Report on Statistics

Automated eyelid ptosis measurement

using video-based oculography

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Medical product: **BulbiCAM**

Automated eyelid ptosis measurement from eye tracking camera

Measurements of the eye margin reflex distances in assessment of eyelid ptosis in the ophthalmic clinic is a manual and subjective assessment. The method is used to assess possible malposition of the upper or lower eyelid due to either mechanical or neurological aetiology. Measurements are important for any mechanical or neurological diagnosis, as well for surgical procedure of ptosis repair or in blepharoplasty. We report on generating facial and eye pictures to introduce a semi-automated measurement of eyelid position that could provide objective, accurate, and reproducible data for the clinician. The aim was to describe an eye tracking based software algorithm for determining the correct position of the eye before a picture was taken. The margin reflex distance 1 was then from the picture manually evaluated in two eye tracking devices, to evaluate the inter-rater reliability. Twelve pictures in total were taken from each participating subject, which were normal subjects and glaucoma patients. Our preliminary results indicate overall good to excellent agreement between devices and an overall good to excellent stability of the method. The methodology needs further investigation to compare with a golden standard of manual assessment.

BACKGROUND

The evaluation of eyelid distance measurement in assessing eyelids drooping (ptosis), includes a handheld millimetre ruler and subjective evaluation of the operator. Two values are normally quantified by this method. The noted values are margin reflex distance 1 (MRD1), and the margin reflex distance 2 (MRD2) (figure 1 and 2). MDR1 is defined by the vertical distance between the upper eyelid margin to the middle of the pupil, which is in clinical measurements noted as the corneal light reflex from a penlight source aligned with the visual axis. MRD2 is defined by the vertical distance between the lower eyelid margin to the middle of the pupil where the middle of the pupil is also defined by the same corneal light reflex[1].
The current clinical methods of ptosis evaluation are subjective and can be influenced by examiner skill, inter-observer variation, patient attention, and cognition. Eye tracking based assessment can provide an objective measure of ptosis to overcome the above limitations.
A software algorithm developed by Bulbitech can identify the visual axis and eyelid margins in the frontal eye plane, as a photograph can be taken when the visual axis is aligned and directed towards the camera.
The aim of this investigation was to introduce this method for a semi-automated ptosis measurement from an eye tracking device (BulbiCAM), and to compare the measurements in two different BulbiCAM devices.

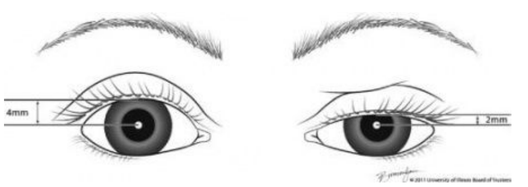


Figure 1 *MRD1 from Putterman AM. Margin reflex distance*

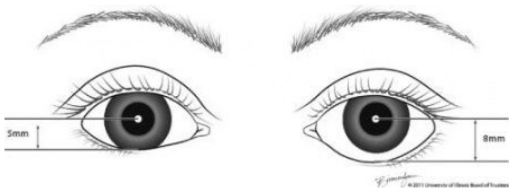


Figure 2 *MRD2 from Putterman AM. Margin reflex distance*

METHOD

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 binocular stimuli were used. The eye tracker frame rate was 400-Hz. The software algorithm of eye tracking was to verify the correct visual axis of the two eyes, as the eyes should be aligned towards a projected central dot on a screen before a photograph is taken of the eyes. If the pupil axis is not aligned, the software algorithm automatically deletes the picture, and a new stimulus is projected for a new photograph taken. To determine the correct vertical eye position, the centre pupil pixel should be between 8 to 20 pixels away from the centre bright pupil glint that is projected in the corneal reflection. If the subject is looking down, those centres are almost in the same position (too small) and if the subject is looking up, the distance is too big. Only vertical corrections were implemented in the eye tracker algorithm, as smaller horizontal positions should not interfere with the MRD1 or 2.

The software algorithm was also set to detect eye blinking, as the eye tracker will lose tracking if the eyelid covers the pupil. If blinking occurred within the time span of 100 milliseconds before and after a photograph was taken, the photograph was deleted, and the procedure was repeated. The distance from the eye to the camera was constant, as the VR headset was used. This also avoided problems with head motions during sampling.

A total of twelve pictures were taken in two different devices (six pictures in each BulbiCAM VR headset) for statistical agreement analysis. The photographs taken were placed behind a grid, which had square lines of one-millimetre distance (Figure 3).

In this trial, a total of 218 eye photographs (right and left) were manually measured to quantify the MRD1. A minimum of three and up to six consecutive measurements were made in the same day, with a wash-out period of 10 min 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 statistical power of 80 %, and 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 had to be included in the substrata, equally divided on the predefined age and disease stage stratum.

The study was performed at the Medical Research Foundation, 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 2/3 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 undistorted eye picture was taken with a high-speed digital infrared camera, which measures eye movements and fixations at a 400-Hz frame rate.

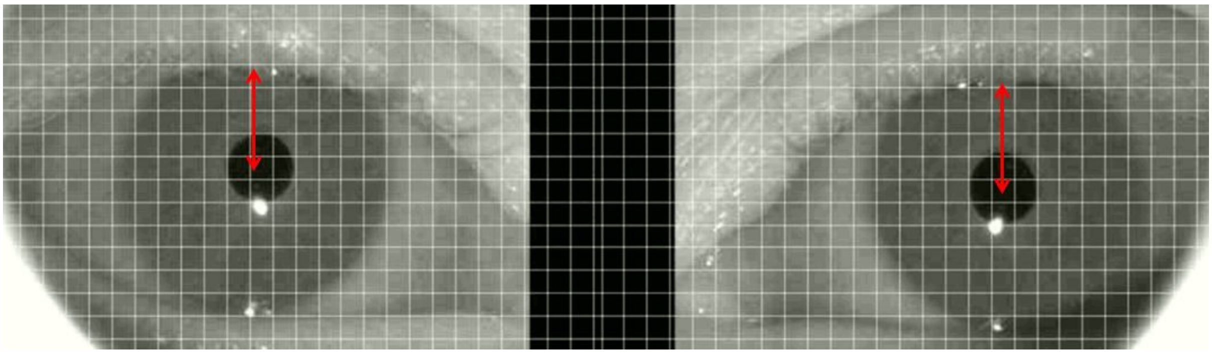


Figure 3 *Manual quantification of the MRD 1 by using the millimetre grid as a millimetre ruler. The quantification was given with 0,5-millimetre margin.*

RESULTS

Statistical method

All results on assumed continuously distributed variables are expressed by Mean values, Standard Deviation (SD) and 95% Confidence interval[2]. Comparison of devices was performed by using analysis of variance with repeated measurement[3]. Contingency Table Analysis was used for categorical data[4]. 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 $Mean_{diff} \pm 2*SD_{diff}$ against $Mean_{pairs}$ [5,6]. Additionally, the number of outliers and the agreement coefficient $AI = 1 – [2*SD_{diff} / Mean_{pairs}]$ is given[7]. 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)

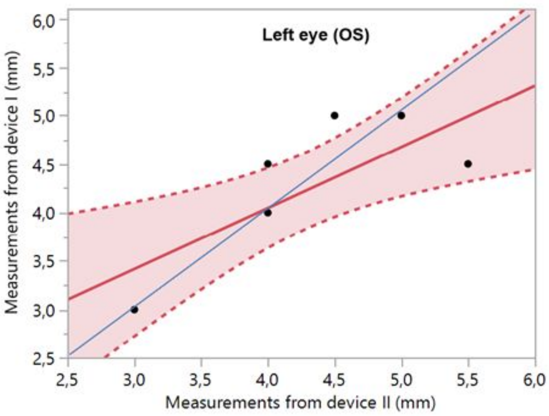
The agreement index of MRD1 between devices was 0,83 for the right eye and 0,73 the left eye. The mean stability index of MRD1 for the right eye was 0,80 and 0,79 for the left eye. In table 1 the agreement between devices can be observed.

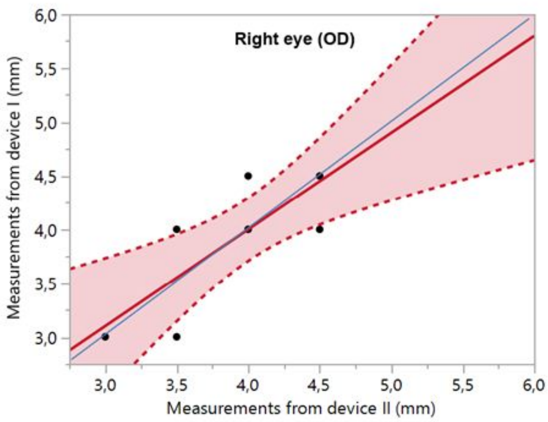
Table 1: Agreement between devices on MRD1

Variable	Parameters	Estimation
MRD1 Left eye	Mean of measurements (SD)	4.25 (0.80)
	Difference between measurements (SD)	0.06 (0.58)
	Agreement Index (AI)	0.73
	% outliers	0.00%
	Correlation between measurements	0.78
	Correlation between mean and absolute difference value	0.66
MRD1 Right eye	Mean of measurements (SD)	4.0 (0.56)
	Difference between measurements (SD)	0.00 (0.35)
	Agreement Index (AI)	0.83
	% outliers	0.00%
	Correlation between measurements	0.82
	Correlation between mean and absolute difference value	-0.21

Regression (Line of equality)

The line of equality is presented for the right and the left eye





Bland-Altman plot presented for the agreement of right and the left eye for MRD1

Agreement between devices

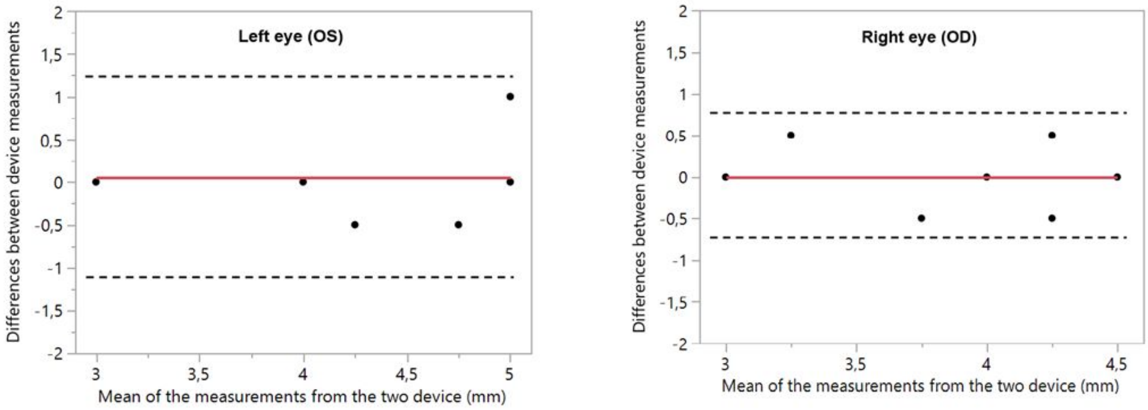


Figure 4: *Agreement plot between devices on Ptosis measured on a) left eye and b) right eye. The line represents the mean measurement on the two devices, the dotted line the agreement limits and the dots the group of observations.*

Stability of agreement between devices on MRD1

Variable	Parameters	Estimation
MRD1 Left eye	Mean of measurements (SD)	4.1 (0.82)
	Difference between measurements (SD)	-0.04 (0.44)
	Agreement Index (AI)	0.79
	% outliers	3/54=5.6%
	Correlation between measurements	0.87
	Correlation between mean and absolute difference value	0.18
MRD1 Right eye	Mean of measurements (SD)	4.0 (0.54)
	Difference between measurements (SD)	-0.03 (0.42)
	Agreement Index (AI)	0.80
	% outliers	2/54=3.7%
	Correlation between measurements	0.75
	Correlation between mean and absolute difference value	-0.17

Bland-Altman plot presented for the stability of agreement for right and the left eye for MRD1

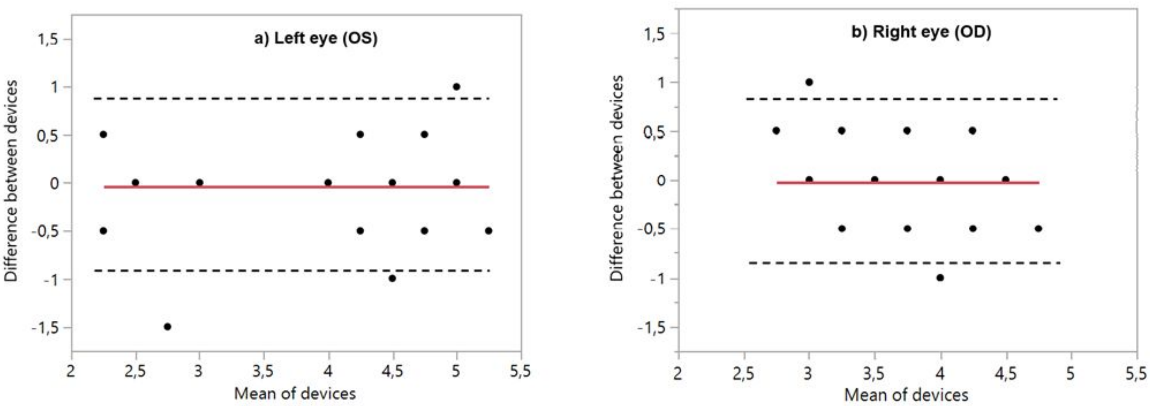


Figure 5: *Stability agreement plot between devices on Ptosis measured on a) left eye and b) right eye. The line represents the mean measurement of all measurements on the two devices, the dotted line the agreement limits and the dots the group of observations.*

DISCUSSION

The software algorithm seems to stabilize the eye gaze position into a vertical axis aligned towards the camera for taking the photograph. There is a good to excellent agreement index between measurements and of the stability agreement index of the devices. The small variability in measurements can either be from a minor misalignment of the eye towards the central axis, or the subjective and manual calculations of the distances in MRD1 made by the operator. As the eye is constantly moving due to micro saccades, there will always be a small variability in gaze fixation, which may explain this physiological and minor misalignment on the vertical axis. The mean variability was 0,5 (± 0,5) millimetre. To provide a more reliable methodology on the distance calculation, a computer-based methodology is preferable.

CONCLUSION

In conclusion, the preliminary results indicate that eye tracking VOG is a promising tool to measure and quantify individual ptosis values of MRD1.

The authors declare no conflicts of interest.

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