Distribution of the Crystalline Lens Power In Vivo as a Function of Age

JONGENELEN, Sien, et al.

Abstract
To observe the age-related changes in crystalline lens power in vivo in a noncataractous European population.

Reference

DOI : 10.1167/iovs.15-18047
PMID : 26523387

Available at:
http://archive-ouverte.unige.ch/unige:90467

Disclaimer: layout of this document may differ from the published version.
Distribution of the Crystalline Lens Power In Vivo as a Function of Age

Sien Jongenelen,1 Jos J. Rozema,1,2 and Marie-José Tassignon1; on behalf of the EVICR.net and Project Gullstrand Study Group

1Department of Ophthalmology, University Hospital Antwerp, Edegem, Belgium
2Faculty of Medicine and Health Sciences, University of Antwerp, Wilrijk, Belgium

Purpose. To observe the age-related changes in crystalline lens power in vivo in a noncataractous European population.

Methods. Data were obtained through Project Gullstrand, a multicenter population study with data from healthy phakic subjects between 20 and 85 years old. One randomly selected eye per subject was used. Lens power was calculated using the modified Bennett-Rabbetts method, using biometry data from an autorefractometer, Oculus Pentacam, and Haag-Streit Lenstar.

Results. The study included 1069 Caucasian subjects (490 men, 579 women) with a mean age of 44.2 ± 14.2 years and mean lens power of 24.96 ± 2.18 dioptries (D). The average lens power showed a statistically significant decrease as a function of age, with a steeper rate of decrease after the age of 55. The highest crystalline lens power was found in emmetropic eyes and eyes with a short axial length. The correlation of lens power with different refractive components was statistically significant for axial length ($r = -0.523$, $P < 0.01$) and anterior chamber depth ($r = -0.161$, $P < 0.01$), but not for spherical equivalent and corneal power ($P > 0.05$).

Conclusions. This in vivo study showed a monotonous decrease in crystalline lens power with age, with a steeper decline after 55 years. While this finding fundamentally concurs with previous in vivo studies, it is at odds with studies performed on donor eyes that reported lens power increases after the age of 55.

Keywords: crystalline lens power, age
a few epidemiological studies available on this topic. In vitro studies show a linear decrease of the isolated lens power with age,22-24 after which some authors report a linear age-related increase after the age of 50 to 60.5,7

The purpose of this study was to verify whether this particular relationship between crystalline refractive power and age may also be observed in vivo by studying the age-related changes in crystalline lens power for a European population, and to examine its relationship with sex and other biometric parameters.

**Materials and Methods**

**Subjects**

Subjects were recruited through Project Gullstrand, a European multicenter study with the goal to determine the average biometric values of human eyes. In total, nine centers in six European countries gathered biometry data of healthy, phakic Caucasian subjects between January 2011 and July 2013. Exclusion criteria for the study were subjects younger than 20 years, a refraction outside the interval 6D, a self-reported age of more than 5 months. The study adhered to the principles of the Declaration of Helsinki and received approval from the ethics committee of the Antwerp University Hospital (Ref. B30020072406) and all other participating sites. Signed informed consent was obtained from each volunteer prior to participation.

In total, 1069 individuals (490 males, 579 females) were included, with a mean age of 44.2 ± 14.2 years (range, 20–85 years). No cycloplegia was used to remain as close to the everyday physiological condition of the eye as possible. This may have introduced a small refractive shift, especially in the subjects below the age of 50.26

**Measurements and Calculations**

The objective refraction was measured with an autorefractometer (varies per center), while the anterior chamber depth (ACD) and corneal shape parameters were collected with a Scheimpflug camera (Pentacam, Oculis Optikgeräte, Wetzlar, Germany; Galilei, Ziemer Ophthalmic Systems, Port, Switzerland; Sirius, CSO, Scandicci, Italy). Finally the axial length was determined with a partial coherence biometer (IOL Master, Carl Zeiss, Jena, Germany or Lenstar, Haag-Streit, Koeniz, Switzerland). At this time the presence of nuclear lens opacification was also checked using the Scheimpflug images. Note that since the biometry was determined with various devices, special statistical considerations are needed to account for between-center differences.27

**Table 1.** Descriptive Statistics of Each Parameter by Sex and in Total

<table>
<thead>
<tr>
<th>Variable</th>
<th>Males, N = 490</th>
<th>Females, N = 579</th>
<th>Total, N = 1069</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE, D</td>
<td>0.93 ± 2.24</td>
<td>0.75 ± 2.09</td>
<td>0.84 ± 2.16</td>
</tr>
<tr>
<td>Skewness</td>
<td>-0.686</td>
<td>-0.814</td>
<td>-0.76</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>1.174</td>
<td>2.438</td>
<td>1.78</td>
</tr>
<tr>
<td>K, D</td>
<td>41.95 ± 1.37</td>
<td>42.34 ± 1.40</td>
<td>42.16 ± 1.40</td>
</tr>
<tr>
<td>ACD, mm</td>
<td>3.49 ± 0.39</td>
<td>3.37 ± 0.38</td>
<td>3.43 ± 0.39</td>
</tr>
<tr>
<td>L, mm</td>
<td>24.12 ± 1.10</td>
<td>23.55 ± 1.05</td>
<td>23.81 ± 1.11</td>
</tr>
<tr>
<td>P L, D</td>
<td>24.23 ± 2.10</td>
<td>25.57 ± 2.06</td>
<td>24.96 ± 2.18</td>
</tr>
</tbody>
</table>

**Table 2.** Distribution of Biometric Parameters by Age for the Entire Group (Average ± Standard Deviation)

<table>
<thead>
<tr>
<th>Age, y</th>
<th>N</th>
<th>SE, D</th>
<th>L, mm</th>
<th>PL, D</th>
<th>ΔPL, D</th>
<th>Homogeneous Subsets, SNK</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>81</td>
<td>1.66 ± 1.87</td>
<td>23.92 ± 1.08</td>
<td>26.17 ± 2.10</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>25–30</td>
<td>133</td>
<td>1.49 ± 1.96</td>
<td>23.97 ± 1.08</td>
<td>25.88 ± 1.98</td>
<td>−0.29</td>
<td>1</td>
</tr>
<tr>
<td>30–35</td>
<td>148</td>
<td>1.37 ± 2.28</td>
<td>23.89 ± 1.19</td>
<td>25.76 ± 2.07</td>
<td>−0.12</td>
<td>1</td>
</tr>
<tr>
<td>35–40</td>
<td>110</td>
<td>1.08 ± 2.05</td>
<td>23.93 ± 1.07</td>
<td>25.39 ± 1.84</td>
<td>−0.37</td>
<td>2</td>
</tr>
<tr>
<td>40–45</td>
<td>97</td>
<td>1.84 ± 2.22</td>
<td>23.90 ± 1.24</td>
<td>25.06 ± 2.17</td>
<td>−0.33</td>
<td>2</td>
</tr>
<tr>
<td>45–50</td>
<td>117</td>
<td>0.81 ± 1.82</td>
<td>23.70 ± 0.95</td>
<td>25.17 ± 1.89</td>
<td>0.11</td>
<td>2</td>
</tr>
<tr>
<td>50–55</td>
<td>107</td>
<td>0.79 ± 2.15</td>
<td>23.83 ± 1.21</td>
<td>24.65 ± 1.68</td>
<td>−0.52</td>
<td>3</td>
</tr>
<tr>
<td>55–60</td>
<td>85</td>
<td>0.33 ± 2.04</td>
<td>23.47 ± 1.08</td>
<td>23.98 ± 2.10</td>
<td>−0.67</td>
<td>4</td>
</tr>
<tr>
<td>60–65</td>
<td>108</td>
<td>0.16 ± 2.11</td>
<td>23.68 ± 1.07</td>
<td>23.64 ± 1.93</td>
<td>−0.34</td>
<td>4</td>
</tr>
<tr>
<td>65–70</td>
<td>46</td>
<td>0.26 ± 1.95</td>
<td>23.62 ± 0.90</td>
<td>23.29 ± 2.02</td>
<td>−0.35</td>
<td>4</td>
</tr>
<tr>
<td>&gt;70</td>
<td>37</td>
<td>0.07 ± 2.58</td>
<td>23.95 ± 1.11</td>
<td>22.51 ± 1.68</td>
<td>−0.78</td>
<td>5</td>
</tr>
</tbody>
</table>

ΔPL, difference with previous age category.
SNK, Student-Newman-Keuls post hoc test.
As lens thickness was not available for all subjects, lens power PL was calculated using the modified Bennett-Rabbetts equation \(^{16}\):

\[
P_L = \frac{L (S_{CV} + K_{tot}) - 1000 \cdot n}{(L - ACD_c - c)(\frac{ACD}{1000} S_{CV} + K_{tot}) - 1}
\]

with \(L\) the axial length, \(S_{CV} = SE/(1 - 0.014 \cdot SE)\) the spherical equivalent refraction at the corneal vertex, \(c = 3.504\) mm the average distance between thin lens position and anterior lens surface, and \(n = 1.356\) the refractive index of aqueous and vitreous humors. \(^{16}\)

We implemented Mann's correction (Manns F IOVS 2014;55:ARVO E-Abstract 5785) to account for the influence of the posterior cornea on the lens power calculation by using the total corneal power \(K_{tot} = K_{ma} + K_{ap} - K_{ma} \cdot K_{ap} \cdot CCT/\pi_c\). Here \(K_{ma}\) and \(K_{ap}\) are the mean anterior and posterior keratometry, respectively; \(CCT\) is the central pachymetry; and \(n_c = 1.376\) the corneal refractive index. This also requires defining the \(ACD\) as the distance between the second principal plane of the cornea and the anterior lens plane, which is calculated by \(ACD = ACD - (CCT \cdot K_{ap})/(1000 \cdot n_c \cdot K_{ma})\).

Although data from both eyes were collected, only one randomly selected eye was used per subject to avoid the influence of high intrapatient correlations of biometric factors.

### Statistical Analysis

This work used biometric data from various sites, which means that minor differences in average age, sex balance, and equipment are to be expected. As this could influence the results, intraclass correlations (ICC) were used to estimate the importance of the between-site differences. If necessary, suitable adjustments could be made.

Each parameter was described by sex and binned per 5 years of age. Student’s \(t\)-test was used to compare the biometric parameters by sex. The lens power for each age category was compared through an ANOVA, followed by post hoc testing to assess the progress of lens power with age. Similarly, the influence of axial length and refraction was determined as well. Correlations of the parameters with biometry were analyzed by Pearson correlation coefficients. A univariate general linear model was applied to the data, and a simple main effects analysis evaluated the interaction between age and sex further. Significance levels of 0.05 were used throughout the analysis. The data were analyzed using SPSS version 21.0 for Windows (IBM Corp., Armonk, NY, USA).

### Results

#### Between-Site Effects

We used mixed effects models to calculate the ICC for \(P_L\), \(L\), \(ACD\), \(K\), and \(SE\) after correction for age and sex differences to estimate systematic between-site effects. These ICC coefficients were found to remain very small (between 0.006 and 0.065), making adjustments for between-site effects unnecessary.

#### Descriptive Statistics

Table 1 gives the descriptive statistics for the total population of 1069 Caucasians from six different countries, split up by sex. The mean spherical equivalent refractive power was \(-0.84 \pm 2.16\) D, while the mean refractive power of the lens and cornea were \(24.96 \pm 2.18\) and \(42.16 \pm 1.40\) D, respectively. The distribution of the lens power had a broad, Gaussian shape (Fig. 1). Significant differences between male and female eyes were found for corneal power (unpaired \(t\)-test, \(P < 0.001\)), \(ACD\) (\(P < 0.001\)), axial length (\(P < 0.001\)), and lens power (\(P < 0.001\)), but not for refraction (\(P = 0.183\)). Women had shorter eyes, shallower anterior chambers, higher corneal power, and a higher lens power than men.

*Figure 1.* The distribution of refractive lens power for the entire cohort (age range, 20–85 years).

*Figure 2.* The distribution of refractive lens power per age category. Error bars represent the 95% confidence interval of the standard error.
Influence of Age

There was a negative correlation between lens power and age (Pearson r = −0.457, P < 0.01). Binned per 5 years of age, lens power undergoes a near-monotonous decrease (Table 2; Fig. 2), which was found to be significant (ANOVA, P < 0.001). A post hoc Student-Newman-Keuls analysis demonstrated that lens power was more similar for younger age categories, while for older age categories these were less similar (last columns in Table 2). This is indicative of a higher rate of lens power decrease for older ages, which contradicts the in vitro reports.

Correlation With Sex and Biometry

The correlation of lens power with biometry was significant for axial length (Pearson r = −0.523, P < 0.01) and ACD (r = −0.161, P < 0.01), meaning that an increase in lens power is correlated with a decrease in axial length or ACD. Spherical equivalent (P = 0.450) and corneal power (P = 0.058) were not significantly correlated with refractive lens power.

The correlation between refraction and lens power was investigated further by dividing refraction into 2-D bins (Table 3). Subsequent ANOVAs showed a significant difference between refraction groups (P < 0.001), with emmetropic eyes having significantly higher lens powers than either high myopes or hypermetropes (Tamhane’s T2 post hoc test). No significant differences were seen between high myopes (SE < −5 D) and hypermetropes (SE > +1 D; Tamhane T2; P > 0.99). This is also seen in Figure 3A, where lens power seems to follow an arc shape as a function of refraction.

Repeating the same analysis by dividing eyes into 1-mm bins according to axial length demonstrated a significant decrease in lens power with increasing axial length (ANOVA, P < 0.001; Fig. 3B, Table 4).

There was also a small but significant interaction between age and sex for lens power (two-way ANOVA, P = 0.012), which accounted for 27.6% of the lens power variation. This interaction was analyzed further using a main effects analysis, which showed that sex influenced lens power significantly in almost every age category except 60 to 65 (F = 1.086, P = 0.298) and >70 (F = 2.740, P = 0.098). A plot of the estimated marginal means of lens power by sex showed nearly parallel lines (Fig. 4), indicating that the changes in lens power occur equally in both sexes.

Discussion

These results suggest that the in vivo crystalline lens power calculated with the modified Bennett-Rabbets method follows a biphasic course, with a flat linear decrease at young ages and a faster decrease after the age of 55. This course is in contrast with the literature, where Glasser and Campbell,5 as well as Borja et al.,7 reported an increase in lens power after the age of 50 to 60.5,7 Jones et al.,23 and Atchison et al.28 found a monotonous linear decrease, and Olsen et al29 reported no correlation between lens power and age between 55 and 100 years of age. Finally, Iribarren et al.30 even reported a very mild increase and subsequent decrease in lens power in Iranian subjects between 40 and 64 years of age. From this overview of the literature we find that, although most of these articles confirm that lens power changes with age and that the rate of this change somehow alters between the age of 50 and 60, in vitro and in vivo studies seem to disagree on the exact course of this altered rate of change (Fig. 5).

The source of this disagreement between studies may lie in the methodology used. In three studies the experiments were performed on postmortem donor material, in which the lenses entered a state of maximal accommodation as they were removed from zonular tension. This can be counteracted by placing the lens in a stretching apparatus, as was done by Glasser and Campbell,5 and Borja et al.7 Jones et al.,23 on the other hand, did not stretch their lenses, and consequently reported lens power values that were considerably higher (Fig. 5). While in either case the age-related decrease in isolated lens power was found to match the in vivo decrease in accommodative amplitude quite well,7,23 the lens powers and the rates of power change with age reported by the in vitro studies are considerably higher than those of the in vivo studies. This may indicate that even when placed in a stretching apparatus, the optical properties of the lens still differ from the physiological suspension inside the eye.

There are also methodological differences between the four in vivo studies, most prominently in the methods used to determine lens power and cycloplegia of the subjects. Olsen et al.29 used a variation of the Olsen IOL formula31 on data from noncyclopleged Icelandic subjects between 55 and 100 years old,29 while Atchison et al.28 performed phakometry on noncyclopleged subjects. Iribarren et al.30 applied the Bennett formula to data of middle-aged Iranian subjects after
The mean refractive lens power stratified by age category and sex.

cycloplegia, and finally the Bennett-Rabbetts formula applied to noncycloplegic Caucasian subjects aged between 20 and 85 years was used in this study. Given the advanced age of the Olsen et al. subjects and the cycloplegia of the Iribarren et al. data, the influence of accommodation can be excluded from these two data sets. The lack of cycloplegia in the current study may have caused some of our subjects below the age of 50 to accommodate during measurement, which would increase lens power in the younger age categories, thus steepening the lens power decrease on the left-hand side of Figure 2. The influence of this effect can be estimated by referring to a recent article by Morgan et al.,26 who found that in subjects aged 20 to 50 years the mean difference between cycloplegic and noncycloplegic refraction can be up to 0.20 to 0.25 D for myopes and emmetropes, and up to 0.50 to 0.65 D for hypermetropes. This corresponds with lens power increases of 0.37 and 0.95 D for myopes/emmetropes and hypermetropes, respectively. Therefore the lens power decrease we found before the age of 50 may have been exaggerated by this amount, although the actual amount is likely to be smaller, as not all subjects will accommodate and the proportion of hypermetropes was less than 20% in the present cohort.

The lens power formulas used in the in vivo studies are unlikely to be a great source of disagreement either, as the Bennett and the Bennett-Rabbetts formulas have been shown to agree well with each other.16 Another issue is the use of the total corneal power (i.e., including the contribution of the posterior corneal surface) rather than the use of the anterior cornea alone. This procedure was first suggested by Manns (Manns F IOVS 2014;55:ARVO E-Abstract 3785), and can be obtained by either adjusting the keratometric refractive index (e.g., to \( n = 1.3515 \)) or by combining both the anterior and posterior surface powers into a total power value. This procedure caused our mean lens power value to be approximately 1 D higher in comparison to the literature.

<table>
<thead>
<tr>
<th>( L, ) mm</th>
<th>(&lt; 22)</th>
<th>(22 &lt; z &lt; 23)</th>
<th>(23 &lt; z &lt; 24)</th>
<th>(24 &lt; z &lt; 25)</th>
<th>(25 &lt; z &lt; 26)</th>
<th>(&gt; 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N )</td>
<td>34</td>
<td>209</td>
<td>401</td>
<td>276</td>
<td>108</td>
<td>41</td>
</tr>
<tr>
<td>( P_L, ) D*</td>
<td>( 27.30 \pm 2.63 )</td>
<td>( 26.47 \pm 2.00 )</td>
<td>( 25.16 \pm 1.87 )</td>
<td>( 24.25 \pm 1.72 )</td>
<td>( 23.08 \pm 1.76 )</td>
<td>( 22.94 \pm 1.66 )</td>
</tr>
</tbody>
</table>

* Mean \( \pm \) SD.

Although the processes behind the gradual decrease in lens power with age are well known,17 it remains unclear why the rate of the lens power decrease seems to change between the ages of 50 to 60 years. Glasser and Campbell5 and Borja et al.7 attributed the increase they found to the presence of cataract in some of their investigated lenses, which is known to cause myopic shifts.32 Similarly, Olsen et al.29 mentioned that the cataract in some of their subjects may have influenced their lens power values. Finally, in Atchison et al.,28 Iribarren et al.,30 and the current study, all subjects with cataractous lenses were excluded, which could be why these studies showed a power decrease after the age of 60.

Note that the studies above are all cross-sectional rather than longitudinal, which implies that the results may have been influenced by gradual changes within the cohorts used. Examples of such effects are the increase in lens power before the age of 50 seen in Iranian adults,30 which was attributed to differences in height, with younger people being taller than older people, or the increasing prevalence of myopia in young subjects, which will undoubtedly influence lens power as well.

According to some studies, refractive error in adults is not significantly associated with crystalline lens power,30,33 while others reported a negative correlation, with higher lens powers in myopes.15,29 This is in contrast to the positive correlation found in children’s eyes, with hypermetropes having higher refractive lens powers than emmetropes or myopes,34,35 while the current study suggests that emmetropic eyes have significantly higher lens powers than in high myopes or hypermetropes. The positive correlation between lens power and spherical refraction in myopes also

Figure 4. Changes in lens power with age reported in the literature by Glasser and Campbell5 (19 eyes, stretched in vitro using ray tracing), Jones et al.25 (20 eyes, unstretched in vitro using magnetic resonance imaging), Borja et al.7 (51 eyes, stretched in vitro using lens meter), Olsen et al.29 (325 eyes, in vivo using Olsen method and non-cyclopleged refraction), Atchison et al.28 (66 eyes, in vivo using phakometry and noncyclopleged refraction), Iribarren et al.30 (1926 eyes, in vivo using Bennett method and cyclopleged refraction), and the current study (1069 eyes, in vivo using Bennett-Rabbetts method and noncyclopleged refraction).

Table 4. Distribution of Lens Power by Axial Length (\( L \))

Figure 5. The mean refractive lens power stratified by age category and sex.
matches the known association between lower lens power and increasing axial length. A myopic eye is usually longer, thus requiring a weaker lens to emmetropize, while a hypermetropic eye is typically shorter, requiring a stronger lens. At a certain age the correlation between spherical refraction and lens refractive power changes from positive to negative, which Iribarren explained through spherical refraction and lens refractive power changes from stronger lens. At a certain age the correlation between while a hypermetropic eye is typically shorter, requiring a usually longer, thus requiring a weaker lens to emmetropize, hypermetropes with a higher lens power. This new balance could reverse the correlation between lens power and refraction, and would explain why in the present study lens power is lower in the hypermetropic group in comparison with the emmetropic group. Still, our study shows higher lens powers in emmetropic subjects than in myopic subjects, similar to the correlation found in childhood. This could be explained by the fact that cataractous lenses were not included in this study, which would have increased lens power in older age due to a cataract-induced myopic shift. Through exclusion of cataractous lenses, the myopic subpopulation consisted largely of myopes since childhood, thus having a lower lens power. This is in contrast with the Reykjavik Eye Study and the CIEMS study, where lens power calculations were based on adults over the age of 50 and where cataractous lenses were not excluded.

In order to shed some light on these issues, we recommend that future population-based studies follow a longitudinal setup to further explore the balance between refraction, lens power, and ocular biometry.

**Acknowledgments**

Project Gullstrand, of which this work is a part, is supported by a grant from the Flemish government agency for Innovation by Science and Technology (IWT 110684).

Disclosure: S. Jongeneelen, None; J.J. Rozema, None; M.-J. Tassignon, None

**References**


**APPENDIX**

**Project Gullstrand Study Group**

Study sponsor: EVICR.net—European Vision Institute Clinical Research Network, AIBILI, Azinhaga de Santa Comba, Celas, 3000-548 Coimbra, Portugal

Coordinating investigator: Jos J. Rozema

Coordinating center: EVICR.net

Data collection by EVICR.net clinical sites (CS):

- CS 02—Mainz (Germany): Katrin Lorenz, Mascha von Trentini
- CS 07—Alicante (Spain): Espranza Sala Pomares, Maria José García Corral, Laurent Bataille, Jorge L. Alió
- CS 12—Antwerp (Belgium): Jos J. Rozema, Sien Jongene-len, Irene Ruiz-Hidalgo, Nadia Zakaria, Sorcha Ni Dhubhghaill, Carina Koppen, Marie-José Tassignon
- CS 27—Leipzig (Germany): Franziska Georgia Rauscher, Maria Teresa Blüs, Jens Dawczynski, Peter Wiedemann
- CS 36—Rome (Italy): Luigi Mosca, Laura Guccione, Monica Riso, Maria Emanuela Toro, Alessandra Rosati
- CS 38—Barcelona (Spain): Francesco Duch, Raimon Escude, Alexia Martinez, Antonio Morilla-Grasa
- CS 51—Valencia (Spain): Cristina Peris-Martinez, Amparo Diez Ajenjo, Carmen Garcia Domene
- CS 51—Girona (Spain): Maria Bozal De Febrer, Teresa Torrent Solans, Alicia Verdugo Gazdik
- CS 60—Tel Aviv (Israel): David Varssano, Barbara Gold
- CS 63—Chieti (Italy): Lisa Toto, Alessandra Mastropasqua, Leonardo Mastropasqua
- CS 67—Milan (Italy): Francesco Fasce, Alessandra Spine-lly, Karl Knutsson, Giovanni Fogliato