EXTENDED REPORT

Age differences in central and peripheral intraocular pressure using a rebound tonometer

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Aim: To evaluate the influence of age on the measurements and relationships among central and peripheral intraocular pressure (IOP) readings taken with a rebound tonometer.

Methods: The IOPs were measured using the ICare rebound tonometer on the right eyes of 217 patients (88 men and 129 women) aged 18–85 years (mean 45.9 (SD 19.8) years), at the centre and at 2 mm from the nasal and temporal limbus along the horizontal meridian. Three age groups were established: young (≤ 30 years old; $n=75$), middle aged (31–60 years old; $n=77$) and old patients (>60 years old; $n=65$).

Results: A high correlation was found between the central and peripheral IOP readings, with the central readings being higher than the peripheral ones. Higher IOP values for the central location were found in the younger patients. Older patients had significantly lower temporal IOP readings than those for the remaining two groups ($p<0.001$), whereas no significant differences were found among groups when IOP was measured at the central and nasal locations. A significant decrease was observed in the nasal and temporal IOP readings as the age increased ($p=0.011$ and 0.006 , respectively).

Conclusion: Older patients had lower IOP values than the middle-aged and younger patients in the temporal peripheral location. A negative correlation was found between age and IOP by rebound tonometry in the corneal periphery but not in its centre.

The assessment of intraocular pressure (IOP) is of major importance in follow-up and treatment of patients with glaucoma. Enormous effort has been made to develop rapid and accurate methods to measure IOP (ie, non-contact tonometry (NCT),^{1,2} dynamic contour tonometer³ and pneumotonometry⁴) in relation to the classic measurement techniques (Goldmann applanation tonometry (GAT)).

However, IOP reliability is compromised after laser corneal refractive surgery procedures as a result of changes in corneal thickness and curvature (see Montés-Micó and Charman⁵ for a review). New instruments to evaluate IOP not based on corneal applanation could be less affected by changes after surgery.

Rebound tonometry⁶ (Tiolat Oy, Helsinki, Finland) measures IOP using the impact of a probe tip over a small area of contact, and could be useful when taking IOP readings after corneal refractive surgery. The reliability of the ICare tonometer in healthy humans has been recently assessed against GAT; it showed good agreement for clinical purposes, with mean differences in the order of 2–3 mm Hg higher for the rebound tonometer than for GAT in its conventional⁷ and portable versions.⁸

Previous research conducted by our group has shown differences in IOP measured at the centre and the periphery of the cornea using rebound tonometry (lower values at corneal periphery).⁹ Topographical differences in the stromal collagen package between the centre and the periphery of the cornea could account for these findings, IOP measurement being a reflection of different biomechanical properties depending on the corneal location.¹⁰ Recent research pointed out that the age of patients influences the IOP measurement using GAT, NCT and pneumotonometry.¹¹

It then becomes necessary to explore the correlation of recorded IOP changes, measured at different locations of the cornea using rebound tonometry, with age. The goal of this study was to analyse the influence of age on the IOP

measured at the centre and the periphery of the cornea using rebound tonometry.

PATIENTS AND METHODS

Patients

In all, 217 people (88 men and 129 women), aged 18–85 years (mean 45.9 (standard deviation (SD) 19.8) years), consented to participate in the study after the nature of the experimental procedures was explained. Only the values obtained on the right eyes were included in the study. The IOP values were recorded using the ICare rebound tonometer (Tiolat Oy, Helsinki, Finland).

None of the participants had any ocular condition or injury, including corneal pathology or corneal scarring, had previously undergone corneal surgery or was taking any ocular or systemic drug likely to induce changes in IOP or corneal properties. All procedures followed the guidelines of the Declaration of Helsinki and were approved by the Scientific Committee of the School of Sciences at the University of Minho, Braga, Portugal.

Three groups of patients were established according to the specifications in table 1, resulting in a similar number of participants within the three age intervals (young, ≤ 30 ; middle aged, 31–60; and old, >60 years).

Measurements

IOP was measured with the ICare tonometer after an ocular health assessment with slit-lamp and fundus examination by direct ophthalmoscopy. Measurements were carried out by a trained clinician, avoiding excessive movement of the instrument as the probe hit the cornea. A new disposable probe was used for each participant. The instrument

Abbreviations: GAT, Goldmann applanation tonometry; IOP, intraocular pressure; NCT, non-contact tonometry

Table 1 Age descriptive statistics corresponding to the three age groups

Age group (years)	n (%)	Mean (SD) age (years)	Age range (years)
≤30	75 (34.6)	22.3 (2.94)	18–30
31–60	77 (35.5)	47.78 (6.86)	32–60
>60	65 (29.9)	70.06 (5.91)	61–85
Total	217 (100)	45.9 (19.8)	18–85

permitted taking a series of six measurements and averaged them to obtain the mean SD. Three valid series were taken at the central, nasal and temporal locations. Measurements at the three locations were randomly taken to minimise the potential effect of initial readings on subsequent ones. The operating protocol followed in the Department of Physics (Optometry), School of Sciences, University of Minho, Braga, Portugal, has been published previously.⁷ Peripheral measurements were taken at a constant distance of about 2 mm from the limbus in the nasal and temporal regions of the horizontal meridian subjectively estimated by the operator as twice the thickness of the probe. For each peripheral measurement, the patients were asked to look at a peripheral fixation target on the right and left sides in front of them to enable the investigator to take nasal and temporal (only the right eye was measured) measurements. After the gaze was reoriented towards the peripheral target, the investigator adjusted the perpendicularity of the probe and the location where the probe was to be applied. This place was estimated as a distance that was twice the thickness of the probe (about 2 mm from the limbus). Similar procedures were followed by previous investigators using Tono-Pen.¹²

Statistical analysis

Data were analysed using SPSS V.14.0. Correlations between the central and peripheral measurements were assessed statistically as the mean of the differences compared with zero. The 95% limits of agreement (LoA) were also calculated as follows¹³:

LoA = mean of the difference ($1.96 \times \text{SD}$ of the differences)
Bias was assessed statistically as the mean of the differences compared with zero. As variables did not present a normal distribution, the Kruskal–Wallis test was used to analyse the statistical significance of the differences. The level of statistical significance was established at $\alpha = 0.05$. Trends for differences between the central and peripheral IOP

readings as a function of age were assessed by regression analysis.

RESULTS

Table 2 shows the mean values of IOP registered at the central, nasal and temporal locations. Despite IOP readings at the corneal centre being slightly superior to those taken at the corneal periphery, those differences were not significant ($p > 0.05$). As data for all variables were not normally distributed, correlations among IOP values were assessed by non-parametric tests (table 3). All correlations were high and significant. The stronger correlation for the whole population was found between the central and nasal measurements, followed by central versus temporal and nasal versus temporal measurements.

Figure 1 shows plots of differences between IOP readings at different corneal locations as a function of the mean value. Narrow confidence intervals were observed, with 95% of the differences lying between 2–3 mm Hg and mean differences close to zero. Nasal IOP values were in closer agreement with central IOP (fig 1A) than temporal ones (fig 1B). However, the highest agreement was observed among nasal and temporal peripheral readings (fig 1C). We found a significant trend towards higher nasal than central IOP values at higher IOP and the opposite for lower IOP ($r^2 = 0.107$; $p < 0.001$). No significant trends were observed when we compared central IOP values with nasal ones ($r^2 = 0.013$; $p = 0.099$) and nasal values with temporal ones ($r^2 = 0.006$; $p = 0.225$).

Table 2 also shows the statistics of IOP readings for the three age groups separately. Apart from the higher central values observed within the same age group, we found a trend for younger patients to have higher IOP values for the three corneal locations where tonometric readings were taken. Box plots in fig 2 show IOP values at the three corneal locations for each age group. As a general behaviour among the three corneal locations, we can highlight that the older group has less variability in terms of interquartile range and upper to lower bar limits range, whereas it was the opposite for the middle-aged group. Although the lower limits were between 9 and 10 mm Hg, the upper limits of the bars show a higher variability and a higher number of outliers. Such a behaviour was also found in a recent experiment that assessed IOP by non-contact tonometry synchronised with cardiac rhythm¹⁴ and reflected that lower IOP values were roughly uniform; on the other hand, higher values showed more variability, even in populations without glaucoma.

Table 3 shows the results of the non-parametric correlations tests between IOP values for different age groups and IOP taken at the three locations. Analysing data by age

Table 2 Descriptive statistics for central and peripheral intraocular pressure measured using the ICare tonometer by age group and for all patients considered as a whole

	Age group (years)	Intraocular pressure (mm Hg)			
		Minimum	Maximum	Mean	SD
Centre	≤30	8	23	15.3	2.9
	31–60	10	25	15.3	3.1
	>60	10	23	14.4	2.5
	Total*	8	25	15.0	2.9
Nasal	≤30	10	24	14.7	2.6
	31–60	10	22	14.6	2.8
	>60	9	23	13.7	2.2
	Total*	9	24	14.4	2.6
Temporal	≤30	9	24	15.1	2.6
	31–60	10	23	15.1	3.1
	>60	10	22	13.9	2.3
	Total*	9	24	14.7	2.7

Total n = 217.

*Considered as a whole.

Table 3 Nonparametric correlations between central and peripheral ICare intraocular pressure readings within each age group and for all patients considered as a whole

	Age group (years)	Spearman's correlation	p Value
Central v nasal	≤30	0.832**	<0.001
	31–60	0.924**	<0.001
	>60	0.833**	<0.001
	Total*	0.869**	<0.001
Central v temporal	≤30	0.787**	<0.001
	31–60	0.879**	<0.001
	>60	0.837**	<0.001
	Total*	0.835**	<0.001
Nasal v temporal	≤30	0.744**	<0.001
	31–60	0.913**	<0.001
	>60	0.806**	<0.001
	Total*	0.826**	<0.001

*Considered as a whole.

**Correlation was significant at the 0.01 level (two tailed).

groups, we observed that the correlation between measurements was stronger for the middle-aged group, followed by the older group, and the least correlation coefficient was found for the younger group for the three combinations (central versus nasal; central versus temporal; and nasal versus temporal).

According to table 4, differences in temporal IOP were found between the older group (>60 years) and the remaining two groups ($p = 0.011$). Differences approached significance only for nasal IOP values ($p = 0.052$), whereas differences were definitively not significant for central IOP measurement ($p = 0.201$).

Figure 3 shows a scatter plot of different IOP readings as a function of age, and a negative correlation between both parameters was observed. This trend towards lower IOP values as a function of age was significant for the temporal ($r = 0.185$; $p = 0.006$) and nasal readings ($r = 0.173$; $p = 0.011$) as obtained from analysis of variance curve-fit analysis. We found no significant trend for central IOP measurement as a function of age ($r = 0.126$; $p = 0.059$).

DISCUSSION

In this study, we found evidence that age could have a significant role in the resistance of the peripheral cornea to the impact of a rebound tonometer. Although we have not taken measurements of corneal thickness, this parameter is not likely to be responsible for the significant trends towards lower IOP with age, as this parameter did not vary significantly as a function of age.¹⁵ For reference purposes, we can consider the values of ultrasonic computed tomography data obtained in a more recent study (unpublished data) carried out on 64 right eyes of patients aged 18–44 years. According to those data, the mean central thickness for a normal average cornea was 532 (SD 37) μm at the centre, and 623 (SD 40) and 597 (SD 46) μm at 4 mm from the centre in the nasal and temporal regions, respectively. These correspond to a distance of about 2 mm from the limbus, which was the place where ICare peripheral measurements were taken in this study.

Tonnu *et al*¹¹ found a significant trend for GAT and ocular blood flow tonometry to overestimate IOP compared with Tono-Pen in eyes of older people—that is, Tono-Pen gives lower values than GAT and ocular blood flow tonometry in eyes of older people. Also, Eisenberg *et al*,¹⁶ in a study on patients aged 4–85 years, found that Topo-Pen measured lower values in older patients than the portable version of GAT. These findings agree in some way with the trend in our study for lower IOP with ICare as age increases.

Figure 1 Differences among intraocular pressure readings as a function of the mean value for (A) central versus nasal, (B) central versus temporal and (C) nasal versus temporal measurements.

A potential explanation for these findings would involve the biomechanical properties and the histological arrangement of the normal cornea and how they change with age.

The macroscopic arrangement of the stromal collagen lamellae seems to be the basis of the shape, strength and

Figure 2 Intraocular pressure values by location and age groups.

Table 4 Paired comparisons between age groups of intraocular pressure readings using ICare

Age group (years)	Central	Nasal	Temporal
≤30 v 31–60	−0.019	0.122	0.042
≤30 v >60	0.823	1.045	1.258*
31–60 v >60	0.842	0.923	1.216*

*Mean difference was significant at the 0.05 level by Kruskal–Wallis test.

transparency of the corneal tissue.¹⁷ The stroma of the human cornea represents 90% of its total thickness and is primarily constituted of collagen fibrils arranged in 200–300 parallel lamellae.¹⁷ Despite the increase in the number of lamellae at the limbus, the number of lamellae across the transparent portion of the cornea has been generally assumed constant by the scientific community. Recent studies have confirmed that the increase in collagen diameter and larger interfibrillar spacing could account for the increased peripheral corneal thickness in the normal cornea.¹⁰ Considering that this collagen network would be responsible for the cornea's mechanical strength, it can be hypothesised that the response of the central and peripheral cornea to rebound tonometry is influenced by differences in the histological arrangement of the stroma.

Boote *et al*¹⁰ showed that collagen fibrils were more closely packed in the prepupillar region than in the peripheral corneal areas; they also found that fibril diameter increases markedly at a distance of 3–4 mm from the corneal centre towards the limbus, resulting in different optical and biomechanical properties across the corneal topography.¹⁰ More interestingly, previous studies using *x* ray diffraction have shown that collagen fibrils increase in diameter with age.¹⁸

The influence of biomechanical properties of the cornea on GAT is well known,^{15 19 20} acquiring special relevance when

measuring IOP after refractive surgery,^{21–24} as well as in the diagnosis and management of glaucoma, with normal-tension glaucomatous and ocular hypertensive eyes having considerably different values of central and peripheral corneal thickness.²⁵ More reliable measurements of the IOP were obtained in the temporal part of the cornea after refractive surgery.¹²

From our previous experiments with peripheral rebound tonometry, we have observed that central and peripheral readings reflected what we considered to be a paradoxical behaviour of IOP, as with lower IOP values at the periphery (despite being thicker) than at the centre (despite thinner thickness). The higher values of IOP at the centre and the correlations between central and peripheral ICare IOP measurements were in agreement with those found in a previous study conducted in our laboratory on a more limited sample.⁹

The results of Boote *et al*¹⁰ showed a mean collagen interfibrillar separation 5–7% larger in the periphery than in the central 3 mm of the cornea. This could partly support the assumption that the central cornea, despite being thinner than the peripheral cornea, could display higher resistance to tonometric devices.

An extension of the work by Boote *et al*¹⁰ on corneas of younger and ageing people could answer this question regarding the stromal organisation in the corneal periphery as a function of age. If such differences in ICare IOP readings are related to changes in the biomechanical behaviour of the human cornea with age, and if such changes could vary from the corneal centre to the periphery, they need to be considered in other specific studies using appropriate instrumentation to quantify such properties. A peripheral thinning in the ageing cornea²⁶ could be involved in some way with changes of the corneal response to rebound tonometry at these places. However, owing to the apparent insensitivity of ICare IOP to large differences in the corneal thickness, other hypotheses can not be ignored.

Figure 3A Regression analysis of intraocular pressure distribution as a function of age for central measurements.

Figure 3B Regression analysis of intraocular pressure distribution as a function of age for peripheral nasal measurements.

Figure 3C Regression analysis of intraocular pressure distribution as a function of age for peripheral temporal measurements.

Another potential explanation that would also help to clarify why differences between central and peripheral rebound tonometry measurements vary among age groups could be related to corneal or ocular rigidity.

Pallikaris *et al*²⁷ concluded that ocular rigidity increases with age; however, despite being statistically significant, their results showed large scatter. On the other hand, Grabner *et al*²⁸ found that the corneal resistance to indentation was positively correlated with IOP values (higher resistance with higher IOP) and corneal thickness (higher resistance in thicker corneas), but inversely correlated with age (younger patients presented higher resistance). So, contrary to the trends of apparent increased ocular rigidity in older patients, younger patients could have more rigid corneas than older patients. Changes in hydration control in elderly people could be partially responsible for such behaviour and could explain, at least partly, the lower values of IOP found in older patients in this study, whose trends were statistically significant for temporal and nasal readings.

Several points with relevance to clinical practice and basic research are highlighted from this study. Correlations between central and peripheral IOP readings were different for different age groups. Contrary to other instruments, when using the ICare rebound tonometer, lower values of IOP can be expected when readings are taken at peripheral locations. Peripheral temporal IOP readings taken with the ICare rebound tonometer in older patients were markedly lower than those taken at the same location in younger patients. Differences between central and peripheral IOP measurements could increase as a function of age, as peripheral readings have a trend to decrease significantly with age, whereas central rebound IOP measurements did not.

In conclusion, we have shown that the ICare tonometer can conveniently measure central and peripheral IOP. Thus, the ICare tonometer is a promising diagnostic modality for the objective assessment of central and peripheral IOP.

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