Contact Lens and Anterior Eye 42 (2019) 575–580

Contents lists available at ScienceDirect

Contact Lens and Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Review article

The refractive index of the human cornea: A review

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ARTICLE INFO

Keywords:
Human cornea
Refractive index
Invasive and non-invasive measurements

ABSTRACT

The refractive index of the cornea and overlying tear film are key factors affecting refraction and overall optical properties of the eye. A figure of 1.376 is often quoted for the refractive index of the human cornea over the visible spectrum. In the 19th century estimates for the average refractive index of the human cornea ranged from 1.335 to 1.4391. Over the last two decades data obtained from either ex or in vivo corneas (under local anaesthesia with or without stromal resection) by contact Abbé refractometry show the refractive index of the cornea changes along its' depth undulating from around 1.400 at the epithelium to 1.380 at Bowman's layer, a low of 1.369 in the mid stroma and 1.373 at the endothelium. The mean refractive index of harvested tear samples is 1.337 rising to 1.482 for the overlying lipid layer. Contemporary measurements obtained in vivo by non-invasive methods reveal the average, or equivalent, refractive index of the tear film-cornea complex along the antero-posterior direction ranges from 1.423 to 1.436. Over the last 200 years calculations, with respect to the optics of the human eye, were based on values for the refractive index of the cornea obtained from invasive techniques. The refractive index of the cornea and overlying tear film appears to be higher than previously accepted and varies from case to case.

1. Introduction

The classical texts identified the cornea as the first refracting surface of the eye [1–3]. The ocular surface is the first and most powerful refractive interface encountered by light rays as they enter the eye. The refractive power of this surface is wholly dependent its' curvature and the change in refractive index between the external environment and the ocular surface. Knowledge of the refractive power of the cornea allows us to further understand the efficacy of any potential treatment designed to correcting refractive error. Thus, the refractive index of the cornea is a paramount feature in the theory and practice of correcting refractive errors by contact lenses, refractive and cataract surgery. There are many non-invasive contactless clinical devices designed to measure corneal surface radii, but none to measure the refractive index of the cornea. Any estimate of corneal refractive power is an assumption based on a perfunctory value for the refractive index of the cornea. The refractive index of a substance is defined as the velocity of a light wave in vacuum divided by the velocity of the light wave in the substance. The exact value for the refractive index depends on wavelength of the radiation and temperature of the medium. Hence, a single value for the refractive index of the cornea is limited. However, for ophthalmic purposes, a value for the refractive index of the cornea should be a figure that encapsulates the visible spectrum under typically encountered ambient conditions.

Tscherning [3] stated the refractive index of the cornea was 1.377 and Gullstrand [4] claimed it was 1.376. These are the most frequently quoted values for human corneal refractive index and widely used throughout the ophthalmic industry. A plethora of new methods for correcting refractive error, and streamlining the overall optical performance of the eye, have been advocated. Some of the newer techniques involve either modulating the refractive index of the normal corneal stroma [5–11] or artificially adjusting overall refractive index of the cornea by inserting implants based on gradient index optics [12]. Other than correcting refractive errors, gradient index systems can be exploited to increase the depth of field of the cornea and aid in presbyopia or affect the higher order optical aberrations of the eye and further improve the overall optical performance of the eye. These novel techniques, alongside the more established ones, depend on having precise knowledge of the refractive index of the cornea in its normal state.

All of this leads to the following series of questions:

Are there earlier estimates for the refractive index of the human cornea? Is it acceptable to employ a perfunctory figure to represent the refractive index of the normal human cornea?

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https://doi.org/10.1016/j.clae.2019.04.018
Received 13 December 2018; Received in revised form 14 April 2019; Accepted 30 April 2019

If not then, what is the typical variation in the refractive index of the normal human cornea?

How were values for the refractive index of the human cornea derived?

The aim of this review is to provide answers to these questions by reviewing the pertinent literature, available evidence, the methods employed for estimating the refractive index of the cornea and determine if the commonly accepted values for the refractive index of the human cornea are still applicable to modern vision science and eye care.

1.1. Historical quotes and methods used to estimate the refractive index of the human cornea

In 1818, Chossat [12] proposed the refractive index of the human cornea was 1.335 and a year later Brewster and Gordon [13] proclaimed the refractive index was 1.3379. In 1864 Donders [1] wrote: ***'For the cornea and aqueous humour we have therefore to assume only one refracting surface of nearly 8 mm radius of curvature, and with a refracting proportion of 1.3366 found by Sir David Brewster for the aqueous humour'.*** Unfortunately, Donders did not provide a specific reference to verify where Brewster, without Gordon, published this figure. Helmholtz [2] claimed that in 1855 Krause [14] found the average refractive index of the cornea to be 1.3507, ranging from 1.3431 to 1.3569. In contrast to this, in a text edited by Norris and Oliver, Baker [15] claimed that the average refractive index was 1.3523 according to Krause not 1.3507. Krause's handbook [14] features two sets of refractive index values for the human cornea. It seems that Baker was quoting from Krause's first set of data while Helmholtz was quoting from the second. Krause took measurements from a single set of 20 eyes. His technique for estimating the refractive index of the cornea required a value for the refractive index of distilled water. For each cornea, Krause calculated two sets of refractive index values using different values for the refractive index of distilled water. The data from Krause's handbook are reproduced here in Table 1. Subjecting Krause's data to statistical analysis reveals no significant difference between the two sets (two tailed paired t-test, $p = 0.2418$). In addition, Krause [14] also tabulated corneal refractive index data obtained by Engel. The mean refractive index of the cornea was considerably higher compared with other estimates. Based on twenty-one samples, reproduced in this paper in Table 2, the mean refractive index according to Engel was 1.4391 (sd = ± 0.0445 range 1.3369–1.5234). Krause did not provide any reference where Engel published these data or how these were obtained. The exact source of Engel's data remains obscure. Baker [15] also provided corneal refractive index values of 1.3754, 1.377 and 1.3825 according to Matthiessen [16], Aubert and Macalister [17] respectively. Incidentally, Baker did not provide a reference regarding the Aubert's value. The value attributed to Aubert was probably taken from a work published twelve years earlier in 1876 [18]. The same text, edited by Norris and Oliver, features a chapter by Jackson [19] in which he wrote *'…corneal tissue having an index of refraction of* 1.3365'. Valk [20] wrote *'We find that the refractive index of the dioptric media will vary, as it will be different in the cornea, aqueous, lens and vitreous body, according to physiological density'.* Therefore, it is reasonable to assume the refractive index of the cornea will be greater compared with the refractive index of the aqueous humour. Following on from this, nineteen years later, Taylor and Baxter [21] assumed the refractive index of the cornea was 1.367 in their calculations on the dioptric powers of the corneal surface. Spooner [22] claimed that one year earlier, in 1907, Freytag proposed the refractive index of the cornea was 1.370. Unfortunately, there is no clear evidence of this in Freytag's original text [23]. Thirty-seven years after Valk's proclamation, Ball [24] asserted that the refractive index of the cornea was 1.337. There is a dichotomy whereby some advocated the refractive index of the cornea was greater than the refractive index of the aqueous and others insisted the two indices were the same.

Table 1
Krause's values for the refractive index of human corneas [14].

Eye №	Corneal refractive index value I (distilled water refractive index accepted as 1.33424)	Corneal refractive index value II (distilled water refractive index accepted as 1.3358)
1	1.3489	1.3473
2	1.3447	1.3431
3	1.3447	1.3431
4	1.3539	1.3523
5	1.3586	1.3569
6	1.3586	1.3569
7	1.3586	1.3569
8	1.3586	1.3569
9	1.3489	1.3473
10	1.3586	1.3569
11	1.3447	1.3431
12	1.3495	1.3479
13	1.3519	1.3502
14	1.3539	1.3523
15	1.3489	1.3473
16	1.3586	1.3569
17	1.3489	1.3473
18	1.3447	1.3431
19	1.3519	1.3502
20	1.3586	1.3569
Mean ± sd	***1.3525 ± 0.0055***	***1.3508 ± 0.0054***

Table 2
The corneal refractive index values attributed to Engel by Krause [14].

Eye №	Corneal refractive index value
1	1.337
2	1.3369
3	1.4532
4	1.4652
5	1.4694
6	1.4356
7	1.4564
8	1.4663
9	1.434
10	1.4462
11	1.4217
12	1.4208
13	1.4217
14	1.4162
15	1.4285
16	1.4207
17	1.5063
18	1.5234
19	1.4627
20	1.4769
21	1.4216
Mean ± sd	***1.4391 ± 0.3246***

Brewster and Gordon [13] used a hollow acute prism with parallel sided glass plates to estimate the refractive index of the cornea. In principle, the same method was employed by Chossat [12]. The hollow prism was filled with macerated corneal tissue. An incident beam of light struck one surface of the prism at 90°, the beam of light exiting the adjacent side of the prism was traced and the angle of exit was measured. The corneal tissue was removed and replaced with water, or another suitable liquid medium, and the procedure was repeated. The RI was calculated using the simple formula:

$$n_1 = n_2 (\sin\alpha / \sin\beta)$$

Where n_1 = refractive index of cornea, n_2 = refractive index of water (or other medium), α = the exit angle when the prism was filled with macerated corneal tissue, β = the exit angle when the prism was filled with water (or other medium).

Krause [14] used a technique based on Brewster and Gordon's method and extended his investigation to include other ocular media such as the aqueous, vitreous humour and crystalline lens. Helmholtz [2] modified the method chosen by Krause when he also determined the refractive indices of ocular tissues. In Helmholtz case, the material in question was sandwiched between a parallel sided glass plate and the concave surface of a plano-concave lens. The focal length of this lens complex was measured. The material was replaced with water, or other suitable liquid medium, and the procedure was repeated. The refractive index was calculated using the simple formula:

$$n_1 = n_2[(1\text{-}r/l_2)/(1\text{-}r/l_1))]$$

Where n_1 = refractive index of the material, n_2 = refractive index of distilled water, l_1 = focal length of the lens complex using the material, l_2 = focal length of the lens complex using distilled water.

The measurement of the refractive index of both liquids and solids was revolutionised after Abbé introduced his technique in 1869. The Abbé refractometer, based on the critical angle method, is the most convenient way of directly measuring refractive index [25]. Thereafter, the Abbé contact refractometer became the instrument of choice for measuring the refractive index of the cornea. According to Helmholtz [4], Aubert and Matthiessen claimed the refractive index of the cornea was 1.372 in 2-day old child and 1.377 in a 50-year old adult. Incidentally, these figures appear in Aubert's handbook [18] and the average, 1.375, nearly matches the figure of 1.3754 attributed to Matthiessen in 1879 by Baker [15]. Gullstrand [4] wrote that in 1891 Matthiessen went on to claim the refractive index was 1.3763. In 1957 Maurice [26] declared the refractive index was 1.375. These uni-index values imply that, under normal circumstances, the cornea is a homogeneous optical medium. Maurice [26] reported the refractive index of the hydrated collagen fibres in the corneal stroma was higher than the refractive index of the background tissue fluid. Duke-Elder and Wybar [27] wrote, ***'Since all the constituents of the stroma have approximately the same refractive index, it is almost impossible to differentiate any structure in a fresh specimen'.*** Therefore, under normal circumstances, the corneal stroma could be averaged as an optically homogeneous uni-index structure. The various layers of the cornea, along the antero-posterior direction, are clearly distinguishable using a simple slit lamp biomicroscope. If the cornea was optically homogeneous then the various structures that make up the corneas would remain invisible. This simple empirical observation informs us that the living cornea is not a simple optically homogeneous medium. The axiom that the whole cornea, under normal circumstances, is optically homogeneous cannot be supported. The various layers of the cornea can only be observed, in the natural living state, when there is a change in refractive index between adjacent regions. Therefore, intracorneal variations of refractive index must occur.

1.2. Variations of refractive index within the human cornea

An optically clear, colourless, object becomes indistinguishable from its' surrounds when immersed in a colourless medium of the same refractive index. Thus, it is possible to estimate the refractive index of corneal epithelial cells by dipping them in a range of colourless liquids of differing refractive index. Tagawa [28] used this procedure on ex vivo samples and estimated the refractive index of corneal epithelial cells lay between 1.40 − 1.47. Fischer [29] measured the proportion of incident light that was reflected from the surface of the eye and calculated the refractive index using the Fresnel formula:

$$Y = [(n1\text{-}n2)/(n1 + n2)]^2$$

Where, Y = proportion of light reflected, n1 = refractive index of the ocular surface, n2 = refractive index of surrounding medium (air).

This was probably the first attempt to measure the refractive index of ocular tissue in vivo. The figures he published for, what he believed was, the refractive index of the corneal epithelium ranged from 1.410 to 1.416. Clearly, these values were much higher compared with the values quoted in the literature for the whole cornea. Fischer did measure the refractive index of the first reflecting surface of the eye. The surface being the desiccated remains of the precorneal tear film not the corneal epithelium. More recently, using a modified Abbé refractometer Patel et al. [30] reported the refractive index of the corneal epithelium in vivo was 1.401 (sd ± 0.005) and Vasudevan et al. [31] stated the refractive index ranged from 1.394 to 1.397 over the surface of the human corneal epithelium. These were the first independently administered studies where the refractive index of corneal tissue was measured in vivo by Abbé refractometry. All previous studies were based on measurements obtained from ex vivo material. According to Berstein [32], the refractive index of corneal endothelial cells fell in the range 1.370 − 1.380. The evidence in hand indicates that the refractive index of the corneal epithelium is greater in comparison with the rest of the cornea.

The refractive index of a chemical mixture can be predicted from the refractive indices of the various constituents and their relative concentrations. The various rules for making these predictions are outside the scope of this review, but sufficiently covered in several general texts (for example Batsanov [33]). The rules according to Biot and Arago [34], Gladstone and Dale [35] are useful starting points to estimate the relationship between the refractive index and hydration of the corneal stroma. Maurice [20], Fatt and Harris [36], Laing et al. [37] and Worthington [38] derived various theoretical models that lead to a common conclusion: expect stromal refractive index to increase as hydration falls and vice versa. The empirical evidence supports this hypothesis when tested, ex vivo, on bovine corneas [39]. Therefore, it is presumed the same occurs in the human cornea in vivo. These theoretical models assumed that the corneal stroma is akin to a homogeneous medium. The histology and structure of the mammalian stroma alters along the antero-posterior direction [40–46]. These variations cause the anterior corneal stroma to be drier and more resistant to changes in water content compared with the posterior corneal stroma [47–50]. Thus, the refractive index should be relatively higher at the anterior section of the stroma. This was confirmed in the human corneal stroma where the refractive indices at the anterior stromal and posterior endothelial surfaces were 1.380 (sd ± 0.005) and 1.373 (sd ± 0.001) respectively [30]. These values were obtained using ex vivo human corneas and a subjective Abbé refractometer. In vivo, using an objective automated hand-held refractometer, the reported mean refractive index values for Bowman's layer were 1.380 (sd ± 0.011) [51] and 1.384 (sd ± 0.004) [52]. And, for the stroma the reported mean values ranged from 1.369 (sd ± 0.007) [51] to 1.377 (sd ± 0.002) [52]. The difference between these mean values for the stroma are probably related to measurements being obtained from different regions along the depth of the stroma [52]. The higher value resulting from measurements taken from regions closer to Bowman's layer. Furthermore, the refractive index of the mid stroma is directly related to age [53]. It would appear, from the front to the back of the average human cornea, the refractive index falls from about 1.400 (epithelium) to 1.380 (Bowman's layer) further reducing to 1.369 (mid stroma) then rising to 1.373 (endothelial surface). This is an approximate view that depends heavily on the distribution of water throughout the cornea. This view totally ignores the tear film. Could the tear film affect the refractive index of the cornea?

1.3. Precorneal tear film and the average, or equivalent, refractive index of tear film-cornea complex

The first refractive interface encountered by light rays is the precorneal tear film. The classical scholars viewed the tear film as a concentric homogeneous medium less than 0.10 mm where the refractive index was about 1.336. The tear film was dismissed as inconsequential in relation to refraction. In 1903 Reiss [54] proposed using refractometry to estimate the concentration of proteins in solutions. This was explored by Barer and Joseph [55] and the protein content, of abnormal tears in allergic conjunctivitis, was estimated by Stegman and Miller [56] using a hand-held refractometer. Craig et al. [57] found the refractive index of tears collected from the lower fornix was directly linked to the concentration of lactoferrin. The mean refractive index of their tear samples was 1.337 (sd ± 0.001) confirming earlier findings [58,59]. The normal tear film has an overall thickness of 3-10μ [60,61], a superficial lipid layer of about 0.1μ thickness overlying an aqueous layer where the concentration of macromolecules probably increases from the underside of the lipid layer towards the corneal epithelium [62]. Therefore, the refractive index of the aqueous layer should gradually increase from the underside of the lipid layer towards the cornea. The average refractive index of the meibomian oil, the bulk of the tear lipid layer, is 1.482 at ocular surface temperature [63]. The refractive index of most proteins lies between 1.53–1.60 [55]. However, there are no reliable estimates for the possible variation in the refractive index of the tear film sandwiched between the underside of the lipid layer and the corneal epithelium. Furthermore, the refractive index in this layer is likely to change as the tear film evaporates between blinks. In short, the precorneal tear film has a superficial layer about 0.1μ in thickness and refractive index of about 1.482 covering a layer up to 9.9μ thick where the average refractive index is about 1.337. Clearly, the precorneal tear film has a non-uniform refractive index that falls and rises gradually along the antero-posterior direction towards the cornea. It can be shown, using the thick lens formula, when the tear film is concentric with a constant thickness over the central pupillary zone of the cornea, the effect on refraction is approximately 0.06DS. The classical scholars were right to dismiss the tear film as inconsequential. However, should the thickness distribution develop an orthogonal characteristic during the interblink interval then, the tear film would affect the total astigmatism of the eye. The thick lens formula predicts, the total astigmatism of the eye is expected to shift by 1.00DC when the difference between the orthogonal surface radii of the precorneal tear film changes by 0.2 mm. It is reasonable to accept that this would influence refractive error and contribute to uncertainty during subjective refraction.

2. Discussion

Fig. 1, approximates the change in average refractive index from the surface of the tear film to the endothelium of the cornea. This is a synthesis of information obtained by invasive techniques. An uni-index model for the refractive index of the tear film-cornea complex has the potential to elevate the precision of contact lens therapy, cataract and refractive surgery. Glancing at Fig. 1 gives the impression the average refractive index of this tear film-cornea complex is about 1.390 – 1.400. Clearly, this exceeds the commonly accepted value of 1.376–1.377 for the refractive index of the cornea. Corneal refractive procedures rely on changing ocular surface power. The clinical assessment of a change in ocular surface radius is indicative of the effectiveness of any such procedure. A change in radius from 7.00 mm to 8.00 mm implies a change in ocular surface power of -6.71DS for a refractive index of 1.376. However, changing the refractive index to 1.400 alters the predicted change in surface power to -7.71DS. Should the actual change in refraction alter by just under 8.00DS then, accepting a constant refractive index value of 1.376, would leave the clinician wondering: Why did the refraction change by more than the anticipated amount? A higher refractive index for the tear film-cornea complex is the likely cause of the difference between the expected and actual.

The shift in refractive index from one layer to the next indicates that variations in curvature between adjacent layers also have the potential to affect overall refraction and optical performance of the eye. In other words, each layer is a potential lenticule. Orthokeratology is a safe procedure [64,65] rising in popularity [66] mainly for the correction of myopia. Besides flattening the central cornea to correct myopia, the technique results in central thinning of the corneal epithelium and paracentral thickening of the corneal stroma [67]. These thickness changes are expected to increase the overall negative dioptral power of both layers, and further contribute to myopia correction.

It would be useful to verify the average refractive index of the tear film-cornea complex in vivo by non-invasive methods with minimal disruption. This has been achieved by a modification of the normally accepted procedure of slit lamp based optical pachymetry. The reported average, or equivalent, refractive index of the human tear film-cornea

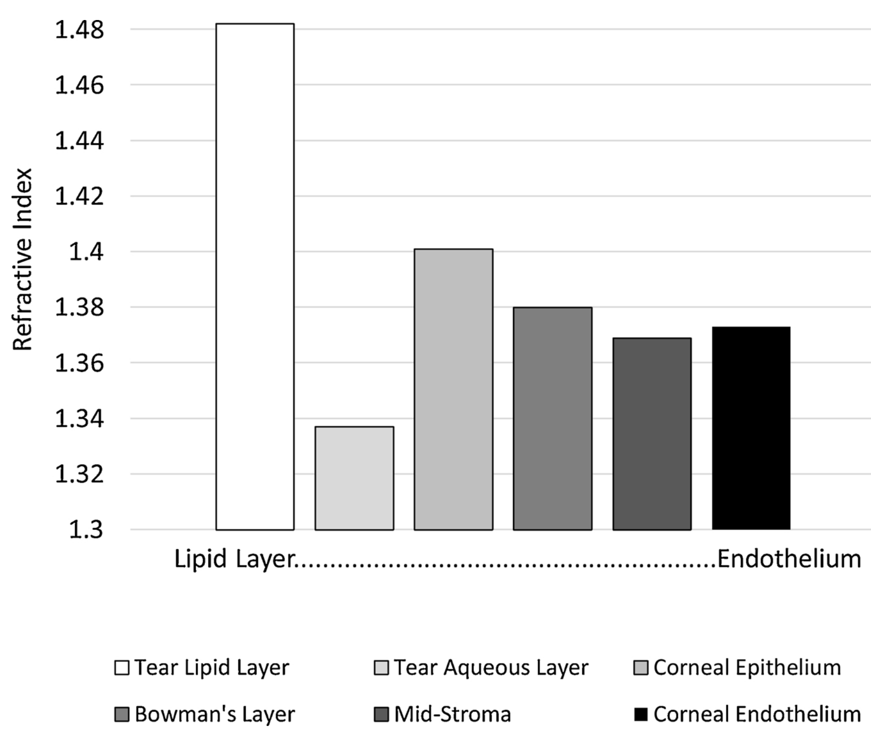

Fig. 1. This shows the change in the average refractive index, along the antero-posterior direction, from the surface of the precorneal tear film to the corneal endothelium.

Table 3
A chronological summary of key published values for the refractive index of the human cornea.

Author	Year	Corneal refractive index value
Chossat	1818	1.335
Brewster & Gordon	1819	1.3379
Krause	1855	1.3507, range 1.3431–1.3569
Engel [I]	1855	1.4391, range 1.3369–1.5234
Aubert [II]	1876	1.377
Aubert & Matthiessen [III]	1876	1.372, two-day old child 1.377, fifty-year old adult
Matthiessen	1879	1.3754
Macalister	1889	1.3825
Matthiessen [IV]	1891	1.3763
Baker [V]	1897	1.3523
Tscherning	1904	1.377
Freytag [VI]	1907	1.370
Taylor & Baxter	1908	1.367
Gullstrand	1911	1.376
Ball	1926	1.337
Tagawa	1926	1.40–1.47, corneal epithelial cells
Maurice	1957	1.375
Berstein [VII]	1984	1.37–1.38, corneal endothelial cells
Patel et al	1995	1.401 (± 0.05), corneal epithelium 1.380(± 0.005), anterior stroma 1.373(± 0.001), posterior stroma
Vasudevan et al	2008	1.394–1.397, corneal epithelium
Patel et al	2008	1.380(± 0.011), Bowman's layer 1.369(± 0.007), mid-stroma
Tutchenko et al	2018	1.432 (range 1.423–1.436) tear film-cornea complex

complex is 1.432, range 1.423–1.436 [68]. The only estimate in the literature that comes close to this is the value of 1.4391 attributed to Engel by Krause [14]. Table 3 summarises the corneal refractive index values reviewed in this paper. The values range from 1.335 to 1.4391 in the 19th century, 1.367–1.380 in the 20th century to the most recent value of 1.432. A more precise value for the refractive index of the cornea is required to refine the accuracy of any prediction relating to the dioptrics of the eye in single cases. For example, the standard Gullstrand model eye [11] predicts the dioptric power of the eye alters by −0.96D when the average value of the refractive index over the depth of the cornea increases from 1.376 to 1.432. In contrast, the Tscherning model eye [3] predicts the dioptric power shift is −1.95D for such a rise in corneal refractive index. Unforeseen refractive errors after contact lens therapy, corneal or cataract surgery could be, in part, explained by disparities of corneal refractive index. Having knowledge of the average corneal refractive index in an individual case and using this to refine the outcome of either corneal or cataract surgery carries the potential to enhance the accuracy of the post-operative refractive outcome and nullify the incidence of refractive surprises.

3. Concluding remarks

The earliest investigators proposed the refractive index of the cornea was nearly identical to the refractive index of water. This view was dismissed with the introduction of the Abbé refractometer. Thereafter, the pioneers gave the impression the refractive index of the cornea was near identical from one person to the next. Helmholtz [2], Tscherning [3] and Gullstrand [11] and others considered the refractive index of the cornea to be a constant. There are approximately 7.3 billion people in the world. Refractive errors, the shape radius and thickness of the cornea, appearance of the iris and pattern of vessels of the retina vary from person to person. It is illogical to accept the refractive index of the cornea remains the same in all 7.3 billion people.

Measurements of corneal refractive index obtained in vivo, by both invasive and non-invasive techniques, have provided us with three facts:

1) The refractive index depends on the region of the cornea where the measurement is being made.

2) The average, or equivalent, refractive index of a cornea is higher than previously envisioned.

3) Significant inter-subject variations in the average, or equivalent, refractive index of the cornea can occur.

The interest in orthokeratology is rising [66] yet there is still a tendency towards a shortfall between a change in anterior corneal surface apical power and actual change in refractive error [64,67]. The shortfall can be explained by the average refractive index of the cornea being higher than previously accepted. A non-invasive, safe, rapid, clinical technique that reliably estimates the refractive index of the cornea in vivo (over the entire depth or individual layers) would improve our understanding of the optical effects of any of the myriad of corneal refractive treatments available today.

Conflict of interest

None of the authors have any financial or conflicting interests to disclose.

Method of literature search

A search was conducted at the British Library, Glasgow Caledonian University Library, on MEDLINE search and Google for relevant publications from the start of the 19th century to the current point in time. Published texts and sources where values for the refractive index of the human cornea were stated were reviewed. Literature stating values that were original, and not readily available elsewhere, are referenced in this paper.

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