THE RANGE OF THE WAVEFORM SCORE OF THE OCULAR RESPONSE ANALYZER (ORA) IN HEALTHY SUBJECTS

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ABSTRACT

Purpose
The waveform score (WS) indicates the reliability of each intraocular pressure (IOP) measurement signal performed with the Ocular Response Analyzer (ORA, Reichert®). We aimed to assess i) the range of waveform score in IOP measurements with ORA in healthy subjects and to ii) identify a cut-off WS value under which an ORA measurement should be discarded.

Methods
Prospective study including three ORA IOP measurements performed in the right eye of 80 healthy normal subjects. The different WS were recorded and the highest WS of the three measurements was analysed. ANOVA test was used to assess variance in repeated measurements.

Results
Mean age of 80 subjects was 46.7±15.6 years. Mean WS of the first IOP measurement was 4.8±2.0 and 4.8±1.7 and 5.0±1.9 respectively for the second and third measurements (p= 0.74). Mean WS of the analysed 240 signals (3 measurements per eye) was 4.9±1.9 (range: 1.2-9.5). The mean value of all the highest values per eye was 6.2±1.8 (range: 2.9 -9.5 and was significantly higher than the mean WS of the 240 signals together (p <0.001). The 10th percentile of all the best values was 3.7 and the 75th percentile 7.5.

Conclusion
ORA measurements with WS <3.7 should be discarded in healthy normal subjects. As much as that the corresponding quality of the waveform ORA scan is satisfying, one single measurement with a WS >7.5 could be considered as sufficient. If this score cannot be reached after three consecutive measurements, the signal with the highest WS should be selected.

KEY WORDS

Goldmann applanation tonometry, Ocular Response Analyzer, corneal viscoelastic properties, waveform score.

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INTRODUCTION

Tonometric measurements were shown to be affected by the overall corneal biomechanical characteristics (1).

Based on a dynamic bi-directional applanation process, the Reichert Ocular response Analyzer (ORA) (Reichert® Ophthalmic Instruments, Buffalo, NY, USA) provides information about the in vivo biomechanical properties of the cornea, such as hysteresis and resistance, and extrapolates an IOP measurement from the calculated biomechanical parameters (2). Recently, the ORA proved to yield good repeatability for CH and CRF in normal subjects (3). Differences in the biomechanical properties of the cornea have been found in glaucoma patients compared to normal subjects and this has given rise to new hypotheses regarding the pathophysiological process by which corneal properties influence the risk of glaucoma (5-9).

In the first generation of the Reichert® ORA, the mean value of four measurements was automatically provided. ORA readings had to have applanation signals with adequate magnitude and symmetry according to the manufacturer's instructions before they were accepted. Based on this, the measured values appeared to be highly dependent on the quality of the generated waveform signals. The recently upgraded software of the Reichert® ORA (version 2.0 and higher) includes a numerical parameter called Waveform Score (WS).

The aim of this study was to identify a cut-off WS value under which ORA measurement should be discarded.

METHODS

Protocol

This was a prospective clinical study of normal healthy subjects recruited from the general consultation and/or accompanying persons in the University Department of Ophthalmology St Luc University Hospital, Brussels, over a seven-month period. The study was discussed with each patient before her/his examination and an informed consent was obtained from all participants in accordance with the tenets of the Helsinki Declaration. Each subject underwent a baseline ophthalmologic examination including recording of medical and ocular history, best corrected visual acuity, slit-lamp biomicroscopy and fundus examination using a 60D lens. Subjects with a previous history of photorefractive surgery or traces of corneal pathology were excluded.

Three good-quality ORA scans, with symmetry in height between the two peaks of the waveform, were performed in each subject by an experienced clinician (MV or SP). The ORA biomechanical parameters and the WS values were saved after each measurement. The ORA measurements were performed before any IOP Goldmann applanation tonometry.

Methods

Basically the ORA determines the corneal biomechanical properties by using an applied force-displacement relationship. A metered collimated air-pulse is used to applanate the cornea and an infrared electro-optical system is used to monitor the process and to record the inwards and outwards applanation events (Figure 1a). The air pulse first deforms the cornea through an initial applanation (peak 1, inwards corneal motion), then into concavity that gradually subsides, thereby allowing the cornea to rebound through a second applanation (peak 2, outwards corneal motion).

Corneal hysteresis (CH) is the measurement that results from the damping of the cornea due to its viscoelastic properties and it is derived from the difference between the two applanation measurements (P1-P2).

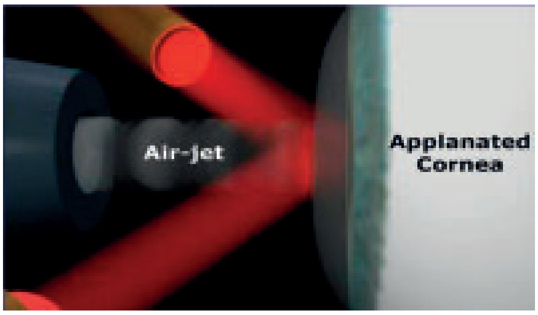

Fig 1a: To determine the biomechanical properties of the cornea, an air-pulse applanates the cornea. An infrared electro-optical system records the entire process and the inward and outward applanation events.

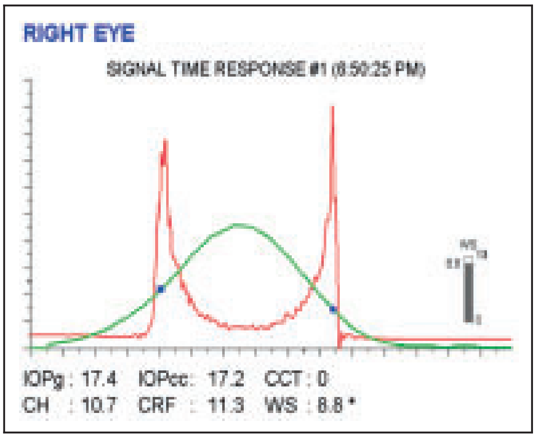

Fig. 1b: To determine the biomechanical properties of the cornea, an air-pulse applanates the cornea. An infrared electro-optical system records the entire process and the inward and outward applanation events. (reproduced courtesy of Reichert®):

These pressure values refer to the blue squares on the green curve in *figure 1b*. ORA in-and out-applanation curves are displayed on the screen together with four numerical parameters expressed in mmHg (*Figure 1b*).

1. Corneal-compensated IOP (IOPcc) is obtained from the difference between the two applanation pressures using the formula P2 -kP1, where the constant k has a value of 0.43 [D. Luce, written communication, September 2005]
2. The Goldmann-correlated IOP (IOPg) corresponds to the mean of the 2 IOP measurements.
3. CH represents the difference between the two IOP values P1 and P2 at the moment of the two applanation processes. It indicates a measure of the viscous damping properties of the cornea.
4. The Corneal Resistance Factor (CRF) is derived from CH and is calculated as a linear function of the two pressures associated with the two applanation processes. It reflects the overall resistance of the eye (4).

The waveform score (WS) assigns a numerical value to the quality of the waveform and allows the clinician to select the best signal based on a score instead of relying on a qualitative and subjective estimation of the waveform. Ranging from 0 to 10, this score provides information about the reliability of the measurements. The higher the WS, the higher the reliability of the measurement.

The waveform score is the result of a complex calculation including five parameters for each applanation peak. These parameters are the a and b indexes (‘smoothness’ of peak 1 and peak 2 and the number of times the response curve changes direction), the p1 and p2 areas of the waveform (the area under peak 1 and 2), the aspects 1 and 2 (ratio width/height), the up slopes 1 and the down slopes 1 and 2 (*figures 2 to 6*) [Data provided by courtesy of Reichert® (Reichert Inc. Buffalo, NY, USA)].

Statistical analysis

The right eye of each subject was selected for the statistical analysis. ANOVA test for repeated measures was used to compare the means of WS1, WS2 and WS3. A paired Student t-test was used to compare the means of the three WS with the best WS. The percentiles of the distributions of the WS were calculated. All statistical tests were twotailed. A p value less than 0.05 was considered as statistically significant. Statistical analyses were performed using SPSS software version 19 (SPSS Inc., Chicago, IL, USA).

RESULTS

Eighty normal healthy subjects (80 right eyes) were studied. *Table 1* shows the characteristics of the studied sample. The mean age of the

Table 1: *Demographic Data of the participants*

Total included subjects n=80 (80 eyes) (M/F: 35/45)	*Mean ± SD*	*Range*
Age (years)	46.7±15.6	19-86
Axial length (mm)	23.7±1.1	21.7-26.4
CCT (m)	538±37	448-614
IOPcc (mmHg)	15.5±3.8	7.2-26.2
IOPg (mmHg)	15.7±3.9	6.6-28.2
CRF (mmHg)	11.0±2.2	5.9-15.5
CH (mmHg)	11.0±2.0	6.9-15.8

CCT= central corneal thickness; IOPcc = corneal compensated intraocular pressure; IOPg= Goldmann-correlated intraocular pressure; CRF= corneal resistance factor; CH= corneal hysteresis; SD= standard deviation

Figures 2, 3, 4, 5, 6: Parameters of the waveform used for the calculation of the Waveform Score (reproduced courtesy of Reichert)

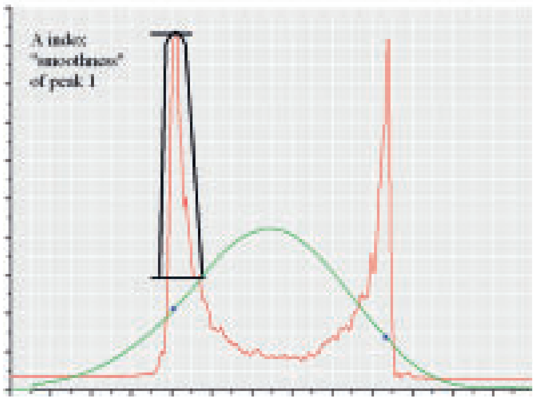

Fig 2: Parameters for the calculation of the WS: *The a index*

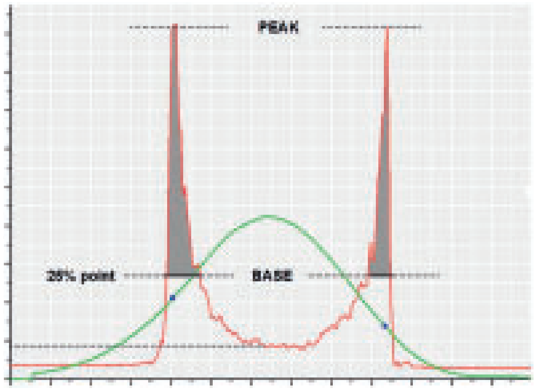

Fig 3: Parameters for the calculation of the WS: The p1 and p2 areas (area under the curve)

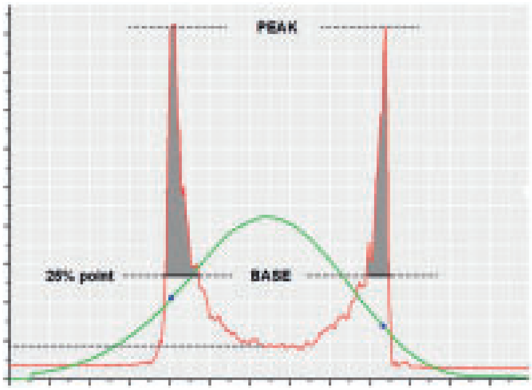

Fig 4: Parameters for the calculation of the WS: The aspect ratio (width/height)

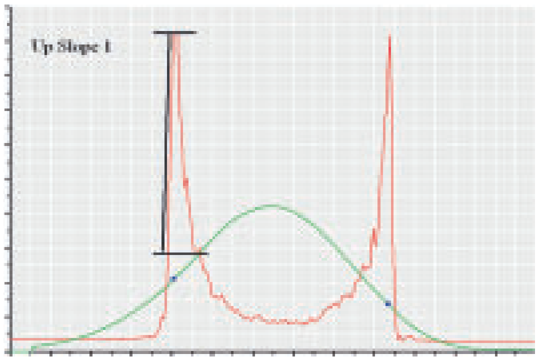

Fig 5: Parameters for the calculation of the WS: *The Up slope 1*

participants ± SD was 46.7±15.6 years (range: 19-86 years). The mean axial length of the globes was 23.7±1.1 mm (range: 21.7-26.4 mm) and the mean central corneal thickness (CCT) was 538±37 .m (range: 448614 .m). Concerning the ORA measurements, the mean IOPcc (15.5±3.8 mmHg) was quite similar to the mean IOPg (15.7±3.9 mmHg). Both CH and CRF were in the normal range with a mean CH being 11.0±2.2 mmHg and a mean CRF being 11.0±2.0 mmHg (10).

The mean values of the first WS measurements (WS1) were 4.8±2.0; the second WS measurements (WS2) were 4.8±1.7 and the third WS measurements (WS3) 5.0±1.9. There were no statistically significant differences between WS1, WS2 and WS3 (p= 0.699).
The mean WS of all (WSA) the 240 analysed signals (80 x 3) was 4.9±1.9 ranging from 1.2 to 9.5. None of the measurements had reached the value of 10, which corresponds to the upper limit of the WS. These results are summarised in *table 2*.

The mean of the highest/best WS values was 6.2 ± 1.8 ranging from 2.9 to 9.5 for the 80 eyes of the studied sample. There was a significant difference between the mean of the highest values and the mean of WSA ($p<0.001$).

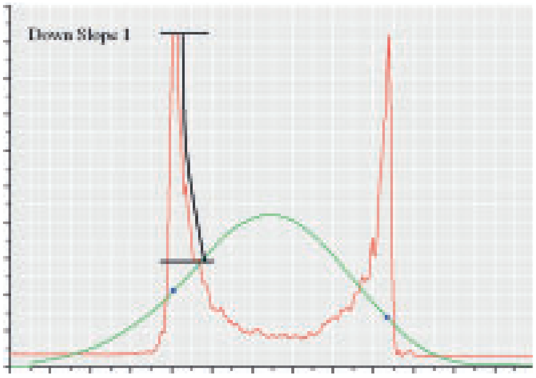

Fig 6: Parameters for the calculation of the WS: The *Down slope 1*

Figure 7 illustrates the cumulated percentages of the highest WS values for the 80 eyes. The lower 10th percentile of all the best values was 3.7 and the 75th percentile corresponds to the numerical value of 7.5.

DISCUSSION

By definition, the waveform score (WS) provides an estimation of the reliability of each ORA measurement. However there is still no complete agreement in the literature regarding a WS cut-off value under which the ORA measurement should be discarded.
The purpose of our study was to define such a reliable cut-off value as well as a minimum value below which data should always be discarded.

From a sample of 80 normal subjects, we found that the threshold WS was 3.7 in the ORA and that, provided that the corresponding quality of the waveform ORA scan is satisfying, one single measurement with a WS >7.5 can be considered as sufficient.

In a study by Ehrlich et al. that studied the agreement between IOP measurements using GAT and Goldmann correlated intraocular pressure by Reichert's ORA (IOPg) in 260 patients examined for glaucoma evaluation, the measurements were repeated until a WS of 6.5 was obtained for each ORA assessment or until five measurements were obtained per eye. Although a higher WS indicated a higher IOPg/GAT correlation, the authors concluded that the influence of the WS was minimal and that the results did not support the use of a specific WS cutoff value to determine the quality of an IOPg measurement (11).
Another study analyzing the usefulness of the WS from the ORA, found similar results to ours with respect to the WS value that should be discarded. In their series of measurements, the 10th percentile of all signals had a WS <3.48. Therefore, the authors also suggested that a score below <3.5 should be discarded and recommended to take three measurements with a WS at least >3.5 to increase the precision of the ORA assessment (12). Moreover in a post-hoc analysis including 100 participants made up by a mixture of patients suspected of having glaucoma and control volunteers, Kotecha et al had found that the variability of repeated ORA IOP measurements was dependent on the magnitude of the ocular pulse so that the eyes with a larger pulse amplitude displayed more intra-session variability in IOPcc readings. Repeated ORA measurements with a lower average numerical WS displayed greater intra-session variability thus giving some weight to the importance of recording repeated, good-quality ORA measurements when assessing a patient (13). In another study that tended to confirm these data, in which the autors have analysed the influence of the Ocular Pulse Amplitude (OPA) on ORA measurements, Xu G. et al. had found that the within-subject variances of IOPg and IOPcc were positively correlated with the OPA unlike the CH and the CRF. They concluded that the measurement reliability of the ORA was only moderate.

Table 2: *Mean Waveform Scores (WS) ± Standard Deviation (SD) of the first, second and third ORA measurements of the eyes considered separately, mean of the WS for all the 240 performed measurements (3 x 80 eyes) and mean of the 80 highest WS (considering the best value for each eye).*

n=80 eyes	*Mean ± SD*	*Range*
WS 1	4.8±2.0	1.2-9.5
WS 2	4.8±1.7	1.6-9.4
WS 3	5.0±1.9	2.0-9.1
Mean WS 1+2+3	4.9±1.9	1.2-9.5
Mean of the highest WS	6.2±1.8*	2.9-9.5

* Difference Mean WS1+2+3 and Mean highest score (p-value<0.001)

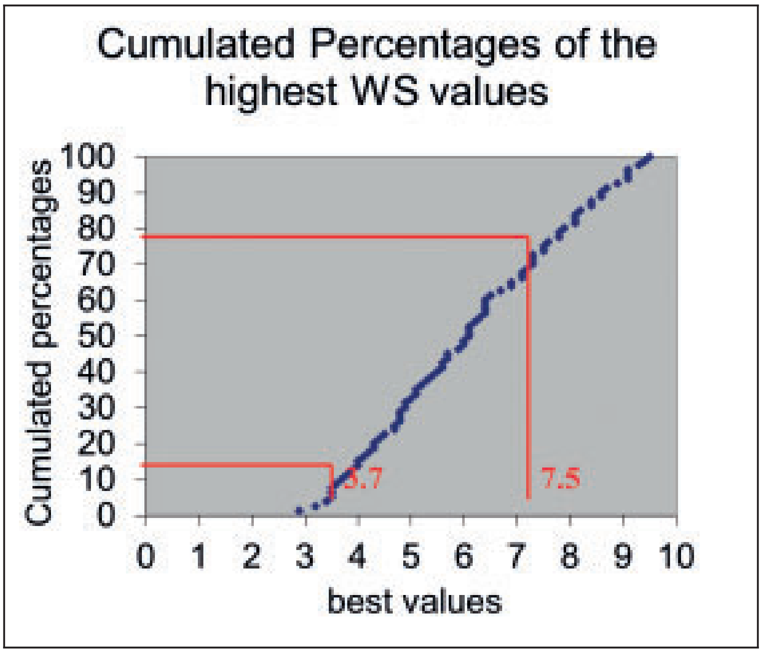

Fig. 7: Cumulated percentages of the highest Waveform Scores (WS) values for each subject (n=80 eyes). The lower 10th percentile had a WS of 3.7 and 75th percentile was 7.5.

Given that the eyes with a large OPA were associated with a higher IOP measurement variability, the authors recommended to consider the average of multiple measurements to obtain reliable ORA measurements (14).

We found that the mean of the highest WS values for each subject was significantly higher than the mean of all generated signals considered together. Therefore, only selecting the value calculated from the signal with the highest WS, as opposed to calculating the mean values of the four parameters (IOPcc, IOPg, CRF, CH) based on three ORA measurements or more in each eye, would be more accurate. Also, as the lower 10th percentile was found to have a WS under 3.7, we suggest that values that do not reach this minimum amount in healthy subjects should be discarded. We also found that the 75th percentile values were under 7.5. Our results are in agreement with those recently reported by Ayala et al (15). With some differences in their methodology compared with ours, the authors recommended that clinicians try to obtain several waveform score measurements of 7 or above, given that waveform scores lower than 7 may render less reliable results.

In the current state of knowledge, Goldmann applanation tonometry (GAT) remains the golden standard for IOP measurement in the diagnosis and the follow-up of glaucoma suspect and glaucoma patients. The ORA mainly aims to estimate the biomechanical properties of the cornea and provides a corrected IOPcc value according to the parameters measured. We suggest to perform a dynamic contour tonometry (DCT) or a GAT before the ORA measurements in order to definitely exclude the lack of reliability in the ORA measurements due to the influence of the OPA. Since GAT measurements with low choroidal pulsations and DCTs with low OPAs have been found to be associated with a lower ORA measurement variability. If it is the case, a single ORA measurement with a WS >7.5 and a satisfying corresponding quality of the waveform ORA scan can be considered as sufficient. If this score cannot be reached after three measurements, the signal with the highest WS should be selected.

Finally, as previously mentioned, glaucoma pa tients have been shown to have altered biomechanical corneal properties compared with healthy normal subjects (9). The cut-off value under which this parameter cannot be considered as reliable enough is possibly different in newly diagnosed glaucoma patients compared with healthy subjects. This potential difference, together with a potential difference between different ethnical groups, reinforces the need for more research in the future.

CONCLUSION

The results of our study suggest that ORA measurements with a WS <3.7 should be discarded in healthy normal subjects. As far as the corresponding quality of the waveform ORA scan is satisfying, even one measurement with a WS >7.5 can be considered as sufficient. If this score cannot be reached after three measurements, the signal with the highest WS should be selected.

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