Report on Statistics

Visual field testing based on Eye Movement Perimetry using video-based oculography

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The visual field test is an important visual function assessment in Ophthalmology and Optometric practice. Perimetry examinations are used to detect malfunctioning in the peripheral vision of a patient, as part of a standardized eye examination. In this research set-up we tested whether video-based oculography (VOG) is suitable to assess, in a clinical setting, the peripheral vision of patients. The variables assessed were seen/unseen and Saccadic Reaction Time (SRT). 26 peripheral monocular targets were tested for both the right and left eye. The study was designed as a Latin square design to test and retest the subjects a minimum of three times for intra-rater reliability and in 2/3 of the subjects the test was performed six times for stability testing of two independent devices. Statistical analysis, applying the agreement index (AI), for reliability and stability is performed. Our preliminary results indicate that high-frame rate VOG is a promising tool to measure and quantify individual peripheral visual function in a clinical setting.

BACKGROUND

The Standard Automated Perimetry (SAP) test uses an apparatus including a computer program to test subjects' visual field. The apparatus is a dome-shaped instrument where the individual is instructed to look at an object in the centre of the dome throughout the test, when small flashes of light are projected in the peripheral areas on the dome. When the test person sees these flashes of light, they will press a button. The computer program will provide the professional a map of the subjects' visual field, providing clinical help to either diagnose or guide towards other clinical assessments.

Glaucoma is treated by lowering the inner eye pressure. Depending on the patient's situation, options are to include prescription of eye drops, oral medications, laser treatment, surgery or a combination of any of these. However, the symptoms of this "silent thief of sight'' start so slowly that initial development can go unnoticed, which hampers early stage diagnostic work-up[1]. At present, no strong functional risk factors are at hand to identify early stages of glaucoma. Especially the functional tests lack sensitivity; elevated inner eye pressure is only present in 50% of cases and SAP shows in general poor reproducibility[2].

With Eye Movement Perimetry (EMP) a developed Virtual Reality (VR) headset is used, relying on natural oculomotor responses of the test subject. A method which may eliminate false positive calls and has shown a fair to good reproducibility[3] in previous research. As in existing SAP, the EMP test assesses the extent of the visual field but it also assesses the visual field responsiveness based on saccadic reaction times (SRTs). Based on these SRTs, the EMP test discriminates well between selected patients with and without glaucoma [4].

SRTs are shown to be significantly increasing with glaucoma progression, from mild stages onwards.

EMP is a well-studied method of testing visual fields in a glaucoma patient population. Furthermore it is fast (90 sec per eye), precise (as it visualizes the patient's eye traces in a diagram) and produces an objective result (instead of the subjective result generated by the patient pressing a button).

METHOD

In this trial we measured SRT values and seen/unseen visual targets during standard visual field test of 26 points with consecutive measurements on the same day, with a wash-out period between measurements. A Latin square study design was used to assess six glaucoma patients, classified as mild to severe glaucoma, in 3 different age groups. Three normal subjects were used as controls. With the significance level of 5 %, a clinically relevant difference of one time the standard deviation, a minimum of nine subjects was included. Due to the stratification in the design a total of at least three subjects must be included in the substrata, equally divided on the predefined age and disease stage stratum.

The study was performed at the Medical Research Foundation, at Sankara Nethralaya Eye Hospital, Chennai, India. The study follows the Helsinki declaration and was ethically approved by the regional ethical board. Subjects underwent a test-retest procedure of three times for inter-rater reliability in two different BulbiCAM devices, and two third of the population underwent six times the testing for stability testing of the devices.

A VR suspended head mounted VOG device from Bulbitech AS (BulbiCAM) was used. The BulbiCAM is based on a two-screen solution, which enables both monocular or binocular stimuli to be presented. In this trial

monocular tests were performed. Eye SRT values were measured with a high-speed digital infrared camera, which measures eye movements at a 400-Hz frame rate.

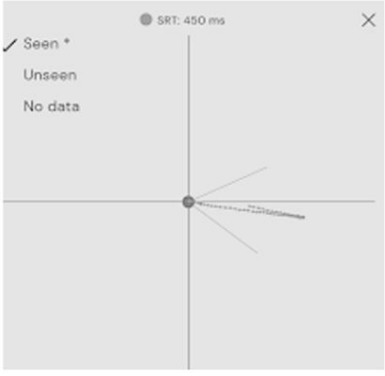


Figure 1 *demonstrates as a "seen" target with an eye movement "departure", starting from an eye gaze on a central target point, moving with a fast eye movement, "arriving" on a gaze fixation point on a peripheral target.*

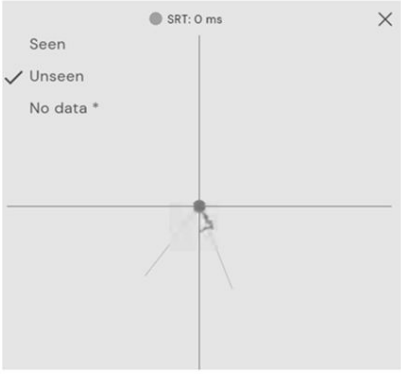


Figure 2 *demonstrates a "unseen" target with no eye movement towards a peripheral target.*

Visual Field diagram for the right and the left eye

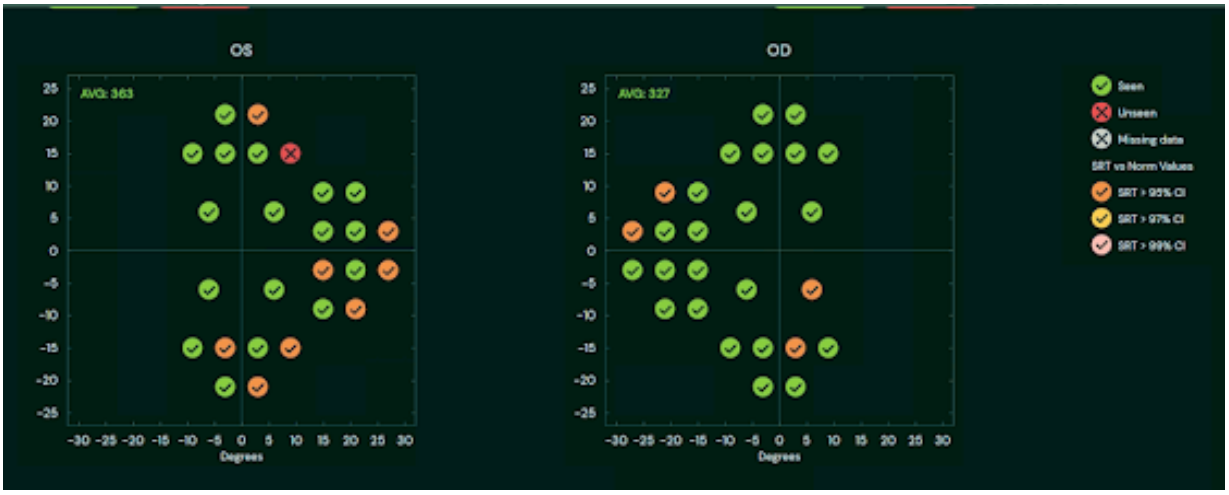


Figure 3 *presenting the Visual Field diagram for the left and the right eye. Diagram providing information on seen targets (green) and unseen targets (red). Slow SRT's are indicated by orange, yellow or pink colours.*

The peripheral white dot on the screen gives a light and contrast stimulus to the eye, triggering light sensitive cells in the retina. From there the neural system interacts, and neural integration in the brain stimulates a voluntary and controlled eye movement towards that specific peripheral target. Three phases can be observed, which is a departure from the central visual target (green dot), a fast eye movement towards a new target, and an arrival with a fixation gaze on a new visual target (white dot). The time from stimulus presentation until an eye movement started and departed away from the green central target, was measured in milliseconds (ms) to determine the SRT value. The SRT variable was measured in a minimum of three to a maximum of six trials in each patient.

The seen/unseen variable was determined by the eye movement into the correct sector as seen in figure 1 and 2. It was also determined by an eye fixation around the peripheral visual target.

The seen/unseen variable was measured in a minimum of three to a maximum of six trials in each patient.

RESULTS

Statistical evaluation of the SRT and seen/unseen variables proposed a four-sector area for analysis. Central, nasal, superior and inferior areas were statistically evaluated for reliability and stability.

Statistical evaluation of the variables was statistically evaluated for reliability and stability.

Statistical method

All results on assumed continuously distributed variables are expressed by Mean values, Standard Deviation (SD) and 95% Confidence interval[5]. Comparison of devices was performed by using analysis of variance with repeated measurement[6]. Contingency Table Analysis was used for categorical data[7]. Differences between devices were considered significant if the p-value was less or equal to the level of 5 %. Pair of observations performed on the same patient on two different devices was used for analysis and estimation of device agreement. The mean of the paired observation (Mean $_{pairs}$) was plotted against the mean difference within pairs (Mean $_{diff}$). The results are graphically given by the Bland &Altman agreement plot as Mean $_{diff}$ ±2*SD $_{diff}$ against Mean $_{pairs}$ [8,9]. Additionally, the number of outliers and the agreement coefficient AI = 1 – [2*SD $_{diff}$ / Mean $_{pairs}$] is given[10]. In order to investigate the stability of the devices, the pair of observations in the same patient on two different devices was repeated at least four times. The stability of agreement was analysed using the same procedure as described for the agreement analyse above.

Categorization of the Agreement Index

<0.40 (Poor), [0.40 - 0.60> (moderate), [0.60 - 0.70> (Good). [0.70 - 0.8> (Very good) og >0.80 (Excellent)

The mean agreement index of SRT between devices in all areas was 0,78 [0,69-0,83] for the right and the left eye. The mean stability index of SRT was 0,75 [0,63-0,86] for the right and the left eye. The mean agreement index of seen/unseen targets was 0,82 [0,63-1,00]. In table 1 the agreement between devices on SRT values can be observed, including the different areas of central, nasal, superior and inferior for the right and the left eye. Notice that any outlier is not because of erroneous device measurements but is due to the variability in the test subject, as this test is based on voluntary eye movements.

Table 1: Agreement between devices on SRT

	Variable	Parameters	Estimation
CENTRAL	SRT* Right eye (OD)	Mean of measurements (SD)	341 (69)
		Difference between measurements (SD)	21.4 (33.4)
		Agreement Index (AI)	0.81
		% outliers	0 (1)
		Correlation between measurements	0.89
		Correlation: mean vs absolute difference value	0.15
	SRT Left eye (OS)	Mean of measurements (SD)	351 (51)
		Difference between measurements (SD)	-8.0 (54.8)
		Agreement Index (AI)	0.69
		% outliers	0
		Correlation between measurements	0.63
		Correlation: mean vs absolute difference value	0.36
NASAL	SRT*) Right eye (OD)	Mean of measurements (SD)	333 (70)
		Difference between measurements (SD)	-5.6 (28.3)
		Agreement Index (AI)	0.83
		% outliers	0 (1)
		Correlation between measurements	0.94
		Correlation: mean vs absolute difference value	0.77
	SRT *) Left eye (OS)	Mean of measurements (SD)	336 (66)
		Difference between measurements (SD)	24.8 (43)
		Agreement Index (AI)	0.74
		% outliers	0 (1)
		Correlation between measurements	0.90
		Correlation: mean vs absolute difference value	0.57
SUPERIOR	SRT **) Right eye (OD)	Mean of measurements (SD)	319 (91)
		Difference between measurements (SD)	-13.8 (31.8)
		Agreement Index (AI)	0.80
		% outliers	0 (2)
		Correlation between measurements	0.94
		Correlation: mean vs absolute difference value	0.18
	SRT*) Left eye (OS)	Mean of measurements (SD)	366 (183)
		Difference between measurements (SD)	-8.0 (32.7)
		Agreement Index (AI)	0.82
		% outliers	0 (1)
		Correlation between measurements	0.99
		Correlation: mean vs absolute difference value	0.31

		Mean of measurements (SD)	358 (139)
		Difference between measurements (SD)	-1.3 (36.0)
	SRT	Agreement Index (AI)	0.80
	Right eye (OD)	% outliers	0
		Correlation between measurements	0.97
		Correlation: mean vs absolute difference value	-0.33
INFERIOR		Mean of measurements (SD)	347 (58)
		Difference between measurements (SD)	-7.4 (53)
	SRT *)	Agreement Index (AI)	0.71
	Left eye (OS)	% outliers	0 (1)
		Correlation between measurements	0.66
		Correlation: mean vs absolute difference value	0.79

*) One value missing; **) Two values missing

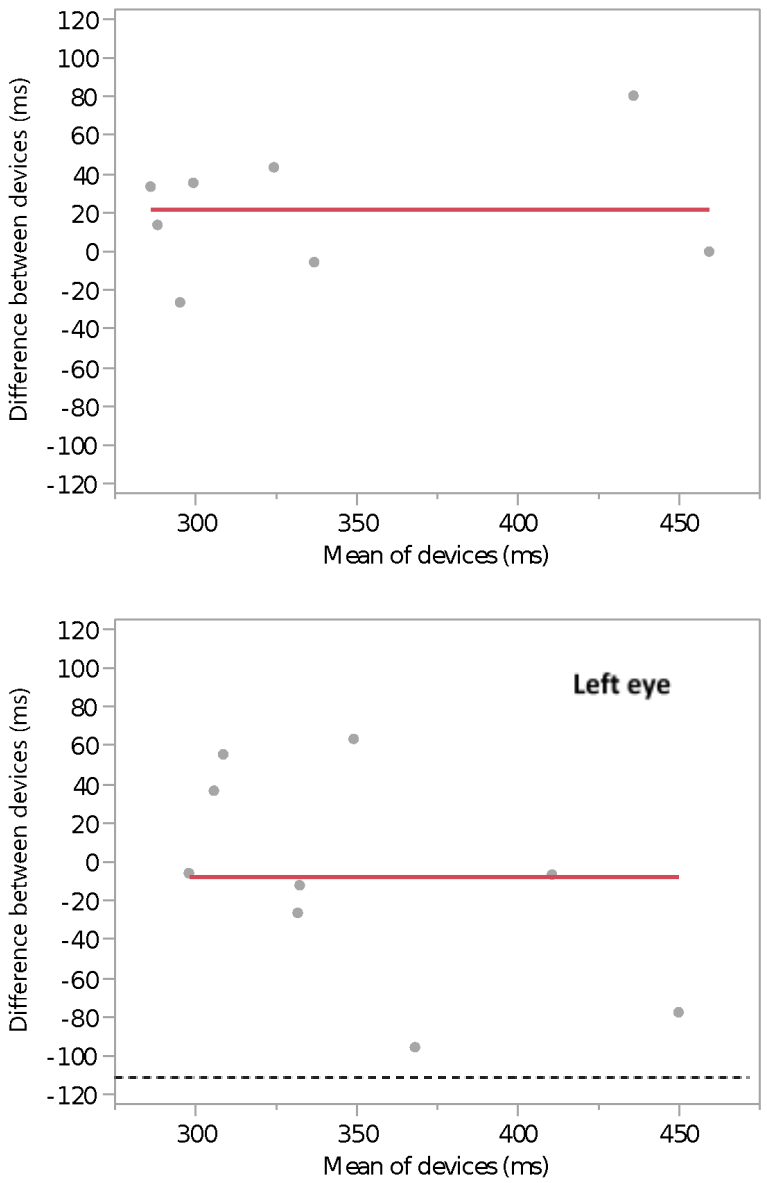


Figure 3: Agreement plot between devices on Central SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.

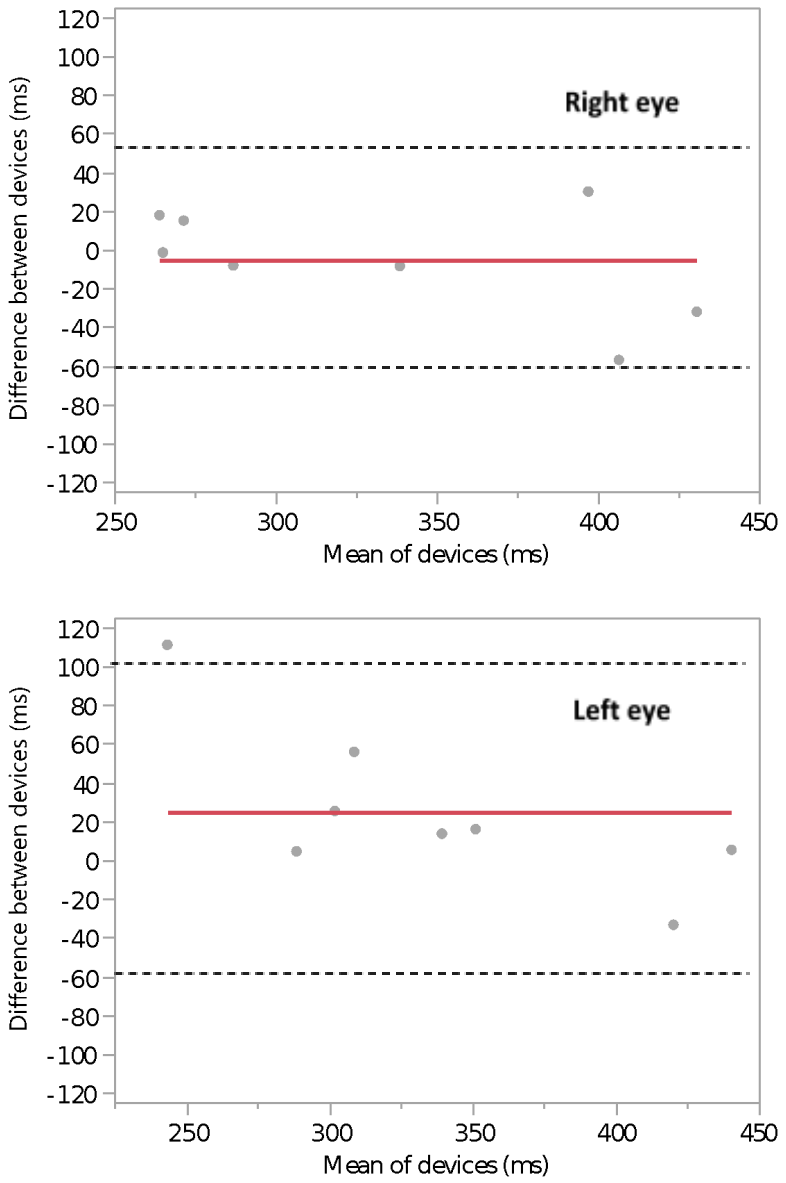


Figure 4: Agreement plot between devices on Nasal SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.

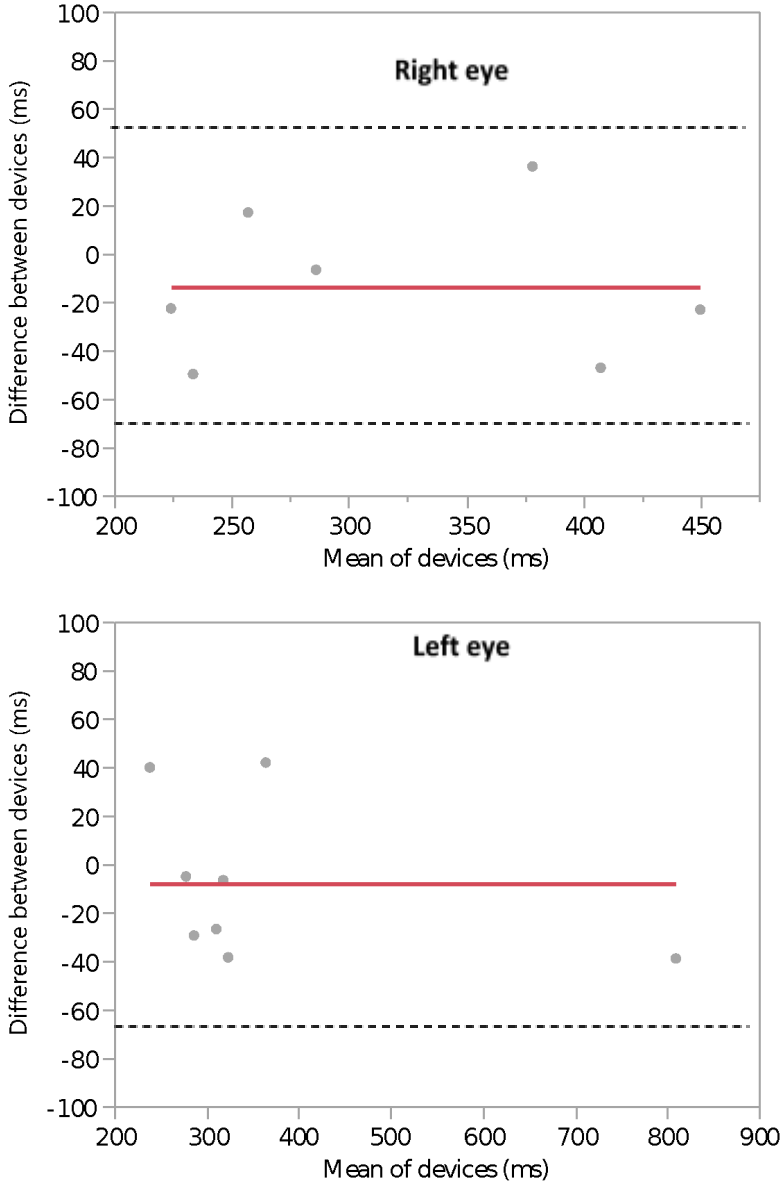


Figure 5: Agreement plot between devices on Superior SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.

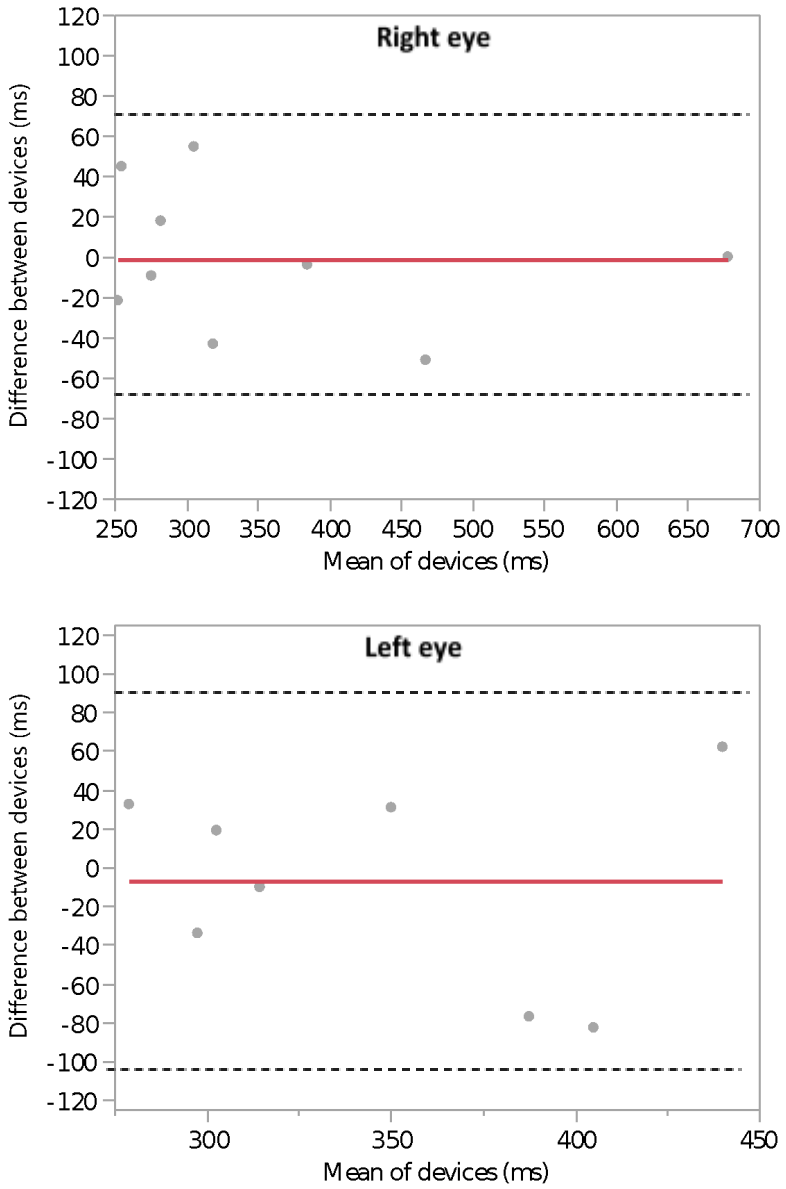
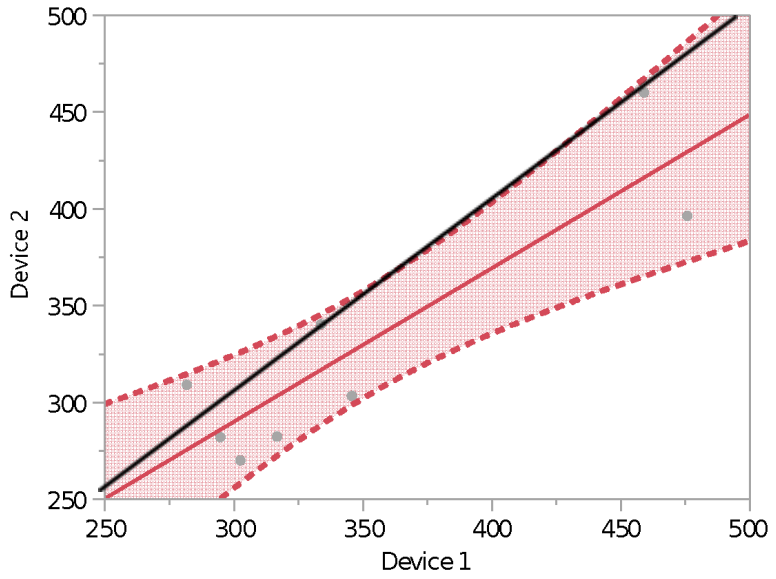


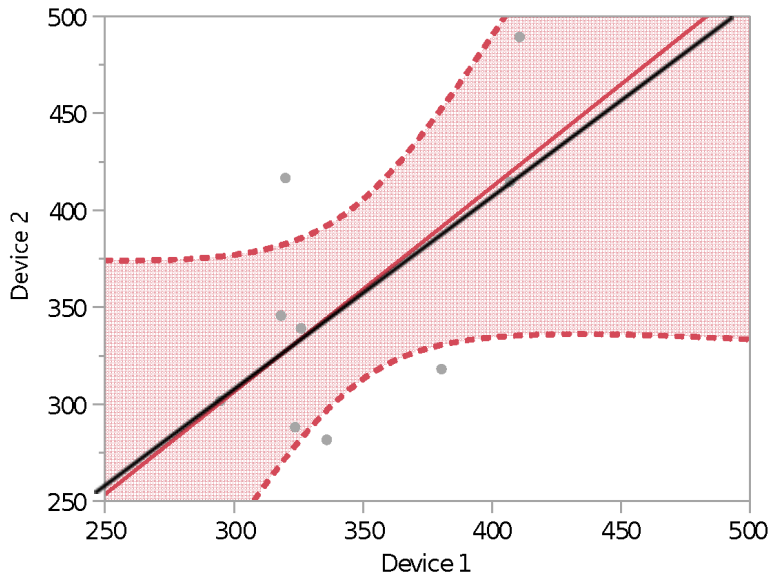
Figure 6: Agreement plot between devices on Inferior SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.

Regression (Line of equality)

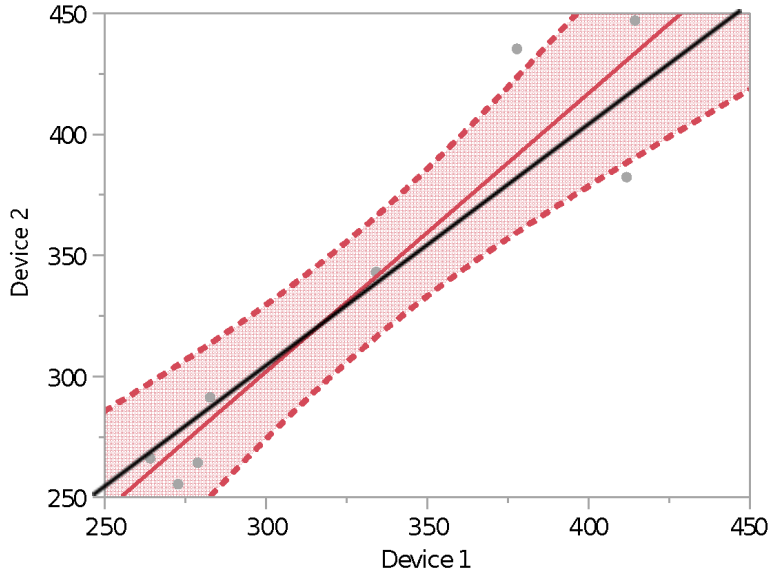
OD: Central SRT index



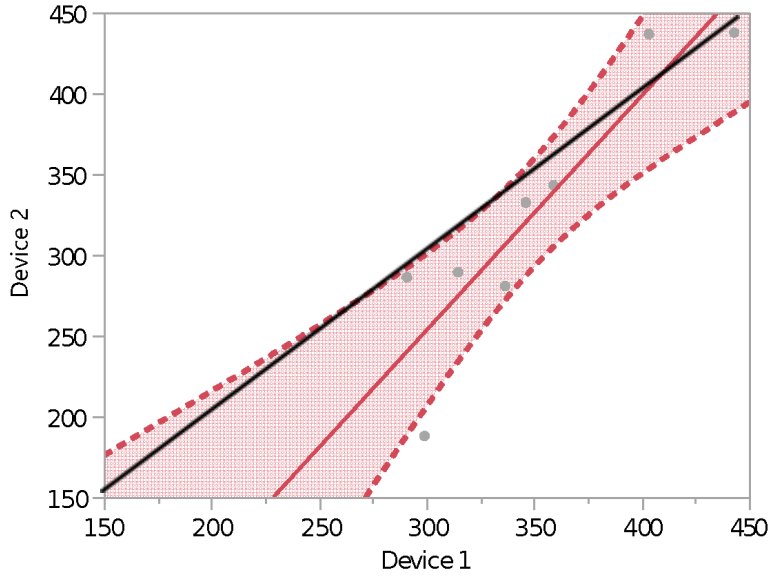
OS: Central SRT index



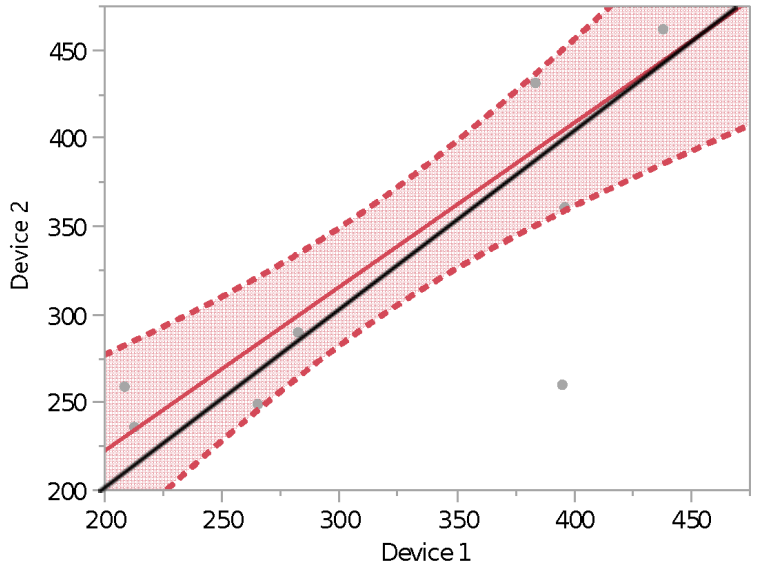
OD: Nasal SRT index



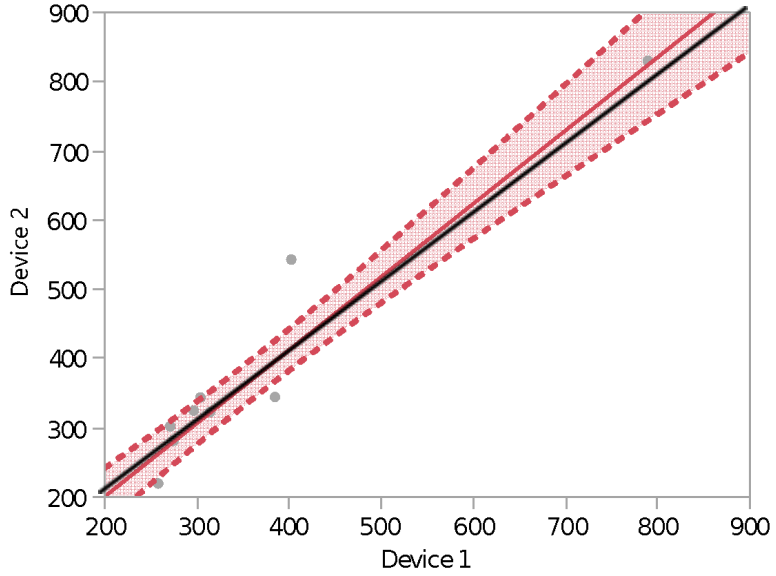
OS: Nasal SRT index



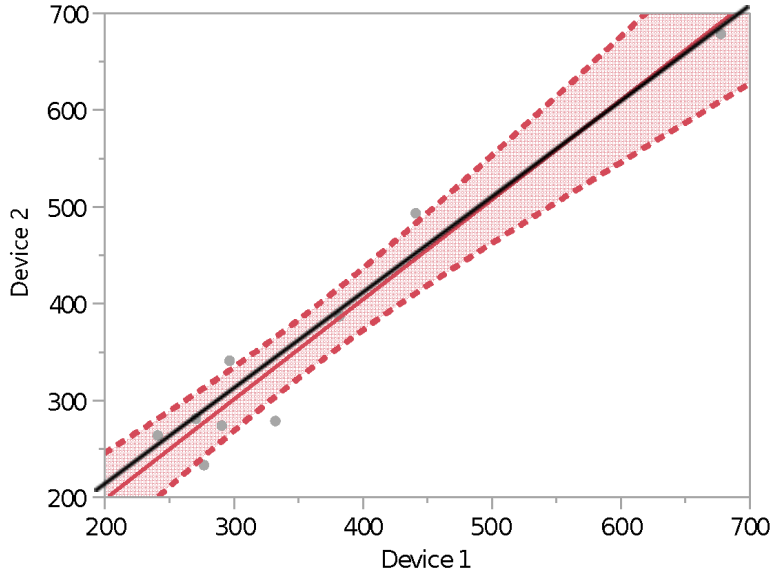
OD: Superior SRT index



OS: Superior SRT index



OD: Inferior SRT index



OS: Inferior SRT index

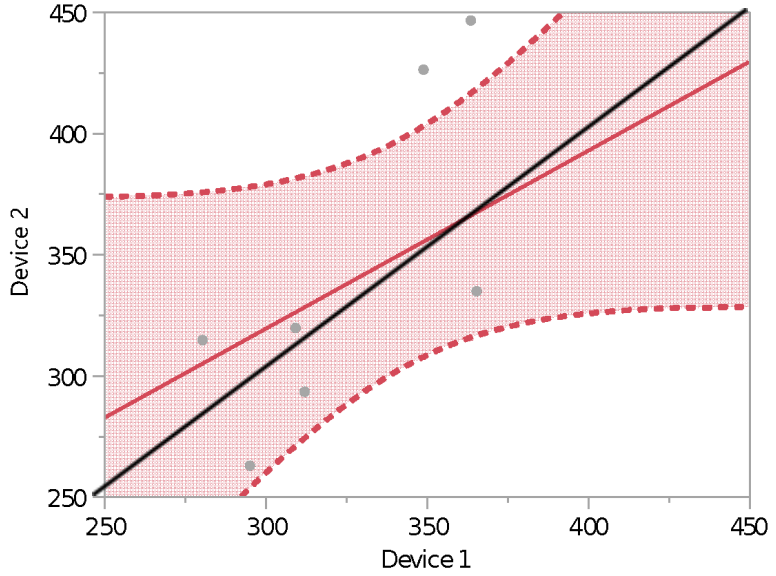


Table 2: Agreement between devices on "Seen / Unseen" index

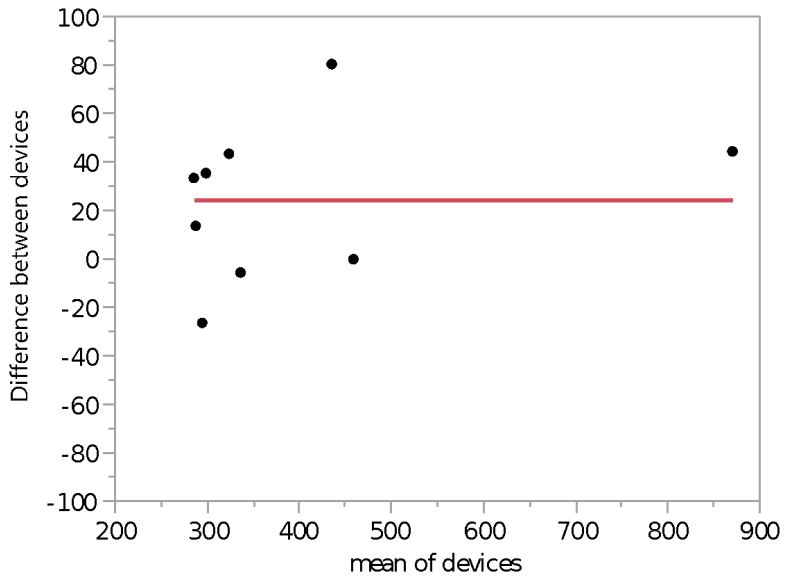
	Variable	Parameters	Estimation
CENTRAL	Seen/Unseen Right eye (OD)	Mean of measurements (SD)	1.30 (0.63)
		Difference between measurements (SD)	0.06 (0.167)
		Agreement Index (AI)	0.74
		% outliers	1/9
		Correlation between measurements	0.99
		Correlation: mean vs absolute difference value	0.85
	Seen/Unseen Left eye (OS)	Mean of measurements (SD)	1.11 (0.33)
		Difference between measurements (SD)	0.00 (0.00)
		Agreement Index (AI)	1.00
		% outliers	0
		Correlation between measurements	1.00
		Correlation: mean vs absolute difference value	0.00

NASAL	Seen/Unseen Right eye (OD)	Mean of measurements (SD)	1.24 (0.56)
		Difference between measurements (SD)	0.04 (0.17)
		Agreement Index (AI)	0.73
		% outliers	1/9
		Correlation between measurements	0.97
		Correlation: mean vs absolute difference value	0.50
	Seen/Unseen Left eye (OS)	Mean of measurements (SD)	1.12 (0.37)
		Difference between measurements (SD)	-0.02 (0.07)
		Agreement Index (AI)	0.88
		% outliers	1/9
		Correlation between measurements	1.0
		Correlation: mean vs absolute difference value	1.0
SUPERIOR	Seen/Unseen Right eye (OD)	Mean of measurements (SD)	1.22 (0.67)
		Difference between measurements (SD)	0.00 (0.00)
		Agreement Index (AI)	1.00
		% outliers	0
		Correlation between measurements	1.0
		Correlation: mean vs absolute difference value	0.00
	Seen/Unseen Left eye (OS)	Mean of measurements (SD)	1.24 (0.66)
		Difference between measurements (SD)	-0.04 (0.11)
		Agreement Index (AI)	0.82
		% outliers	1/9
		Correlation between measurements	0.99
		Correlation: mean vs absolute difference value	-0.04
INFERIOR	Seen/Unseen Right eye (OD)	Mean of measurements (SD)	1.29 (0.67)
		Difference between measurements (SD)	0.09 (0.28)
		Agreement Index (AI)	0.63
		% outliers	1/9
		Correlation between measurements	0.92
		Correlation: mean vs absolute difference value	0.16
	Seen/Unseen Left eye (OS)	Mean of measurements (SD)	1.01 (0.06)
		Difference between measurements (SD)	-0.04 (0.11)
		Agreement Index (AI)	0.78
		% outliers	1/9
		Correlation between measurements	0.00
		Correlation: mean vs absolute difference value	1.00

Table 3: Stability of agreement between devices on SRT

	Variable	Parameters	Estimation
CENTRAL	SRT* Right eye (OD)	Mean of measurements (SD)	399.7 (188.0)
		Difference between measurements (SD)	23.9 (32.2)
		Agreement Index (AI)	0.84
		% outliers	0/9
		Correlation between measurements	0.99
		Correlation: mean vs absolute difference value	0.24
	SRT Left eye (OS)	Mean of measurements (SD)	350.6 (51.2)
		Difference between measurements (SD)	-8.0 (54.8)
		Agreement Index (AI)	0.69
		% outliers	0/9
		Correlation between measurements	0.63
		Correlation: mean vs absolute difference value	0.36
NASAL	SRT*) Right eye (OD)	Mean of measurements (SD)	395.3 (199.4)
		Difference between measurements (SD)	-2.4 (28.2)
		Agreement Index (AI)	0.86
		% outliers	0/9
		Correlation between measurements	0.99
		Correlation: mean vs absolute difference value	0.29
	SRT *) Left eye (OS)	Mean of measurements (SD)	364.3 (75.8)
		Difference between measurements (SD)	-4.9 (56.4)
		Agreement Index (AI)	0.69
		% outliers	1/9
		Correlation between measurements	0.93
		Correlation: mean vs absolute difference value	0.69

SUPERIOR	SRT **) Right eye (OD)	Mean of measurements (SD)	404.0 (262.8)
		Difference between measurements (SD)	-10.9 (73.8)
		Agreement Index (AI)	0.63
		% outliers	1/9
		Correlation between measurements	0.97
		Correlation: mean vs absolute difference value	0.63
	SRT*) Left eye (OS)	Mean of measurements (SD)	372.4 (172.1)
		Difference between measurements (SD)	-11.4 (32.3)
		Agreement Index (AI)	0.83
		% outliers	0/9
		Correlation between measurements	0.99
		Correlation: mean vs absolute difference value	0.33
INFERIOR	SRT Right eye (OD)	Mean of measurements (SD)	357.6 (138.6)
		Difference between measurements (SD)	-1.3 (36.0)
		Agreement Index (AI)	0.80
		% outliers	0/9
		Correlation between measurements	0.97
		Correlation: mean vs absolute difference value	-0.33
	SRT *) Left eye (OS)	Mean of measurements (SD)	364.6 (75.8)
		Difference between measurements (SD)	1.7 (56.7)
		Agreement Index (AI)	0.69
		% outliers	0/9
		Correlation between measurements	0.76
		Correlation: mean vs absolute difference value	0.79



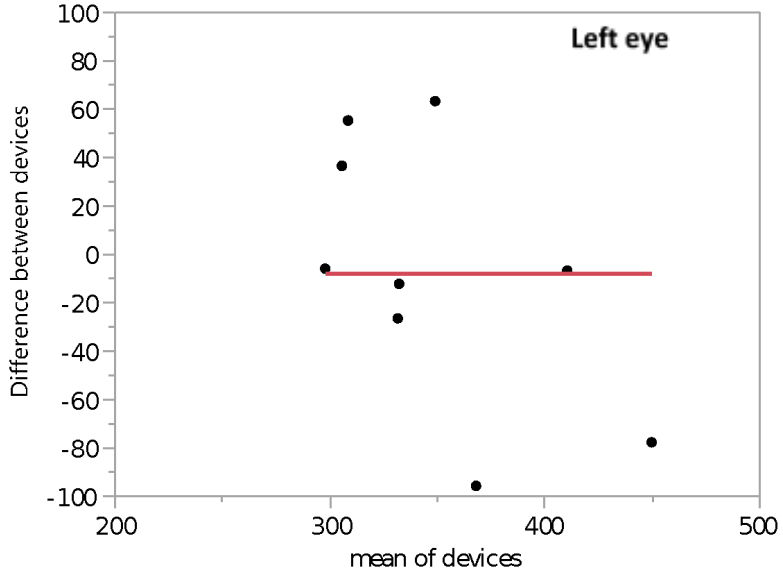
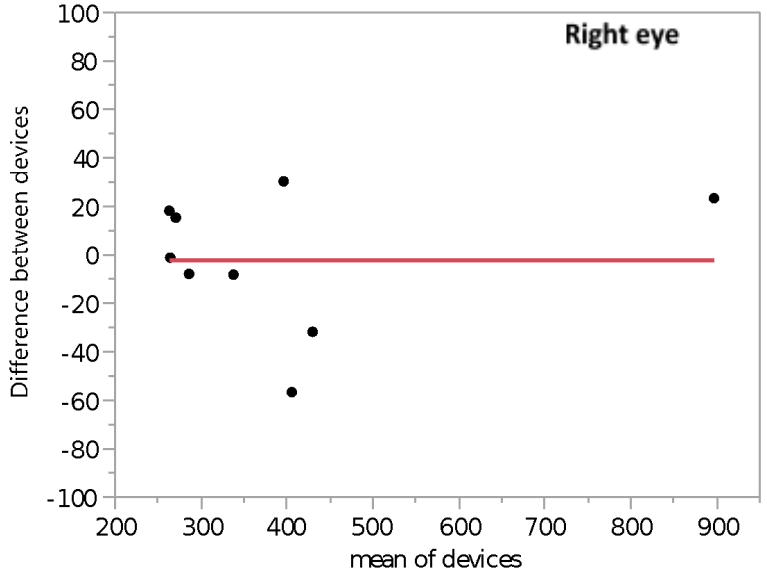


Figure 7: Stability agreement plot between devices on Inner SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.



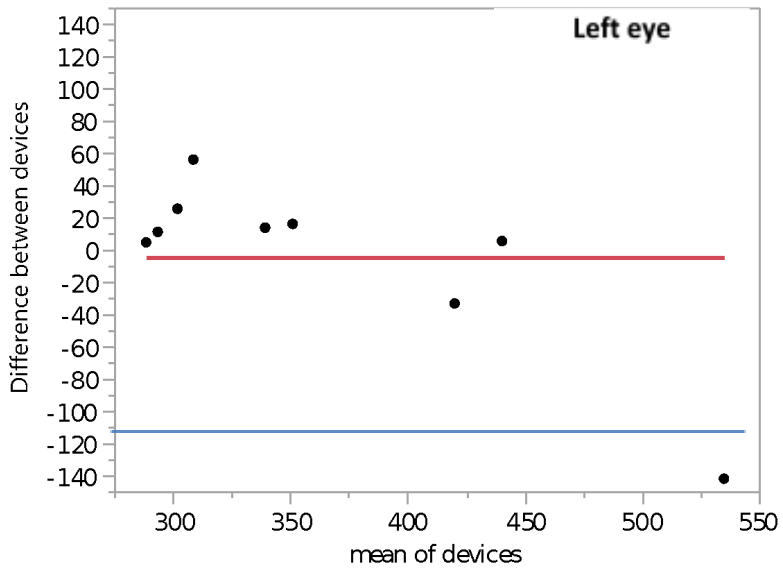
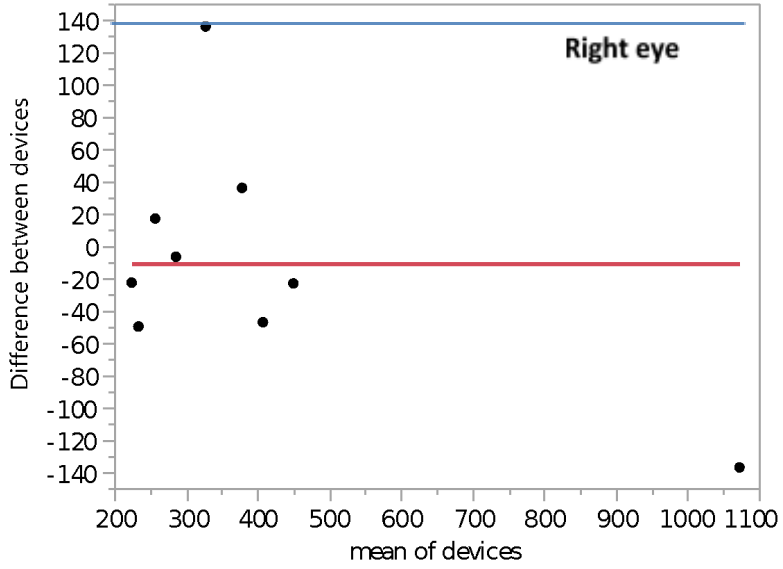


Figure 8: Agreement plot between devices on Nasal SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.



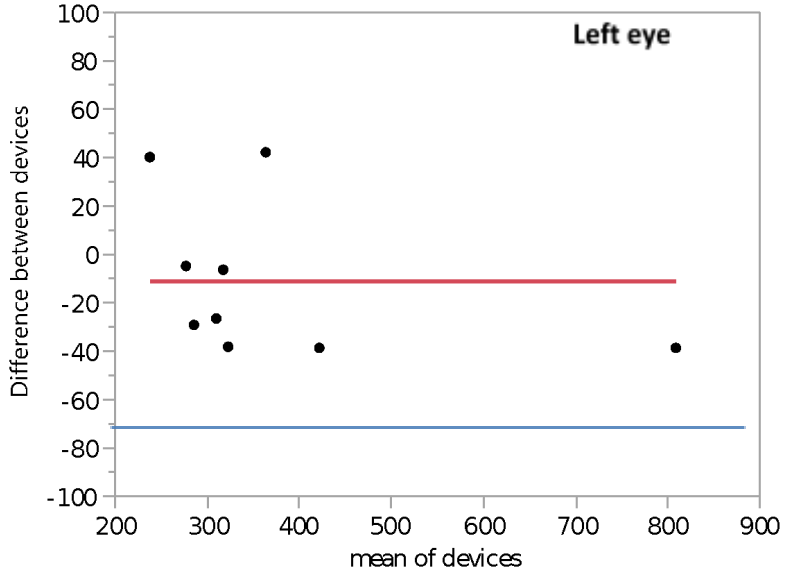
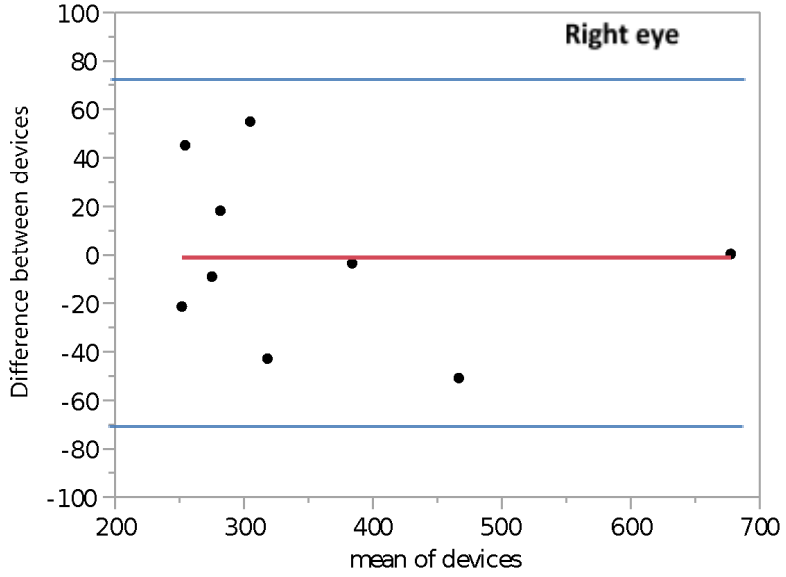


Figure 9: Stability agreement plot between devices on Upper SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations



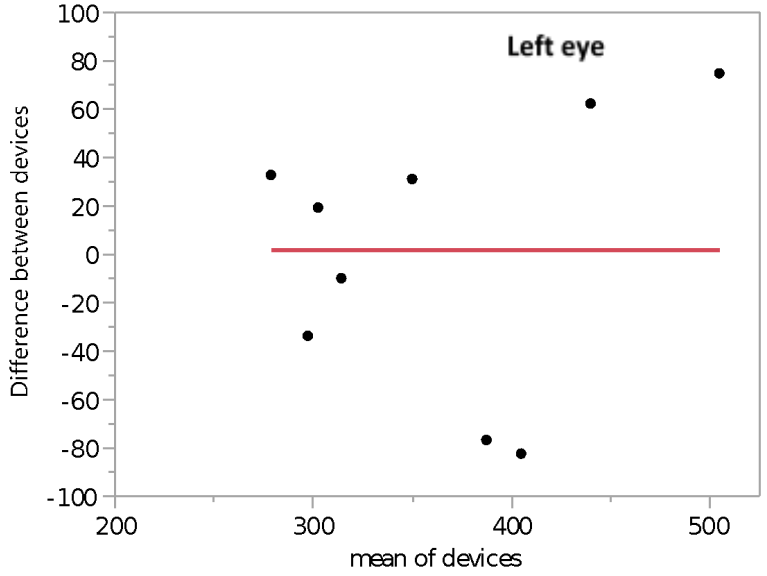


Figure 10: Stability agreement plot between devices on Lower SRT index measured on a) right eye and b) left eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.

CONCLUSION

In conclusion, our preliminary results indicate that high-frame rate VOG, is a promising tool to measure and quantify individual SRT values and seen/unseen visual targets in a visual field test using Eye Movement Perimetry.

The authors declare no conflicts of interest.

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