | P = .04|     |
| Preschool children (2–6 y; n = 73) | Mean | 1.51| 2.23|
|                           | SD   | 1.97| 1.95|
|                           | Min  | −1.46| −1.08|
|                           | Max  | 8.44| 8.78|
| ARnc compared with ARc     | P = .02|     |
| Schoolchildren (7–15 y; n = 72) | Mean | 1.24| 1.61|
|                           | SD   | 2.45| 2.65|
|                           | Min  | −8.02| −8.60|
|                           | Max  | 7.12| 8.08|
| ARnc compared with ARc     | P = .38|     |

Refractive error data (right eyes) from three measurements. The most positive was elected for M. The astigmatic components J0 and J45 are averages. The upper rows present descriptive statistics for all subjects, the middle rows display descriptive statistics for pre-school children, and the lower rows depict descriptive statistics for schoolchildren. We emphasize the large span (>16 D) of our data for the spherical equivalent. P values are provided for the difference between the cycloplegic and noncycloplegic findings.
is estimated relative to the most positive value measured. Fig. 5 displays the distribution for the two investigated conditions. In addition to the histogram of the probability density, calculated from the empirical data, a fit is added for the exponential distribution. The inverse of the only fit parameter $\lambda$ equals both the mean value and the standard deviation. There are very few contributions

![Figure 1](image_url)
beyond the limit of 2 D, which are not visible at this scale. Therefore, the abscissa is truncated at 2 D.

As expected, children under the ARc condition do accommodate very little, with a mean (standard deviation) value of 0.185 (0.185) D (confidence interval, 0.17 to 0.21 D). This number is probably an upper limit because the current data represent a typical clinical, not an optimal environment.

Under the ARnc condition, the distribution becomes much broader, and the mean (standard deviation) value increases by a factor of 2.4 to reach a value of 0.448 (0.448) D (confidence interval, 0.40 to 0.50 D). All values are obtained from the fitted distribution. Numbers calculated directly from the empirical distribution agree nicely regarding the mean value for both ARc and ARnc. A higher result is obtained for standard deviation (0.57 D) in the ARnc condition. This difference in standard deviation indicates a deviation from the exponential distribution, most probably due to outliers.

The empirical 95% percentiles are 1.49 D for ARnc and 0.50 D for ARc, which means that the width of the ARc reference interval is a third of the ARnc case; see Table 3 for full results. For the comparison with other data, one has to keep in mind that this width spans the total interval, not only ± the half, as it is commonly used.

An effective standard deviation is affiliated by the formula \( SD_{\text{eff}} = \frac{1.49 D}{2 \times 1.96} = 0.38 D \). This effective standard deviation would reproduce the 95% reference interval limits under the assumption of a normal distribution of data.

It is of interest to investigate which of the three measurements lead to the most positive value. Because in cycloplegia accommodation is substantially reduced, no preference for any of the measurements, or in other words an equal distribution, is expected. This is the actual result: all measurements, independently of the number of repetition, contribute identically with 33% to the most positive value. Under the ARnc condition, the distribution is different, namely, 44, 26, and 30% for the first, second, and third measurements. Therefore, repeated measurements definitely improve the results.

Finally, the propensity to accommodate is compared in a qualitative way. Two measures are considered: (a) the differences to the most positive value from the triple measurements and (b) the actual accommodation distribution, as determined by the differences between the values for M under the ARc and ARnc conditions. Both distributions are shown in Fig. 6. Note that the first blue bar (ARc minus ARnc) includes all contributions from negative values (up to −0.5 D) of accommodation.

The general appearance of both distributions agrees remarkably well. After a substantial decline toward 0.75 D, a slight increase between 1.0 and 1.5 D can be observed. The intrinsic measure from three measurements alone overestimates smaller accommodation and underestimates the width of the distribution.

### DISCUSSION

#### Feasibility

Wavefront-based measurement with the tabletop based ZEISS i.Profiler plus was feasible in this clinic-based setting to determine

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**TABLE 2. Agreement between non-cycloplegic (ARnc) and cycloplegic (ARc) measurement conditions for all subjects (n = 145, right eyes) and separated for pre-school children and schoolchildren**

| Condition          | ARc minus ARnc (D) | M  | J0  | J45 |
|--------------------|--------------------|----|-----|-----|
| All children       |                    |    |     |     |
| Mean               | \( P < .001 \)     | 0.55 | -0.03 | 0.02 |
| SD                 |                    | 0.56 | 0.11 | 0.09 |
| 2.5 percentile     |                    | -0.22 | -0.26 | -0.13 |
| 50 percentile      |                    | 0.42 | 0.02 | 0.02 |
| 97.5 percentile    |                    | 1.84 | 0.15 | 0.22 |
| \( \pm LoA \)      |                    | 1.05 | 0.16 | 0.17 |
| Preschool children |                    | \( P < .001 \) | \( P = .13 \) | \( P = .002 \) |
| Mean               |                    | 0.72 | -0.02 | 0.03 |
| SD                 |                    | 0.59 | 0.11 | 0.09 |
| 2.5 percentile     |                    | -0.11 | -0.28 | -0.13 |
| 50 percentile      |                    | 0.56 | -0.01 | 0.04 |
| 97.5 percentile    |                    | 2.22 | 0.16 | 0.24 |
| \( \pm LoA \)      |                    | 1.16 | 0.22 | 0.17 |
| Schoolchildren     |                    | \( P < .001 \) | \( P = .004 \) | \( P = .10 \) |
| Mean               |                    | 0.38 | -0.03 | 0.02 |
| SD                 |                    | 0.48 | 0.09 | 0.08 |
| 2.5 percentile     |                    | -0.30 | -0.20 | -0.12 |
| 50 percentile      |                    | 0.30 | -0.02 | 0.02 |
| 97.5 percentile    |                    | 1.56 | 0.14 | 0.19 |
| \( \pm LoA \)      |                    | 0.93 | 0.17 | 0.16 |

The computation of ARc minus ARnc for the comparison of agreement of the measurement conditions (all entries are in diopters) showed a statistically significant difference for \( M \) and for some entries of J0 or J45. However, the computed difference between astigmatic components is clinically insignificant. \( LoA \) = limit of agreement.

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**TABLE 3. Repeatability of wavefront-based autorefraction results without cycloplegia (ARnc) and in cycloplegia (ARc) for all subjects and separated for pre-school children and schoolchildren under each condition**

| Condition          | ARnc (D) | ARc (D) |
|--------------------|----------|---------|
| All children (n = 145) |          |         |
| SD                 | \( 0.57 \) | \( 0.11 \) |
| 95% Total empirical interval | \( 1.49 \) | \( 0.36 \) |
| Preschool children (n = 73) |          |         |
| SD                 | \( 0.56 \) | \( 0.13 \) |
| 95% Total empirical interval | \( 1.47 \) | \( 0.41 \) |
| Schoolchildren (n = 72) |          |         |
| SD                 | \( 0.57 \) | \( 0.07 \) |
| 95% Total empirical interval | \( 1.61 \) | \( 0.28 \) |

Results for the SD of astigmatic components J0 and J45 are based on three repeated measurements per eye, which are pooled for all eyes. All entries are given in diopters. For the spherical equivalent \( M \), the most positive value was elected as a reference, and the spread is one-sided. The reference interval for 95% of all data is provided. In the case of J0 and J45, this is the whole interval for the difference between two measurements. In the case of \( M \), it is the whole interval for the range of differences to the most positive value.
refraction data in children with repeated measurements. We expect that dropout experienced (22% for analysis based on strictly three measurements) could be reduced significantly by improved explanation to children and parents, time management, and preparations.

Limitations

First, we would like to discuss the limitations of our study regarding cycloplegia. (1) We have to acknowledge that 0.5% of tropicamide is not the recommended standard dose, and it is possible that adequate cycloplegia was not always achieved. Because the application of this dose is a common approach in clinical care in Germany, the data might be of interest for this specific dose, even if the highest degree of cycloplegia may not have been achieved. (2) Because pupil diameter in children is not indicative of accommodation, residual accommodation was assessed—as a proxy—by investigation of the absence of fluctuations of the neutral retinoscopic reflex. We are aware that this is not the standard parameter of examining residual accommodation in children. Furthermore, this assessment of the retinoscopic reflex depends on the experience of the practitioner and contains a subjective component. However, in the given environment, other assessments of accommodation were not possible. (3) From these limitations, one might conclude that application of a stronger agent might lead to different results. We cannot exclude this argument. However, we share the view of Mutti et al. that “the role of cycloplegia may be to inhibit accommodation rather than to paralyze it,” as described in the discussion of their publication. Then, relaxing accommodation, for example, by appropriate fogging implemented during refraction, will support to achieve a better estimate of distance correction, which is the desired quantity. This view is supported by the results of Fan et al. They did not find a significant difference for cycloplegic refraction using tropicamide 0.5% compared with using a combination of tropicamide 1.0% and cyclopentolate 1.0% in a group of moderately hyperopic children. Nevertheless, whenever the term cycloplegia is used for our data, it is linked to a nonstandard dose of 0.5% tropicamide.

Agreement of Noncycloplegic and Cycloplegic Data

Data on astigmatism show excellent agreement from a clinical perspective. Furthermore, these data reconfirm convincingly that accommodation is no issue in the case of astigmatic components of refraction data. It was shown before that the mean change in astigmatism with each diopter of accommodation was only 0.036 D. Stability and agreement for both conditions can be explained by the fact that accommodations work equally on both principal meridians of the eye lens. Because astigmatism is based on differences of powers in two meridians, an equal offset to both of them cancels out in the final result. Therefore, cycloplegia does not show different or better results for the astigmatic components.

In the case of the spherical equivalent, however, the situation is different; a bias of 0.55 D was observed. It has to be emphasized that this was found for the wide range from −8 to +9 D of the data, with much more hyperopic than myopic subjects, as can be expected for young subjects (Table 1). A linear regression demonstrated that the best linear fit is represented sufficiently by the bias of 0.55 D (the offset). Thus, the bisecting line is parallel transported to fit the data. A parameter value different from 1 for the slope does not result in statistically significant improvements.
Here, the few data points that lie far away from the regression line and have short error bars (like the one at \(-0.4\) and \(2.5\) D) indicate a stable accommodation during all three measurements. To allow for a connection to the Bland-Altman plot, the limits of agreements by the two dashed lines are added. Despite using techniques such as fogging to induce de-accommodation, the refraction of hyperopes to date is a delicate matter. That is why cycloplegia dramatically fosters the refraction measurement, especially in children. Only under cycloplegia, the problem of accommodation is controlled, and the refraction procedure is as objective as it can be. In the current data, exactly this effect can be observed. Repeatability is improved under cycloplegic conditions by a factor of 3, most likely due to lack of accommodation, as all other parameters remained constant. Strangely enough, in some studies, the effect of cycloplegia on repeatability is not conclusive; see Rosenfield and Ciuffreda.\(^{12}\) We cannot explain their results.

For one reason or another, the option of cycloplegia is not always possible. Then, as second best, an autorefraction without cycloplegia has to be considered. Depending on the requirements and purpose of the measurements, the results of the ZEISS i.Profiler plus will serve well. The bias of roughly half a diopter could be corrected for a posteriori by a recalibration of the instrument. However, this does nothing to the variance of the data. That is why repeatability, for example, given as 95% reference interval, is such an important piece of information. Bland and Altman\(^{31}\) stated that, without knowing the repeatability of methods, it is difficult to compare them in a useful way. In other words, agreement depends on repeatability.

**Repeatability**

The total reference interval for 95% of all data is 1.4 D for repeatability. This is an astonishingly good result for the total interval, especially if we consider that data were obtained in a typical hospital environment. Systematically high accommodation in the noncycloplegic condition for children can be ruled out by our data. Because accommodation is bounded, more than 84% of the children accommodate less than 1 D (Fig. 6). These data do not leave room for higher systematic accommodation but obviously do not exclude outliers.

This promising result depends largely on repeated measurements, which allow for election of the most positive value; for example, in the current study, only 44% of the first ARnc measurement rendered this result. The quality of measurements can be further enhanced by a sensible operator who can judge the data immediately and improve the refraction result by adding a further measurement. The time span of less than a minute is not at all a time-consuming process, given the advantages linked to it.

Fixation and (de-)accommodation can be a severe obstacle to reliable results without cycloplegia, as can be seen from the findings of Dahlmann-Noor and colleagues,\(^{34}\) where differences up to 8 D were observed, and only 20% of all difference values fell into an interval of ±0.50 D. Obviously, the effects depend on the technology applied. In the current approach, an autorefractor was considered, which addresses the problem of accommodation by...
fogging the target image. To the best of our knowledge, there are currently no data on the quantitative effect of this procedure in general.

The current study extracted results on the propensity to accommodate in children for the instrument applied. The method might seem as a crude approach. Nevertheless, it has to be considered as a first step to gain quantitative knowledge on how accommodation influences the measurement and eventually how accommodation can be controlled. It would be interesting to compare different instruments regarding the propensity to accommodate and learn about their different strategies to deaccommodate.

Accommodation is a dynamic process in noncycloplegic refraction. A real-time monitoring of the spherical equivalent, for example, on the device display, would be an interesting and yet feasible approach. The most positive value from such an approach would deliver a much better estimate of refraction data in the natural eye. Not only the spherical equivalent but also additional parameters, which are correlated with accommodation, could be monitored continuously. In adults, the change of pupil size and spherical aberration clearly indicate accommodation. However, in children, there is no correlation between pupil size and accommodation. Little is known about the change of spherical aberration with accommodation in children; here, further investigations would be helpful.

In addition, the measurement process itself could be complemented to introduce cognitive deaccommodation, for example, by asking questions. This is a well-known fact in adults. In passing, we mention that this study observed similar effects in children. However, this was not investigated in a systematic way.

Interestingly, only a few other studies carried out a similar setup to the current investigation to facilitate overall comparison when agreement was established based on ARc and ARnc data within one instrument. Two larger studies on non–wavefront-based devices found a bias for ARc minus ARnc for $M$ values of 1.18 (1.05 to 1.30) for 6-year-olds and 0.84 (0.81 to 0.87) for 12-year-olds, both on the Canon RK-F1 (Tokyo, Japan), and a bias for $M$ of 0.71 for 5- to 10-year-old children was established on the Topcon KR8000 (Tokyo, Japan), the latter data being similar to two earlier studies who found comparable bias in their devices.

In line with the current study, there is only one study in children (SVOne) and only one study in adults (COAS), which reported data that would allow for comparison of noncycloplegic and cycloplegic wavefront-based measurements within one device. Salmon and van de Pol kindly agreed to allow to report their agreement data for 28 adults (mean age, 24.7 ± 3.3 years) as part of the current study. Agreement for cycloplegic minus noncycloplegic wavefront-based data in their cohort was 0.56 ± 0.36 D for $M$. Agreement data within one instrument by Salmon and van de Pol on the COAS system therefore presented similar agreement and variability in their adult groups of subjects compared with the children of the current study. It has to be highlighted that their results were obtained for a range of refractive errors that spanned between −1.83 and +0.62 D, whereas the current study investigated children between −8 and +9 D (Table 1).

**CONCLUSIONS**

Repeatability and agreement of noncycloplegic and cycloplegic wavefront-based autorefraction were analyzed for the first time in...
children of this range of age and refractive errors. Refraction measurements were obtained by ZEISS i.Profiler plus with and without cycloplegia. The agreement and repeatability of astigmatic data are excellent under both conditions. Regarding agreement for the spherical equivalent, ARc presented with higher positive values than did ARnc. The shift can be explained by variations in relaxation of accommodation among subjects when wavefront-based autorefraction was measured without cycloplegia. Agreement and repeatability in children show comparable results with data obtained with wavefront-based devices in adults.

If cycloplegia is not an option, only then can noncycloplegic data be considered. The first strategy is to correct results from ARnc for the bias of roughly half a diopter. This correction scheme does not depend on the individual subject but represents a “one-size-fits-all” approach. However, the most promising strategy, as can be concluded from the current results on the propensity to accommodate, is the repetition of measurements or, even better, a real-time measurement approach with continuous data. Accommodation, as a dynamic process, is best controlled by dynamic means for each individual. From the point of technology, all components are available to realize such a progress.

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