Nerve fibre layer measurement of the Hong Kong Chinese population by scanning laser polarimetry

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Abstract

Purpose **To obtain normal retinal nerve fibre layer (RNFL) measurements by scanning laser polarimetry in a local Hong Kong Chinese population and to identify the correlation of the measurements with age.**

Methods **One hundred and fifty-nine normal Hong Kong Chinese volunteers of different ages were recruited for this study. RNFL values were measured using a Nerve Fibre Analyzer GDx (Laser Diagnostic Technologies, CA).**

Results **Mean peripapillary RNFL measurements at the superior, inferior, temporal and nasal regions were 95.0 ± 15.6, 97.0 ± 16.3, 47.0 ± 9.0 and 43.9 ± 15.1 μm respectively (mean ± SD). There was a highly significant negative correlation in average RNFL values with increasing age (~1.9 μm per decade, $p = 0.001$). A significant negative correlation with increasing age was also identified in the RNFL values in all four regions and they decreased by similar amounts ($p < 0.05$). No correlation with age was observed for relative ratio parameters such as superior/nasal ratio, inferior/nasal ratio and max. modulation ($p > 0.05$).**

Conclusion **RNFL values of the Hong Kong Chinese population appeared to decrease over time cross-sectionally. Since they decreased by similar amounts at four regions, use of relative ratio parameters for analysis has an advantage over absolute values, as they were not affected by age.**

Key words Age, Chinese, Nerve fibre layer analyzer, Retinal nerve fibre layer, Scanning laser polarimetry

Scanning laser polarimetry (Nerve Fiber Analyzer, NFA, GDx version; Laser Diagnostic Technologies, San Diego, CA), is a new diagnostic computerized technique for rapid, quantitative, objective and *in vivo* estimation of retinal nerve fibre layer (RNFL) thickness. It indirectly assesses this thickness based on the amount of polarisation change, or retardation, induced by the RNFL on a polarised laser beam passing through it. This instrument is potentially useful in glaucoma screening since glaucoma disease is associated with diffuse as well as localised thinning of the RNFL. Before introducing the tool into clinical practice, it is necessary to develop a norm and ascertain its correlation with age. Previous studies have shown ethnic variation in that Caucasians have significantly higher RNFL values than Afro-Caribbeans in terms of both average thickness[5] and relative ratios[4] (superior/nasal ratio and inferior/nasal ratio). Moreover, RNFL values have been shown to decrease significantly, albeit gradually, with age.[1–5]

The aim of this study was to determine the normal RNFL measurement profile in a local Hong Kong Chinese population. This profile may be useful in the evaluation of RNFL and provide a reference for comparison with glaucoma patients.

Methods

After full informed consent had been obtained, 159 normal Hong Kong Chinese individuals (78 males, 81 females; age range 10–78 years) were recruited at the Queen Mary Hospital Ophthalmology Clinic, Hong Kong. Most volunteers were staff and medical students, or friends and relatives of hospital personnel. Subjects were classified as 'Chinese' by their self-identification. The subjects were subdivided into seven age cohorts: 10–19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, and 70 years or above. Each subject underwent a complete ophthalmological examination. Inclusion criteria were best-corrected visual acuities of 6/9 or better, refractive errors between +6.00 and −6.00 with less than 2.00 dioptres of astigmatism, no diabetes, and no history or family history of glaucoma. Each eye had an intraocular pressure of 21 mmHg or less (by Goldmann applanation tonometry), a cup/disc (C/D) ratio of less than 0.6, no asymmetry in the C/D ratio between fellow eyes exceeding 0.2, no peripapillary

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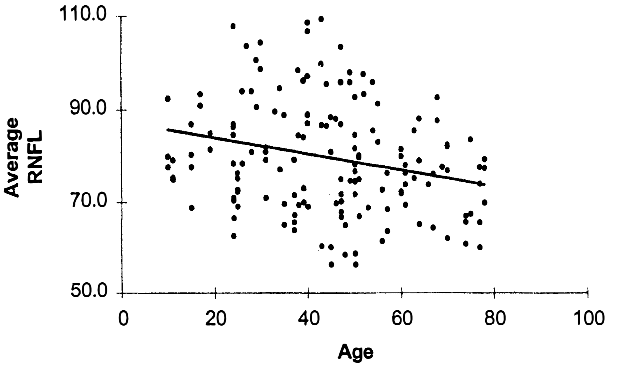

Fig. 1. *Average RNFL value as a function of age* (p = *0.001,* r = *0.25,* y = –0.18x+*87.6).*

atrophy and no optic nerve head abnormality as determined by slit-lamp biomicroscopy. All subjects underwent Humphrey Field Analyser 24-2 threshold perimetry. Visual fields were accepted only when false responses and fixation losses were 15% or less. Single, isolated defects of 10 dB or less at the edge of the 24-2 field were ignored.

After applying all the above criteria we excluded 28 subjects. The reasons for exclusion were: previously undiagnosed glaucoma (2 subjects), ocular hypertension (7 subjects), retinal degeneration (1 subject), high refractive errors (9 subjects), and inability to satisfy the reliability criteria for visual field perimetry (9 subjects). Only the right eye of each subject was included for evaluation.

RNFL estimations were obtained with the NFA GDx. This consists of a laser source, a polariser, a scanning unit, a polarisation modulator, a compensator and a polarisation detector. When a polarised near-infrared light source (wavelength 780 nm) is projected across the ocular media to the retina, the incident and reflection beams double-pass the RNFL before emerging from the eye. The parallel microtubules within the retinal ganglion cell axons in the RNFL are thought to be the birefringent medium. They induce a change in the reflected light's state of polarisation – termed a retardation – which is detected and quantified by the NFA. A total of 65 536 retinal locations are measured within 0.7 s to create a retardation map corresponding to RNFL thickness over a 15° × 15° (256 × 256 pixels) retinal area. The amount of polarisation retardation in the reflected light has been shown to correlate with RNFL thickness.[7] Thus, retardation is a measure of relative, not absolute, RNFL thickness.

While undergoing scanning, the pupils of the subjects remained undilated. All examinations were performed by one experienced operator (K.H.M.). At least three measurements were taken for each eye, and the mean of three good images was used for analysis in this study. According to the manufacturer, a good image is defined as one which has even illumination, which is properly focused as characterised by sharp and well-defined edges for blood vessels, and which lacks red saturation. Red saturation is an indication of image overexposure and this impairs the sensitivity of the machine's polarisation detector. A measuring ring placed around the inner margin of the peripapillary scleral ring by the operator approximated the optic disc margin. Another measuring ring was then automatically placed 1.75 disc-diameters away and concentric with the margin of the optic disc. Default region positions were applied: the peripapillary band was divided into superior and inferior regions of 120° each, a temporal segment of 50°, and a nasal region of 70°. Linear regression analysis was applied to determine the effect of age on RNFL values in our normal population. Although there was an array of parameters provided by the instrument, only the average, superior, inferior, temporal and nasal values were analysed in the present study since most parameters are calculated from these values.

Results

Mean peripapillary RNFL values at the superior, inferior, temporal and nasal regions were 95.0 ± 15.6, 97.0 ± 16.3, 47.0 ± 9.0 and 43.9 ± 15.1 μm respectively (mean ± SD). Using regression analysis, we found a significant negative linear correlation (p = 0.001) between average RNFL value and age (Fig. 1), suggesting a decrease of about 1.9 μm per decade. There were also significant negative and gradual correlations with age in the superior ($p < 0.01$), inferior ($p < 0.01$), temporal ($p < 0.05$) and nasal values ($p < 0.01$) (Table 1). They all decreased to a similar extent (about 1.8 μm) per decade). No correlation with age was observed among the ratio

Table 1. *RNFL values by age groups in the population*

n	Age (years)	Average values	Superior values	Inferior values	Nasal values	Temporal values
16	14 ± 3	81 ± 8	102 ± 10	104 ±12	48 ± 10	45 ± 6
24	25 ± 2	85 ± 15	99 ± 17	99 ± 16	51 ± 11	48 ± 15
24	35 ± 3	80 ± 12	95 ± 16	97 ± 15	48 ± 9	44 ± 15
32	45 ± 3	83 ± 16	97 ± 19	102 ± 20	48 ± 9	44 ± 17
27	53 ± 3	77 ± 11	90 ± 14	95 ± 14	44 ± 7	41 ± 14
20	64 ± 3	77 ± 8	94 ± 13	95 ± 15	46 ± 7	45 ± 13
16	75 ± 3	72 ± 8	85 ± 10	83 ± 9	44 ± 6	40 ± 11
R		−0.27	−0.31	−0.28	−0.22	−0.12
p value		0.001	<0.001	<0.001	<0.001	0.04

Values are the mean ± SD. R, linear regression correlation betwen age and RNFL measurements.

Table 2. *Average relative ratios provided by the NFA by age groups*

n	Age (years)	S/N	I/N	S/T	I/T	Max	S/I
16	14 ± 3	2.2 ± 0.6	2.2 ± 0.4	2.3 ± 0.4	2.3 ± 0.4	1.6 ± 0.5	1.0 ± 0.1
24	25 ± 2	2.0 ± 0.3	2.0 ± 0.3	2.3 ± 0.7	2.2 ± 0.7	1.4 ± 0.6	1.0 ± 0.1
24	35 ± 3	2.0 ± 0.3	2.0 ± 0.5	2.4 ± 0.8	2.5 ± 0.8	1.7 ± 0.7	1.0 ± 0.1
32	45 ± 3	2.0 ± 0.2	2.0 ± 0.3	2.4 ± 0.6	2.5 ± 0.8	1.7 ± 0.6	1.0 ± 0.1
27	53 ± 3	2.0 ± 0.3	2.0 ± 0.4	2.4 ± 0.7	2.5 ± 0.8	1.7 ± 0.7	1.0 ± 0.1
20	64 ± 3	2.0 ± 0.3	2.0 ± 0.3	2.4 ± 0.6	2.5 ± 0.8	1.6 ± 0.6	1.0 ± 0.1
16	75 ± 3	2.0 ± 0.3	2.0 ± 0.2	2.3 ± 0.6	2.2 ± 0.6	1.5 ± 0.5	1.0 ± 0.1

S/N, I/N, S/T, I/T, Max. and S/I are the ratios of superior/nasal values, inferior/nasal values, superior/temporal values, inferior/temporal values, max. modulation and the ratio of superior/inferior values respectively in the population.
No significant correlation with age among relative ratios was observed ($p > 0.05$).
Values are the mean ± SD.

parameters such as superior/nasal, inferior/nasal, superior/temporal, inferior/temporal, superior/inferior, or max. modulation ($p > 0.05$) (Table 2).

Discussion

We determined the distribution of RNFL thickness as measured by NFA in the normal Hong Kong Chinese population, and its correlation with age. Consistent with previous studies[1–5] on other ethnic groups, the peripapillary RNFL topography in all our subjects exhibited a double-hump pattern: RNFL values were highest in the superior and inferior regions (two humps) and lowest in the temporal and nasal regions (two troughs). In this cross-sectional study we found a significant but gradual decrease in the average RNFL values with age. This decrease is consistent with previous reports and the amounts of thinning were also similar.[1,5] The observation is also consistent with histological studies indicating that about 4000 to 5000 retinal ganglion cell fibres are lost annually in the human as the result of ageing.[8,9] Even though pupil size becomes smaller in the elderly, the decrease in the RNFL values seems unlikely to be a result of this fact since such measurements have been shown not to be influenced by pupil size.[10] Linear regression in our local population showed that RNFL values decreased similarly in all four regions; thus ratio parameters such as the superior/nasal ratio, inferior/nasal ratio, superior/temporal ratio, inferior/temporal ratio, superior/inferior ratio and max. modulation were found to be constant across the age groups.

In contrast, Chi *et al.*[3] reported that only RNFL thickness in the nasal and inferior regions decreased with age in their 75 subjects (presumably Japanese volunteers). It was postulated that the observed decrease in these regions was mainly due to a loss of large-diameter fibres. However, a histological study by Mikelberg *et al.*[8] showed that with increasing age, mean axon diameter increases while total axon count decreases, inferring that small-diameter axons are preferentially lost with increasing age. Other studies found a weak but significantly negative correlation between the superior/nasal and inferior/nasal ratios with age in the white population,[1,4] but not in the black.[4] The reasons for these discrepancies with our results are unclear and they may be due to a difference in detection sensitivity between earlier and later scanner versions, or a true ethnic difference.

Older versions of the NFA (such as NFA I) did not have an absolute calibration. There was no method of minimising the influence of image intensity during measurement. Although newer versions such as NFA II and NFA GDx introduced a standardisable intensity adjustment which then allowed absolute polarimetric measurements, using relative ratios for analysis still appears to be advantageous over absolute readings in some important aspects. Relative ratios have been reported to score higher reproducibility than absolute values.[11] Since we take measurements in a peripapillary circle 1.75 disc-diameters away from the optic disc, the RNFL at this site is naturally thinner and their corresponding absolute retardation values, smaller. Nevertheless the ratio parameters appear to be fairly insensitive to this effect, which presumably means that this centrifugal decrease in measurement occurs evenly in all regions.[12] Finally, while the RNFL thicknesses were shown to decrease with increasing age in a similar fashion for all four regions in the present study, the relative ratios were insensitive to this change. Therefore, use of these ratio parameters to assist in identifying pathological states appears to be significantly more advantageous than absolute values from any region.

Since the repeatability for the nasal region measurement was reported to be high,[2] it has been used as a reference in the calculations of relative ratios.[2,4] More importantly, two of the relative ratio parameters (superior/nasal ratio and inferior/nasal ratio) have been shown to be sensitive discriminators of both glaucoma suspects[2,13] and glaucoma patients[13–15] from the normal population.

We have now obtained estimated normal RNFL values for the Hong Kong Chinese population as determined by scanning laser polarimetry. RNFL values of the Hong Kong Chinese population appear to decrease cross-sectionally with age. These normal values may serve as a reference during screening procedures for glaucoma.

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