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Reproducibility of transcranial Doppler ultrasound examinations of the ophthalmic artery flow velocity

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Abstract

Transcranial Doppler ultrasound measurements of ophthalmic artery velocity were made on 88 patients predominantly suffering from glaucoma. Of the four observed parameters, peak velocity, mean-enveloped velocity, diastolic velocity, and resistivity index, the latter was found to be the most reproducible (CV=5·2%). The variability between patients was approximately twice that of the variability between consecutive measurements. Measurement error appeared to decrease as the operator gained experience.

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Transcranial Doppler ultrasound was introduced in 1982[1] to study non-invasively the blood flow velocity of some intracranial vessels for the examination of cerebral vascular diseases. The transcranial Doppler instrumentation consists of a 2 MHz pulsed Doppler with a fast Fourier transformation which is used to derive and analyse the spectrum of returning echoes of various frequencies.[2] It has been shown that there is considerably less attenuation of the sound beam in bone and soft tissue with the transcranial Doppler.[1] The technique has been used to obtain information from a number of intracranial arteries based on an understanding of their anatomy.[2–4] It has recently been shown that the method could be used to study the ophthalmic flow velocity.[4] Such quantitative measurements may provide more information on the physiological responses and pathological changes of the ocular circulation. The intraorbital course and branching of the ophthalmic artery are variable.[5] No previous studies have reported the reproducibility of transcranial Doppler ultrasound flow velocity measurements of the ophthalmic artery. It was the purpose of this study to determine the reproducibility of such measurements.

Patients and methods

Eighty eight subjects, comprising 22 normal and 66 patients predominantly suffering from glaucoma, were studied. Consent was obtained for all subjects. In order to evaluate the influence of the experience of the operator on the test, the data were divided into the initial group and a later group, each with 44 subjects. Twenty of the patients in the initial group had participated in more than one testing session, 4 and 24 hours after the initial test. In all testing sessions more than five measurements on an eye were recorded. The mean number of measurements per eye per test was 8·5.

The ultrasound beam was set at a depth of 40–50 mm from the eyelid as there is less variation in the course of the ophthalmic artery in the posterior orbit.[5] The ultrasound beam has to penetrate the eye and the orbital soft tissues which produce many different interfaces causing considerable attenuation of the ultrasound energy. It has been shown that the optimum ultrasound frequency in (MHz) which can be used at a given depth is approximately equal to 90 divided by the depth in mm. At any given depth this frequency is generally smaller than that used for imaging purposes.[6] Doppler frequencies ranging from 2–4 MHz have been found suitable for such purposes. In our experience it has been found that the 2 MHz pulse of the Doppler gives better quality spectrograms than the 4 MHz, both of which were available to us. If one wishes to study smaller vessels located more anteriorly than higher ultrasound frequencies may be more suitable.

For this study the Medasonic II Transpect transcranial Doppler ultrasound system (Medasonics, CA, USA) was used. It was equipped with a 2 MHz pulsed Doppler, real time fast Fourier transformation spectrum analyser as well as a 4 MHz continuous Doppler ultrasound. The maximum acoustic output water value was 161 mW/cm² (spatial peak temporal average intensity at 3·8 cm) which gives 95 mW/cm² intensity in situ. The power could be adjusted stepwise from 5–100% of the maximum power. We normally used 10% of maximum power to minimise unknown effects on the ocular tissues along the path of the ultrasound. The current guidelines of the Food and Drug Administration for ophthalmic application is 17 mW/cm² (ref 7) so that the intensity of 16·1 mW/cm² which we usually selected was well

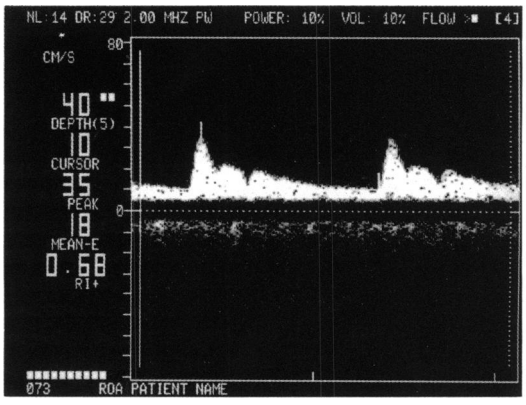

Figure 1 A videographic print-out of a pulsed Doppler ultrasound (2 MHz) of the ophthalmic artery is shown. The numbers on the left show from the top the gated depth in mm the diastolic velocity in cm/s, the peak velocity in cm/s and the mean enveloped velocity in cm/s. The lowest figure is the calculated resistivity index as outlined in the text.

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under this safety limit. The unit employs a microprocessor, a black and white monitor, and a hard disc for data storage. Our system was also equipped with an extra colour monitor and a videographic printer. Peak flow velocity and the other parameters such as the mean-enveloped flow velocity, the pulsatility index, and resistivity index were calculated and updated automatically in real time on the display screen. A remote control foot switch facilitated the operation of the equipment.

All tests were performed by one of us (PR). The subjects were tested in the supine position. The transcranial Doppler transducer probe was placed over the upper eyelid approximately 5 minutes after patient rested to maximise cardiac stability. Ultrasound coupling gel was applied liberally. This technique for the examination of the transorbital approach is now widely accepted.[4 8] In most cases the probe was placed on the superotemporal part of the eyelid. It was usually tilted approximately 20–30° to the sagittal plane and pointed towards the orbital apex. The gated depth was usually set at 40 mm and the volume sampled was 7–13 mm long. Adjustment of the angulation and the position of the probe as well as the gated depth and the subject's gaze were changed to optimise the displayed spectrogram. In almost all cases consistent and strong signals were obtained before recording. An audible pitch could be used as an additional guide once the operator had gained the necessary experience. The identification of the ophthalmic artery was based on the position of the probe, the depth of the sample volume, the direction of the flow, the relative flow velocity, and the instant observation of the spectrogram. The signal from the ophthalmic artery was normally recognised by its high resistance pattern. According to the Doppler equation the Doppler shift is proportional to the speed of the moving object,[9] in this case the blood flow velocity, which we wanted to measure. The angle between the line of motion and the observer has an effect on the Doppler shift. If the direction of the sound propagation is directly opposite to the flow direction, the maximum positive Doppler shift is obtained. It is difficult to determine the angle between the ultrasound beam and the direction of the ophthalmic artery since we had no duplex scanners which combine real-time cross-sectional ultrasound imaging with transcranial Doppler to help effectively to outline the ophthalmic artery. Allowing for a range of angles between the ultrasound and the course of the ophthalmic artery from 0–30° (cosine varying between 1 and 0·86) should give an error of less than 15% in most instances.[1]

The peak systolic blood velocity (peak), the mean-envelope velocity (Mean-E), end diastolic flow velocity, and the resistivity index were measured and calculated by the machine. Systolic blood velocity is defined as the maximum systolic peak velocity. The Mean-E velocity is defined as the mean of the peak frequency envelope which outlines all the frequency peaks forming a single signal in one cardiac cycle. End diastolic flow velocity is the minimum flow velocity at the end of the diastolic phase prior to the next cardiac cycle. The resistivity index is the ratio of peak velocity minus diastolic velocity divided by peak velocity.

Statistical analysis

There were four potential sources of variability affecting the measurements; they were measurement error (residual), temporal variation (between tests), variability between patients, and difference between eyes of a patient. In order to assess the relative magnitude of the variability of these four factors, analysis of variance, using different design models, was carried out. The first analysis employed a nested three-factor design (patient, test, eye) with replication. Since all of the later patients underwent only one test, and with only one test it is impossible to estimate the variability between tests, only data from the initial group of 44 patients were included in this analysis.

The second analysis was a nested two-factor design (eyes nested within patients) with replication. The variance component associated with tests was not included in this model in order that the entire data set could be analysed under this model. In the case of those patients in the initial group who had participated in more than one examination, one of their tests was randomly selected and only the measurements from that test were used.

Both analyses were performed on the four variables, peak velocity, mean-E velocity, diastolic velocity, and resistivity index. From the analysis of variance results, estimates of the components of variation were made. Coefficients of variation (CV) based on these components were then calculated by taking the square root of the component and dividing it by the group mean. In order to do this, it was necessary to determine the mean number of measurements per test, mean number of tests per patient, and mean number of eyes measured per test. Since the numbers varied from test to test and patient to patient, harmonic means rather than arithmetic means were used (see Appendix).

Results

Coefficients of variation for peak velocity, mean-E velocity, diastolic velocity, and resistivity index are shown in Table 1. These figures are based on 1447 measurements from the initial group of 44 patients, all of whom were examined more than once. It can be seen that for some of the parameters the interpatient CV is almost three times as great as the CV for the measurement. For the intermeasurement variability it can be seen that the least variation is shown by the peak velocity (CV=6·32%) whereas the

Table 1 Coefficient of variation (%) based on components of variance. Data from initial group of 44 patients (n=1447)

	Components of variance			
Doppler parameter	*Measurement*	*Test*	*Eye*	*Patient*
Peak velocity	6·32	8·38	11·68	17·69
Mean-E velocity	7·85	9·57	12·31	14·00
Diastolic velocity	10·01	11·86	11·71	19·80
Resistivity index	5·20	3·82	3·53	9·20

mean-E and diastolic velocity had coefficients of variation of 7·85 and 10·01% respectively. The resistivity index has the best reproducibility (CV=5·2%). The inter-test variability (temporal variation) was least variable for the resistivity index (CV=3·82%), followed by the peak velocity (CV=8·38%), Mean-E velocity (CV=9·57%), and diastolic velocity (CV=11·85%).

The effects of operator experience are shown in Table 2. The coefficients of variation are based on the measurement error. The estimates given in the first column are from the initial 44 patients and based on 807 measurements for peak, mean-E, and diastolic velocities, and 421 measurements for the resistivity index. The estimates in the second column are from the later group of patients and are based on 429 measurements for the peak and mean-E velocities, 419 for the diastolic velocity, and 417 for the resistivity index. The variability is less in the later group for three out of the four parameters measured. It appeared to the operator that the measurements were done more quickly for the second group but the actual timing was not recorded.

Table 2 Coefficient of variation (%) based on measurement error for initial group and later group

Doppler parameter	Coefficient of variation (%)			
	Initial group	(n)	Later group	(n)
Peak velocity	6·67	(807)	4·67	(429)
Mean-E velocity	7·38	(807)	6·88	(429)
Diastolic velocity	9·19	(807)	9·86	(419)
Resistivity index	4·97	(421)	4·46	(417)

Discussion

The principles of Doppler ultrasound are well known.[9,10] Doppler instruments can produce continuous wave and pulsed wave ultrasound emissions. Transcranial Doppler is a pulsed wave Doppler which provides discriminated Doppler signals from specified depths and well defined regions with little attenuation which is normally produced by the ocular and orbital soft tissues. It has made the non-invasive examination of the ophthalmic artery and some other intracranial vessels possible.[4] The first part of the ophthalmic artery before it curves over or under the optic nerve shows the least variability as shown by Hayreh.[5] In order to minimise the incident angle between the ultrasound and arterial course this appears to be the best part of the vessel to study. Our study has shown that the coefficient of variation between patients was large but the variation of the measurements was very acceptable. The large interpatient variability is not surprising as we included patients of different sex, ages, and disease states. A variation of the angle between the ultrasound beam and the direction of the blood flow, which affects the velocity values displayed from the spectrogram between the two eyes, is possible. In order to minimise such errors Canning and Restori[11] proposed using ultrasound indices instead of absolute velocity values. Our study confirms that when the two eyes are compared the resistivity index is much less variable than the other parameters. Our patients, however, did not have their carotid arteries examined and therefore some of the variation between the two eyes may be due to carotid disease. The variability of repeated readings in the same individual separated in time by 4–24 hours was of the order of 8% for the peak velocity which would indicate quite a good reproducibility of the readings on different occasions. Greater experience of the operator also improves the reproducibility of the results.

The present study suggests that the reproducibility of the transcranial Doppler ultrasound measurements of the ophthalmic artery is such that it can be used as a clinical tool in evaluating a number of physiological and pathological changes of the ophthalmic artery. Studies might now be useful in evaluating some disease states.

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Appendix

The harmonic mean (HM) is defined as

$$\frac{1}{HM} = \frac{1}{n} \frac{n}{\sum_{i=1}} \left(\frac{1}{x_i}\right)$$

where – for example, in our case we wanted to calculate the mean number of measurements per eye per tests, the 'x_i' would be the number of measurements on a given eye during a given test, and 'n' would be the total number of times – that is, over all patients, all tests and all eyes, such a set of measurements was made.