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Clínica Universitária de Oftalmologia

# Characteristics of the pupil and its role in vision: a revision and study

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# Abstract (EN)


CONTEXT: the pupil has become increasingly important in Ophthalmology since the advent of refractive and pseudophakic surgery. Its pre-operative evaluation and comparation to standard values is therefore important since it can condition post-operative results.

OBJECTIVES: a literature review of the schematic eye models and the role of the pupil in them, as well as of the pupil's characteristics and difficulties in measuring them. A retrospective study of the pupil parameters was then done. Pupil diameter and decentration in right eyes were analysed and characterised, as well as their relation to each other and to eye side, white-to-white distance and anterior chamber depth in a population from Hospital da Luz, Lisbon. Results were compared to the available literature.

METHODS: a population of 1013 patients (763 right and 844 left eyes) that were to be submitted to cataract surgical treatment was measured with Lenstar LS 900 (Haag-Streit) in photopic conditions. The device was operated according to the manufacturer's indications.

RESULTS: mean pupil diameter (PD) was 4.109 ± 0.532mm, difference between right and left eyes was significant ($p$=0.005). ACD and WTW were not correlated with PD (*Pearson coefficient* of 0.06 and 0.087). Mean horizontal pupil decentration (PCX) was 0.259 ± 0.165mm, Vertical (PCY) was -0.010 ± 0.153mm and Absolute decentration was 0.312 ± 0.144. PCX and Absolute decentration were significantly correlated to PD (*Pearson coefficient* of 0.183 and 0.174, respectively, and $p$<0.001).

CONCLUSION: even though pupil is still not contemplated in most eye models, it is important on vision quality. Results show generically similar values to reference, with some differences and limitations. Standard pupillometry conditions should be proposed, and the possibility of inter-populational variation of parameters should be tested.


**Key Words:** pupillometry; schematic eye models; pupil centre; pupil diameter.

# Resumo (PT)


CONTEXTUALIZAÇÃO: a pupila tem ganho importância na Oftalmologia desde a introdução da cirurgia refrativa e pseudofáquica. A sua avaliação pré-operatória é importante, uma vez que esta estrutura pode condicionar os resultados pós cirúrgicos.

OBJETIVOS: fazer uma revisão da literatura acerca dos modelos esquemáticos do olho e o papel da pupila nestes, bem como das características da mesma e as dificuldades na sua medição. Será depois analisada e caracterizada a sua biometria (diâmetro e descentramento), a relação entre si e com o lado da órbita, diâmetro do limbus (WTW) e profundidade da câmara anterior (ACD) na população do Hospital da Luz Lisboa. Os resultados foram comparados com a literatura.

RESULTADOS: o diâmetro pupilar (PD) médio foi de 4.109 ± 0.532mm, e a diferença entre olhos direitos e esquerdos foi significativa ($p$=0.005). ACD e WTW não estavam correlacionados com o PD (*Pearson coefficient* de 0.06 e 0.087). O descentramento pupilar horizontal (PCX) era de 0.259 ± 0.165mm, o vertical (PCY) de -0.010 ± 0.153mm, e o descentramento absoluto de 0.312 ± 0.144. O PCX e o descentramento absoluto correlacionavam-se com o PD (*Pearson coefficient* de 0.183 e de 0.174, respectivamente, e $p$<0.001).

CONCLUSÃO: apesar de a pupila não ser contemplada na maioria dos modelos esquemáticos revistos, tem um papel significativo na qualidade de visão. Os resultados mostram valores genericamente similares à literatura, com algumas diferenças e limitações. Condições estandardizadas para pupilometria deviam ser propostas, e a possibilidade da existência de variabilidade inter-populacional dos parâmetros deveria ser testada.



**Palavras-chave:** modelos esquemáticos do olho; pupilometria; descentramento pupilar; diâmetro da pupila;

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# 1. Introduction

The pupil has become increasingly important in Ophthalmology. It has long been studied its impact on post-operative quality of vision in refractive and phakic surgery, but researchers still find dissonant results in what concerns to pupil biometrics. As so, the aim of this study is to do a bibliographic review of both schematic eye models (in which optometry is based) and the role of the pupil on them, as well as the pupil's characteristics and its impact on vision.

A populational study will then be made using databases from a device used in Hospital da Luz Lisboa, to characterize pupil biometry in that population and posteriorly compare and discuss those results with the currently available references.

# 2. The study of the eye and vision

Vision has always been a subject of interest for humans. Since the times of ancient Greece, with Democritus and Galenus being the most notable ones, to the Arabic scholars and Renaissance Europe through the work of Descartes, or more recently Snell's law and Gauss' paraxial theories, studies were conducted and theories were formulated to explain such phenomenon and its properties. (Atchison & Thibos, 2016; Smith, 1995) From the description of the detailed eye anatomy to the explanation of the optical system, step by step and aided by many instruments, the human knowledge of vision has increased to an extent where one can fully understand its functioning.

In order to summarise and organise our ever-growing understanding of the eye as an optical system and to study particular properties of human optics and retinal image formation, various authors have dedicated their work to the development of schematic eye models. (Atchison & Smith, 2000) Their purposes are numerous, ranging from the study of retinal image sizing and light levels, to refractive errors, aberrations and retinal image quality, design of spectacles, lenses and individual customization, or even development and calibration of optical instruments (Atchison & Thibos, 2016). To account for different populations and to allow customization, some can even be stratified by age, gender, ethnicity, refractive errors and accommodation. (Atchison & Thibos, 2016) As much as each model is different, the same applies to their intended purposes and focus.

The first schematic eye model dates back to the $19^{th}$ century, but previous attempts had already been made. (Atchison & Smith, 2000; Smith, 1995) Since then, many others were formulated, each pretending to address particular questions. As complex as they may be, they can essentially be grouped into two types: Paraxial models and Finite models.

## 2.1 Paraxial Models

Paraxial models are simpler ones. They mechanistically summarise what we know about the optics of the eye (Atchison & Thibos, 2016), while describing refractive surfaces as spherical and centred on a common optical axis. Refractive indices are constant within each medium. (Smith, 1995) These models are only accurate within the paraxial region and are not capable of predicting aberrations and retinal image formation for large pupils or angles that are far from the optical axis. Since structures are centred and refractive surfaces are spheric while the lens is generally of constant refractive index, paraxial models are poor predictors of monocular aberrations such as spherical aberration and sagittal/tangential power errors, and lack on prediction of light distribution with larger field angles (Smith, 1995). Nonetheless they are sufficient for calculating entrance and exit pupil positions and diameters, retinal image sizes and effects of refractive errors. For that reason, they are commonly used as a learning tool for the theory of visual optics. (Atchison & Thibos, 2016).

At last, Paraxial models may be further divided into three groups as follows, according to the number of refractive surfaces each offers. (Atchison & Smith, 2000; Atchison & Thibos, 2016; Esteve-Taboada et al., 2018)

### 2.1.1. Exact paraxial models

Exact models try to represent the most accurately they can the optical structure and so they must include at least 4 refractive surfaces: two for the cornea and for the crystalline lens, each. Some of the models included in that group are the following:

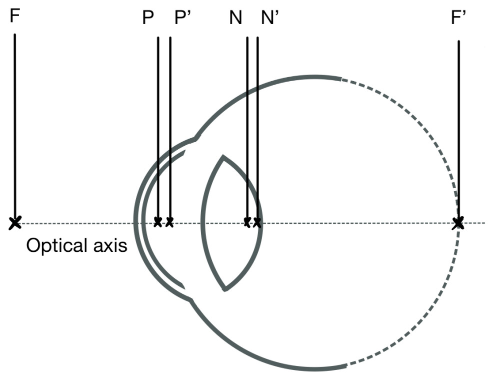



Figure 1 - Representation of an Exact Paraxial eye model and its cardinal points, with a dual surface cornea and lens. (Image not to scale)

- Tscherning (1900) – allegedly the first model to include a posterior corneal surface; (Smith, 1995)

- Gullstrand's number 1 eye (1909) – was built with 6 refractive surfaces, of which the lens is composed by 4, divided in a higher refractive power nucleus and a lower power cortex - a gradient index lens. It also features adaptation to 2 levels of accommodation, being one of the few paraxial models that have this particularity. Despite that, Gullstrand's model presents an exaggerated spherical aberration, much higher than that of real eyes; (Smith, 1995)

- Le Grand's Full theoretical eye (1945) – a modification of Tscherning's, it is presented in both relaxed and accommodated forms; (Smith, 1995)

- Blaker's eye (1980) – modified from Gullstrand's number 1 eye, it is the only paraxial model to feature a continuous gradient index for the lens. It is also called an adaptive model since parameters such as the lens gradient index, lens surface curvature, thickness and the anterior chamber depth vary as linear functions of accommodation. It was posteriorly revised to include the effects of age.

### 2.1.2. Simplified paraxial models

Simplified models have a total of 3 refractive surfaces – one for the cornea and two for the lens. For paraxial calculations, these models are now considered to be more adequate than many exact eyes which are often more complex than required. Some of them are:

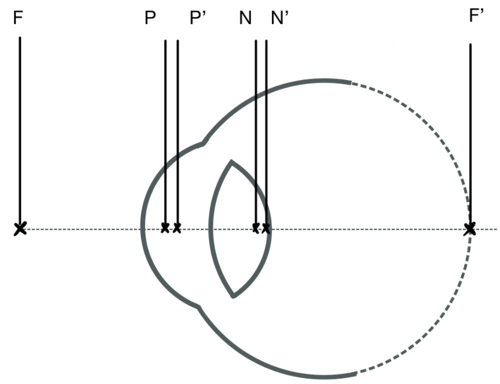



Figure 2 - Representation of a Simplified Paraxial eye model. Simplified paraxial models feature a single surface cornea and a dual surface lens. (Image not to scale)

- Gullstrand's number 2 eye (1909) – while close to its Exact counterpart, its lens, even though two-surfaced, has zero thickness which limits its usefulness; (Smith, 1995)

- Le Grand's simplified eye (1945) – similar to Gullstrand's number 2 eye in terms of features; (Smith, 1995)

- Gullstrand-Emsley eye (1952) – modified from Gullstrand's number 2 eye to simplify calculations, including the same lens thickness as in Gullstrand's number 1 eye, with changed aqueous', vitreous' and lens' refractive indices. This model offers 2 accommodation levels as does Gullstrand's number 2 eye but the lens' refractive index is constant; (Smith, 1995)

- Bennett & Rabbetts' simplified eye – a modification from the Gullstrand-Emsley eye in its relaxed form with different parameter values obtained through data from a larger study, with a mean power closer to 60 D. It also included four levels of accommodation , an "elderly" version of the eye, and a refractive error of 1 D hypermetropia; (Smith, 1995)

### 2.1.3. Reduced paraxial models

Reduced eyes have a single refractive surface – the cornea - along with shorter axial length and corneal radius of curvature. In these models, principal points (P and P') and nodal points (N and N') coincide since there is only one refractive surface. As a consequence of the absence of a crystalline lens, they cannot be used to study the optical consequences of accommodation nor the changes in lens properties on refractive error including aphakia and pseudophakia (Smith, 1995). Some examples are Emsley's and Bennett & Rabbetts' reduced eyes. (Smith, 1995)

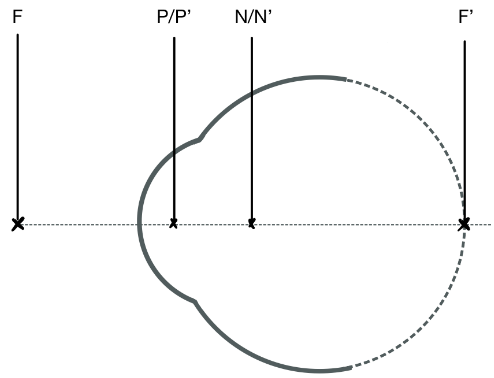



Figure 3 - Representation of a Reduced Paraxial eye model. Notice the single refractive surface that is the cornea. (Image not to scale)

## 2.2 Finite Models

Finite models are more complex than Paraxial models and their primary interest is a reliable representation of the eye's functional capabilities instead of its constitution (Esteve-Taboada et al., 2018) – the reason why some models are actually incorrect from an anatomical point of view, or even oversimplify important features of the eye. They may be represented as a physical device used to test and calibrate equipment, or a mathematical equation that provides analytical descriptions of the eye's behaviour, or even a computer program intended to describe the eye's optical aberrations. Their aim is to represent optical aberrations and retinal quality as closely as possible as they occur *in vivo*. In order to do so authors make use of aspherised surfaces (e.g. conicoids and ellipsoids), curved retinas (which is not a part of Paraxial models, albeit regularly

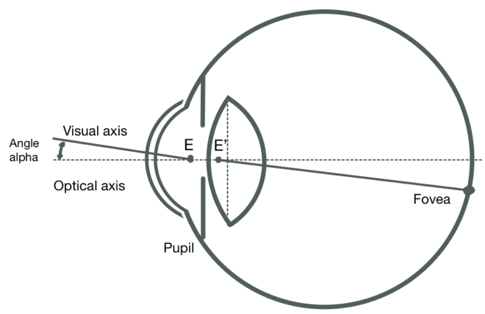



Figure 4 - Representation based on Liou & Brennan's Finite eye model. This model features pupil decentration in a nasal direction, as well as non-coincident visual and optical axis. *E* represents the entrance pupil level, and *E'* represents the exit pupil level. (Image not to scale)

illustrated), decentration of surfaces/the aperture stop, or even gradient index lenses, whether through shell structures or continuous gradient (Esteve-Taboada et al., 2018; Smith, 1995).

Practical applications of such models are various including the calculation of retinal image sizes, magnification, retinal illumination, entrance and exit pupil positions and sizes, especially for objects imaged with wide pupils or away from the optical axis. Thus, they are frequently used in everyday clinical optometry. Finite eye models can be used for a range of research and development purposes including spectacle lens design, simulation of on-eye contact lens performance, predicting the outcomes of ortho-keratology procedures, refractive surgery or IOL implantation and studying the features of optical component systems. (Bakaraju et al., 2008) Some of those models are:

- Lotmar (1971) – modified from Le Grand's full theoretical eye with anterior corneal aspherization and a paraboloid posterior crystalline surface. (Lotmar, 1971) However, it was shown that an ellipsoid shape for the anterior corneal surface would be a better fit, and the model is based on an anatomically inaccurate shape of the anterior lens surface. A constant 8mm centred pupil of zero thickness was considered in the construction of this model.

- Drasdo and Fowler (1974) – based on a schematic eye attributed by Stine to Cowan, the purpose of this model was to determine the retinal projection of the visual field using spherical lens surfaces since data supported the insignificance of such alteration. No mention to the pupil was found in the paper. (Drasdo & Fowler, 1974)

- Kooijman (1983) – based on Le Grand's full theoretical eye it intends to predict retinal illumination. Corneal surfaces are aspherical, and the anterior lens surface is hyperbolic, while the posterior surface is parabolic. This model has two versions with retinal shape variations: spherical and elliptical. The author used this model to study the influence of pupil size on retinal light distribution homogeneity, concluding that it is minimal. (Kooijman, 1983)

- Liou and Brennan (1997) – This model includes conicoid corneal and lenticular surfaces and a parabolic gradient index lens and was based on anatomical values of eyes around 45-years-old. Its primary purpose was to model the spherical aberration of real eyes, while also intending to mimic normal levels of chromatic aberration – which was not well-succeeded. Additionally, it features a displacement of the aperture stop 0.5mm to the nasal side and an angle between the line of sight and the optical axis (angle alpha) of 5 degrees regarding real eyes. (Liou & Brennan, 1997)

- Navarro & Escudero-Sanz (1999) – based on Le Grand's full theoretical eye with slightly modified anterior corneal radius and corneal index, it is a variable accommodating model in which the lens parameters and anterior chamber depth are expressed as functions of accommodation in a logarithmic manner. Anterior corneal and lenticular surfaces are conicoids while the retina is spherical. The entrance pupil (image of the pupil seen from the object space) is located 3.04mm from the anterior corneal surface, while the exit pupil (image of the pupil seen from the image space) is located 3.92mm from the posterior lenticular surface. It's diameter is adaptable even though it's not decentred, and good results were obtained using medium-large pupil sizes. (Escudero-Sanz & Navarro, 1999)

- Atchison (2006) – Based on Liou and Brennan's, two models were proposed: one with centred surfaces, and another one accounting for the displacement of the retina from the visual axis. The most distinctive features are the inclusion of a gradient index lens, a thoric retina and its variation with refractive errors (in particular, myopia). The pupil lies on the same plane as the lens' vertex, centred on the visual axis, and a diameter of 6mm was used to calculate aberrations. (Atchison, 2006; Bakaraju et al., 2008)

Liou & Brennan's and Atchison's models are the ones who show the most similarities to in-vivo eyes. (Bakaraju et al., 2008) Lotmar's, Kooijman's and Navarro & Escudero-Sanz' attempts were as accurate as Liou & Brennan's and Atchison's at mimicking the performance of real eyes reasonably well for on-axis and small pupil diameters. For large pupil diameters, however, they were more inaccurate. Opposingly, Liou & Brennan and Atchison created schematic eyes that presented close to *in vivo* experimental values among spherical and higher order aberrations, even eccentrically, and to peripheral refraction profiles for larger pupil diameters. Their corneal and lens spherical aberration and coma were similar but opposite in sign, which results in a good real eye representation. (Smith et al., 2008) Of the two models, Liou & Brennan's was considered the most reliable both anatomically and practically, even without considering the characteristic pupil nasal decentration. (Bakaraju et al., 2008; De Almeida & Carvalho, 2007) If lens tilt is taken into account, as well as retinal tilt and decentration, then Atchison's model has a peripheral refraction profile that doesn't well match real eye data. Eccentric variation of coma-like aberration was, however, much higher than expected in every model as was retinal image quality probably due to the lack of scattering among the optical media. (Bakaraju et al., 2008)

Even though some schematic eyes can accurately represent the real eye to a considerable extent, it is notable that the vast majority of presented schematic models (both paraxial and finite) doesn't contemplate the existence nor the importance of the pupil, a structure which has been shown to have an impact on quality of vision under several circumstances. Even when they do, limited comprehension of its functioning is offered. As a result, those models have limited applicability on modern ophthalmology including refractive and IOL implantation surgery, where quality of vision is becoming increasingly important by the day. New models should, therefore, be developed that included pupillometry data to better suit those needs.

## 3. The pupil and its role in vision

The pupil is an important structure in optical dynamics. It can have a substantial impact on quality of vision and on aberration levels depending on its size and position (Bakaraju et al., 2008; Salati et al., 2007). It is defined as the aperture stop formed by the iris, composed by the sphincter pupillae and dilator pupillae. The pupil has an elliptic shape (Aguirre, 2019) and is situated about 3.05mm behind the anterior surface of the cornea.

The pupil is frequently represented by its image as seen from the object space – the entrance pupil -, and may also be represented as seen from the image space – the exit pupil. (Aguirre, 2019; Atchison & Smith, 2000) Its elliptic shape varies depending on the position of the viewer – the wider the viewing angle, the more elliptic the entrance pupil is. (Aguirre, 2019) It is important to note that the entrance and exit pupils are not the same as the real pupil: due to corneal magnification of its image (Aguirre, 2019), the entrance pupil is 13% larger than the real pupil, while the exit pupil is 9% larger due to refraction in the ocular media. (Atchison & Smith, 2000) As a consequence, the term “pupil” in clinical practice generally refers to the entrance pupil since it is the actual measured parameter in pupillometry.

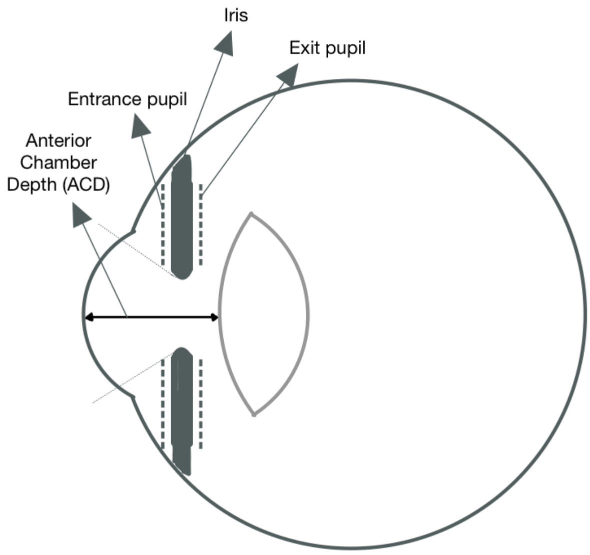



Figure 5 – Representation of the iris and the entrance and exit pupils. (Image not to scale)

The most important pupil parameters to be considered are diameter and decentration. (Atchison & Smith, 2000)

### 3.1 Pupil Diameter

Pupil size is under autonomic control, responding to a variety of factors: illumination (the predominant one), accommodation, psychological factors such as fear, joy and surprise, and drugs. (Atchison & Smith, 2000; Kelbsch et al., 2019) Age also has an impact on pupil size and on reactiveness through the *Senile myosis* phenomenon (Atchison & Smith, 2000), with a relatively predictable decrease per decade of about 0.28mm under mesopic and 0.15mm under photopic conditions (Fernández et al., 2020b).

IOL Implantation following phacoemulsification surgery is also associated with a statistically significant reduction in pupil size of about 10%, with variations among studies between 9-16mm. (Fernández et al., 2018, 2020a, 2020b; A. J. Kanellopoulos et al., 2015) Evidence suggests that this might be due to two factors: the increased anterior chamber depth and volume after replacement of the thicker crystalline by a slimmer IOL, allowing the iris muscles to move more freely; or the enhanced clarity and transparency of the implanted IOL compared to the cataract, which results in some degree of myosis. (A. J. Kanellopoulos et al., 2015)

Some studies tried to establish a correlation between Pupil diameter (PD) and other biometric parameters. Horizontal White-to-White distance (WTW) and Anterior Chamber Depth (ACD) were two of them. (Cakmak et al., 2012) WTW is the diameter of the cornea, and has interesting applications in cataract surgery since it can be used to select the most suitable anterior chamber lens or calculate the lens power, for instance. (Hashemi et al., 2015) ACD, on its turn, is the distance that goes from the anterior surface of the cornea to the anterior surface of the lens. It is a helpful parameter in the preoperative evaluation that serves as an indicator of the postoperative axial position of the implanted IOL, or the effective lens position (ELP). Considering ACD into the calculation of the IOL power is probably an effective method to reduce postoperative errors. (Ning et al., 2019) WTW and ACD were suggested to be moderately correlated to PD ($R=0.236$, $p=0.039$ and $R=0.513$, $p<0.001$, respectively) (Cakmak et al., 2012).

Pupil size is important in vision and has a number of effects which shouldn't be disregarded on depth-of-field, retinal illumination, retinal image quality, and on visual performance. (Atchison & Smith, 2000; A. J. Kanellopoulos et al., 2015; Salati et al., 2007) As a result, it might influence the results of cataract surgery in terms of visual acuity and quality of vision and should be considered.

Diameter is believed to range from 2mm under photopic conditions to 8mm under scotopic ones (Alberto & Romão, 2003; Atchison & Smith, 2000; Watson & Yellott, 2012), but even then, some other researchers present different values for a generic estimation:

>6 mm for scotopic pupil, 4-6 mm for mesopic, 3-4 mm for photopic. (Liu et al., 2019) It is easy to understand that since many factors play a role in pupil diameter, it is difficult to establish an accurate or absolute value for it. For instance, different studies present different results depending on the conditions in which measurement took place (especially illumination and monocularity/binocularity) (Fonseca et al., 2019), characteristics of the studied populations (i.e. age), and the device chosen. Since variables are not constant across literature it becomes difficult to compare studies and results. A summary of some references is presented on *Table 1*.

Nonetheless, some authors were able to develop formulas which intended to express pupil size as a function of luminance, taking into account field diameter as well as age and monocularity/binocularity. (Watson & Yellott, 2012) Such formulas present a good estimation of the mean pupil size, but even their authors warn for interindividual variability and other factors such as mental activity, accommodation, contrast, attention, and many others that can influence actual diameter.

| Reference | No of enrolled eyes/patients | Age Mean ± SD (Min-Max) | Device | Illuminance | Light conditions | PD (mm) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Mean | SD |
| (Koch et al., 1991) | 121 eyes | (20-70) | White light photography | 0 ft-c | . | 4.90 | 0.8 |
| | 132 eyes | | | 20 ft-c | . | 3.30 | 0.7 |
| | 131 eyes | | | 80 ft-c | . | 2.70 | 0.5 |
| | 132 eyes | | | 320 ft-c | . | 2.60 | 0.5 |
| | 131 eyes | | | 1000 ft-c | . | 2.20 | 0.3 |
| (Colvard, 1998) | 200 eyes | 28 (18-50) | Colvard | 3 lux | "scotopic" | 6.20 | . |
| (Boxer Wachler & Krueger, 1999) | 14 eyes | (28-42) | Rosenbaum card | 0.42 lux | . | 5.40 | 1.1 |
| | | | | 25.55 lux | . | 4.40 | 1 |
| | | | | 344.33 lux | . | 3.50 | 0.6 |
| | | | Iowa pupillometer | 0.42 lux | . | 4.95 | 1.08 |
| | | | | 25.55 lux | . | 4.09 | 1.16 |
| | | | | 344.33 lux | . | 3.22 | 0.41 |
| (Atchison & Smith, 2000) | . | 10 | . | . | scotopic | 7.60 | . |
| | | | | | photopic | 4.80 | . |
| | | 45 | . | . | scotopic | 6.20 | . |
| | | | | | photopic | 4.00 | . |
| | | 80 | . | . | scotopic | 5.20 | . |
| | | | | | photopic | 3.40 | . |
| (Schnitzler et al., 2000) | 66 eyes | 36 ± 9 (19-55) | Colvard | 0.5-0.6 lux | "scotopic" | 6.08 | 1.16 |
| | | | VIVA pupillometer | 0.5-0.6 lux | "scotopic" | 6.24 | 1.28 |
| (Boxer Wachler & Krueger, 2000) | 14 eyes | (28-42) | C-Scan | 25.55 lux | high mesopic | 3.35 | 0.54 |
| | | | Masterview | 344.33 lux | photopic | 2.96 | 0.22 |
| | | | Eyemap | 33.99 lux | high mesopic | 2.33 | 0.21 |
| | | | IR photography | 0.05 lux | low mesopic | 5.94 | 0.81 |
| (Rosen et al., 2002) | 58 patients | 46 ± 11.7 | Procyon P2000 SA | 0.02 lux | scotopic | 6.61 | . |
| | | | | 0.15 lux | low mesopic | 4.84 | . |
| | | | | 10.6 lux | high mesopic | 3.30 | . |
| (Schmitz et al., 2003) | 56 eyes | 23 ± 3 | Colvard | - | "darkness" | 0.61 | . |
| | | | Procyon P2000 SA | - | "darkness" | 6.56 | . |
| | | | Wasca | - | "darkness" | 6.30 | . |
| (Kohnen et al., 2003) | 100 eyes | 38.8 ± 10.7 (20-59) | Procyon P2000 SA | 0.07 lux | low mesopic | 5.90 | 0.97 |
| | | | Colvard | 0.28 lux | low mesopic | 5.78 | 0.98 |
| (Brown et al., 2004) | 40 eyes | 31.6 ± 7.3 (20-49) | IR photography | 1 lux | low mesopic | 7.00 | 0.75 |
| (Kohnen et al., 2004) | 100 eyes | 36.8 ± 10.28 (19-60) | Procyon P2000 SA | 0.07 lux | scotopic | 6.10 | 0.86 |
| | | | | 0.88 lux | mesopic | 4.73 | 0.92 |
| | | | Colvard | <0.05 lux | scotopic | 5.68 | 1.07 |
| | | | Zywave (target off) | 0.27 lux | | 5.91 | 1.01 |
| | | | Zywave (target on) | 0.44 lux | | 5.09 | 1.14 |
| | | | Wasca | 0.51 lux | | 5.59 | 0.99 |
| | | | Orbscan II | 480/28.2 | | 3.75 | 0.67 |
| (Netto et al., 2004) | 192 eyes | 36 ± 11 (22-61) | Procyon P2000 SA | - | scotopic | 6.54 | 0.88 |
| | | | | 0.4 lux | low mesopic | 5.62 | 0.95 |
| | | | | 4 lux | mesopic | 4.09 | 0.76 |
| (Twa et al., 2004) | 45 eyes | 36 ± 11 (22-61) | IR photography | <0.63 lux | "dark" | 6.24 | 1.03 |
| | | | | 5 lux | mesopic | 5.99 | 1.11 |
| | | | | 1000 lux | photopic | 2.72 | 0.42 |
| | | | IR video | <0.63 lux | "dark" | 6.28 | 1.03 |
| | | | | 5 lux | mesopic | 6.03 | 1.09 |
| | | | | 1000 lux | photopic | 2.72 | 0.41 |
| | | | Colvard | <0.63 lux | "dark" | 6.03 | 1.05 |
| | | | | 5 lux | mesopic | 5.67 | 1.15 |
| | | | | 1000 lux | photopic | 3.02 | 0.47 |
| | | | Ruler | 5 lux | | 5.47 | 1.20 |
| | | | | 1000 lux | | 2.56 | 0.46 |
| | | | Semicircular Template | 5 lux | | 5.64 | 1.15 |
| | | | | 1000 lux | | 2.68 | 0.43 |
| (Shankar et al., 2008) | 67 eyes | 35.5 ± 14.8 (7-65) | Pentacam | . | "natural light" | 3.04 | 0.45 |
| (Robl et al., 2009) | 300 eyes | 35.4 ± 10 (18-58) | Procyon P2000 AS | 0.03 lux | scotopic | 6.82 | 0.87 |
| | | | | 0.82 lux | low mesopic | 5.64 | 1.02 |
| (Bradley et al., 2010) | 50 eyes | 35 (19-62) | IR photography | 1 lux | | 7.00 | . |
| | | | Neuroptics PLR-200 pupillometer | 1 lux | | 6.90 | . |
| (Yazici et al., 2010) | 100 eyes | 25 (21-32) | Visante OCT | . | mesopic | 4.87 | 1.09 |
| | | | Orbscan | . | mesopic | 4.00 | 0.67 |
| | | | Pentacam | . | mesopic | 3.05 | 0.59 |
| (Cakmak et al., 2012) | 60 eyes | 29.41 ± 0.90 (20-48) | ORK wavefront analyzer | 0.6 lux | mesopic | 6.39 | 0.80 |
| (Gedik et al., 2012) | 72 eyes | 26.2 ± 8.1 (19-43) | Lenstar LS 900 | 2 lux | mesopic | 5.82 | 0.99 |
| (Domínguez-Vicent et al., 2014) | 80 eyes | 30.36 ± 7.32 (20-40) | Galilei G4 | . | "complete darkness" | 3.22 | 0.58 |
| | | | Pentacam HR | . | "complete darkness" | 3.22 | 0.52 |
| (J. Kanellopoulos & Asimellis, 2014) | 86 eyes (Group A) | 70.58 ± 10.33 (42-89) | WaveLight Oculyzer II | 4.79×10-2 mW/cm2 | "dim" | 2.83 | 0.53 |
| | 75 eyes (Group B) | 53.14 ± 16.27 (35-64) | | 4.79×10-2 mW/cm2 | "dim" | 3.03 | 0.31 |
| (Koktekir et al., 2014) | 25 eyes | 27.09 ± 1.72 (20-40) | Lenstar LS 900 | 3 lux | mesopic | 6.36 | 0.94 |
| | | | | 150 lux | photopic | 4.86 | 0.70 |
| (A. J. Kanellopoulos et al., 2015) | 40 eyes | 67.9 ± 10.5 (51-82) | Topolyzer vario | 0.7 lux | mesopic | 4.67 | 0.78 |
| | | | | 44.0 lux | "photopic" | 2.83 | 0.47 |
| (Y. Wang, 2019) | 78 eyes | (<60) | Lenstar LS 900 | . | photopic | 4.18 | 1.03 |
| | 95 eyes | (60-70) | Lenstar LS 900 | . | photopic | 4.19 | 1.05 |
| | 94 eyes | (>70) | Lenstar LS 900 | . | photopic | 3.70 | 1.04 |

Table 1 - Summary of other references on Pupil Diameter. Results are divided by device type in color categories: Photography (Orange), Comparative Methods (yellow), Infrared pupillometry (Green), Topography – Placido ring, Slit-scan or Scheimpflug-based (Blue)- , Aberrometry (Gray), Optical Coherence Tomography/OCT (Pink) and Optical Low-Coherence Reflectometry (purple). According to literature, light conditions are as follow: scotopic - <0.5 lux, mesopic – 0.5-50 lux, photopic - >50 lux. When studies did not provide an accurate illumination level or light condition designation is not correct according to considered levels, said condition will appear as "condition" in the table.

### 3.2 Pupil Decentration

The position of the entrance pupil controls the direction of the light beam's path passing into the eye, and therefore affects the amount and type of aberrations, such as transverse chromatic aberration and coma, which decrease spatial visual performance, hence retinal image quality. (Atchison & Smith, 2000)

In any rotationally symmetric optical system, the pupils are centred. However, this is not true in real eyes. Pupil decentration is defined as the distance between the pupil center and the optical axis/corneal vertex. (Atchison & Smith, 2000) The pupil was found to be horizontally displaced to the nasal side between 0.25mm and 0.5mm (Atchison & Smith, 2000; Iskander et al., 2004; Kaschke et al., 2014; Walsh, 1988; Wildenmann & Schaeffel, 2013), as may be seen in Table 2, with some studies reporting individual cases of up to 0.6 mm of decentration. (Liou & Brennan, 1997) To what concerns to vertical displacement, literature is both scarce and discordant, mainly because vertical displacement is frequently not as evident as nasal displacement or because a high variability is often found. (A. J. Kanellopoulos et al., 2015; Wildenmann & Schaeffel, 2013; Wyatt, 1995) Results of some studies are presented in Table 2.

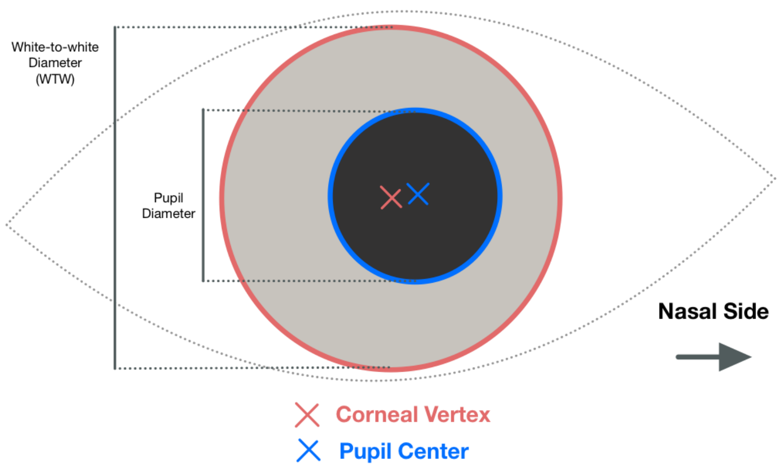



Figure 6 - Pupil centre (blue cross) is not coincident with corneal centre (red cross). It is displaced nasally and slightly superiorly.

| Reference | N (eyes/patients) | Age Mean ± SD (min-max) | Device | Light conditions | PD (mm) | | | Pupil Centre | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Mean | SD | Parameter Evaluated | Axis/Absolute | Mean (mm) | SD |
| (Wyatt, 1995) | 23 eyes | 35.18 ± 13.2 (22-71) | Photography | 100 cd/m$^2$ | | 3.09 | . | Center Position | Horizontal | 0.28 | 0.09 |
| | | | | | | | | | Vertical | 0.18 | 0.18 |
| | | | | Darkness | | 4.93 | . | Center Position | Horizontal | 0.25 | 0.15 |
| | | | | | | | | | Vertical | 0.14 | 0.12 |
| (Liou & Brennan, 1997) | . | . | . | . | | . | . | Centre Position | Horizontal | **0.5 *** | . |
| (Wildenmann & Schaeffel, 2013) | 20 eyes | (25-58) | IR video camera | 800 lux | OD | 4.75 | 0.52 | Center Position | Horizontal (OD) | 0.17 | 0.2 |
| | | | | | | | | | Vertical (OD) | 0.26 | 0.28 |
| | | | | | OS | 4.74 | 0.52 | Center Position | Horizontal (OS) | 0.12 | 0.22 |
| | | | | | | | | | Vertical (OS) | 0.2 | 0.25 |
| | | | | Flash light | | 4 | 0.2 | Center Position | Horizontal (OD) | 0.18 | 0.19 |
| | | | | | | | | | Vertical (OD) | 0.3 | 0.3 |
| | | | | | | | | | Horizontal (OS) | 0.14 | 0.22 |
| | | | | | | | | | Vertical (OS) | 0.27 | 0.29 |
| (Kaschke et al., 2014) | . | . | . | . | | . | . | Center Position | Horizontal | **0.5 *** | . |
| (A. J. Kanellopoulos et al., 2015) | 40 eyes | 67.9 ± 10.5 (51-82) | Topolyzer vario | 0.7 lux | | 4.67 | 0.78 | Center Position | Horizontal (OD) | 0.2 | 0.11 |
| | | | | | | | | | Vertical (OD) | -0.03 | 0.18 |
| | | | | | | | | | Horizontal (OS) | 0.14 | 0.22 |
| | | | | | | | | | Vertical (OS) | 0.03 | 0.16 |
| | | | | 44 lux | | 2.83 | 0.47 | Center Position | Horizontal (OD) | 0.16 | 0.11 |
| | | | | | | | | | Vertical (OD) | 0.02 | 0.16 |
| | | | | | | | | | Horizontal (OS) | 0.09 | 0.15 |
| | | | | | | | | | Vertical (OS) | 0.06 | 0.03 |
| (X. Wang et al., 2018) | 140 eyes | 10 ± 2 (7-18) | Lenstar LS 900 | . | | 3.84 | 0.79 | Center Position | Absolute | 0.19 | 0.12 |
| (Walsh, 1988) | 63 eyes | < 30 | Photography | Flash light and Darkness | | . | . | Centre Change (constriction -> dilation) | Horizontal | -0.09 | 0.17 |
| | | | | | | | | | Vertical | -0.03 | 0.15 |
| | | | | | | | | | Absolute | -0.19 | 0.12 |
| (Wildenmann & Schaeffel, 2013) | 20 eyes | (25-58) | IR video camera | 800 lux and flash light | | . | . | Center change /mm of dilation | Horizontal Nasal (OD) | -0.03 | 0.07 |
| | | | | | | | | | Vertical (OD) | -0.04 | 0.06 |
| | | | | | | | | | Horizontal Nasal (OS) | 0.03 | 0.04 |
| | | | | | | | | | Vertical (OS) | -0.05 | 0.12 |
| (Mathur et al., 2014) | 20 eyes | 22 ± 2 (18-25) | COAS-HD aberrometer | 6100 cd/m$^2$ and 0.01 cd/m$^2$ | | . | . | Center change with dilation (max illumination > min) | Horizontal | -0.2 | 0.09 |
| | | | | | | | | | Vertical | -0.18 | 0.05 |
| | | | | | | | | | Absolute | -0.26 | 0.08 |
| | | | | | | | | Center change /mm of dilation | Horizontal | -0.022 | . |
| | 19 eyes | 49 ± 4 (45-58) | COAS-HD aberrometer | 6100 cd/m$^2$ and 0.01 cd/m$^2$ | | . | . | Center change with dilation (max illumination > min) | Horizontal | -0.17 | 0.05 |
| | | | | | | | | | Vertical | -0.22 | 0.1 |
| | | | | | | | | | Absolute | -0.26 | 0.08 |
| | | | | | | | | Center change /mm of dilation | Horizontal | -0.039 | . |

Table 2 - Summary of references on Pupil Decentration. Because the pupil centre changes with pupil size, Pupil diameter is also presented when available in the references' results. Absolute pupil decentration refers to the distance between corneal apex and the centre of the pupil. In the horizontal axis, a positive value means a nasal sided shift or position, and a negative value means a temporal sided shift or position. In the vertical axis, a positive value means a superior shift or position, and a negative value means an inferior shift or position. In absolute terms, a positive value means an increase in decentration with dilation, while a negative value means a decrease with dilation. Values in bold are purely descriptive and weren't obtained in an investigation paper.

Pupil centre itself moves with changes in pupil diameter. (Liu et al., 2019) Many studies have analyzed this movement, suggesting a mean shift of between 0.18 mm (Donnenfeld, 2004; Wildenmann & Schaeffel, 2013) and 0.26 mm (Mathur, 2014) in absolute terms in nasal and superior directions with pupillary constriction, with a mean shift of between 0,03-0,05 mm/1 mm of constriction. (Walsh, 1988; Wildenmann & Schaeffel, 2013) However, many others reported significant inter-subject variations (Walsh, 1988), individual shifts of up to 0.5mm (Mathur et al., 2014), or shifts in temporal and inferior directions. (Wildenmann & Schaeffel, 2013). It is also difficult to precisely predict pupil decentration shift on an individual basis, since a correlation between a subject's baseline pupil diameter and decentration shift was not found. (Wildenmann & Schaeffel, 2013) As a result, pupil decentration can be highly variable, and so, difficult to generalize.

### 3.3 Measuring the Pupil

As previously seen, different studies have found different values for the same pupil parameters due to different methodologies. To a great extent, that might be attributed to some difficulty in establishing or achieving standard conditions during pupillometric evaluation. As a result, comparing data from literature might be a challenging task, which is a frequently reported problem (Boxer Wachler & Krueger, 1999; Bradley et al., 2010; Twa et al., 2004). Parameters which are recommended to be streamlined in pupil diameter measurement are room illumination levels, constant illumination at the corneal plane, time for dark or light adaptation before measuring, accommodation, correct positioning of the subject and examiner, and subject alertness state. (A. J. Kanellopoulos et al., 2015; Kelbsch et al., 2019; Watson & Yellott, 2012) If such variables are similar across studies, extrapolation and comparison of results become both easier and more relevant.

Another variable of importance is the choice of measuring device. (Liu et al., 2019) Nowadays, there is a wide range of devices at a clinician's disposal. They go from more basic tools such as rulers, templates and pupillary cards – called comparative methods - to more sophisticated techniques. Some of them are based on Infrared lighting imaging

(IR photography, pupillometers such as the Procyon P2000 SA, the Oasis Medical Colvard pupillometer, Neuroptics pupillometer). Other ones are Corneal Topographers which can be Scheimpflug (e.g. Pentacam, Alcon Wavelight Oculyzer), Placido ring-based (Orbscan II), or both (Galilei G4). Hartmann-Shack aberrometers (Zywave, Wasca, ORK wavefront analyzer) are also used to evaluate pupil biometry, as are anterior segment Optical Coherence Tomographers, or OCT (Visante OCT), and Optical low-coherence reflectometres or OLCR (Haag-Streit Lenstar LS900). (Boxer Wachler & Krueger, 1999; Bradley et al., 2005, 2010; Kohnen et al., 2004; Liu et al., 2019; Robl et al., 2009; Schmitz et al., 2003; Twa et al., 2004) A multitude of authors has tried to study the differences between those methods regarding accuracy, validity, variability and reliability of measurements.

Comparative methods (millimetric ruler, semicircular templates and Rosenbaum/Bernell cards) have shown to be significantly inferior to other methods for measuring pupil diameter. Validity and repeatability are limited since they have a higher user-dependency (Twa et al., 2004) as well as lower accuracy than Infrared (IR) pupillometers (Liu et al., 2019), and are hard to use under dark conditions. Pupil cards have also shown a tendency for overestimation of pupil size. (Boxer Wachler & Krueger, 1999; Chaglasian et al., 2006)

Figure 7 – The Rosenbaum Card features a pupil gauge in its lower end. Credit: https://www.precision-vision.com

The Colvard pupillometer has been widely used in clinical practice (Bradley et al., 2010). It was shown to have a high user-dependency, subjectivity and intra/inter-individual variance (Kohnen et al., 2004; Liu et al., 2019; Schmitz et al., 2003) as well as a steep learning curve (Bradley et al., 2005), despite being more accurate than the Rosenbaum card and the ruler (Chaglasian et al., 2006; Schmitz et al., 2003).

IR video or photography analysis is often used as a reference term. (Liu et al., 2019; Twa et al., 2004) While measurement is performed by the examiner using collected images, some studies claim those methods to have high accuracy (Liu et al., 2019), insignificant inter-examiner variability and high validity and repeatability in contrast to comparative procedures, even though IR photography had slightly less repeatable measuring under bright conditions than IR video analysis. (Twa et al., 2004) Nonetheless, problems derived from defocus, device positioning and correct use may impact measuring. (Twa et al., 2004).

Automated instruments such as the Procyon pupillometer are capable of dynamic pupillometry (Schmitz et al., 2003). Unlike the Colvard pupillometer, it features binocular occlusion providing highly reliable scotopic results (Schmitz et al., 2003). Furthermore, it has great repeatability and is capable of obtaining multiple measurements in a small amount of time (Chaglasian et al., 2006) at standardized illumination levels (Robl et al., 2009; Schmitz et al., 2003).

Figure 8 – The Colvard pupillometer. Credit: https://www.oasismedical.com/

Corneal topography systems, for instance, are devices whose primary purpose was not pupillography but became capable of doing so through software advancements. The Orbscan II showed larger deviations from expected values for darker settings because of the bright luminance of Placido rings therefore underestimating pupil size. Mean values obtained for “scotopic” pupil diameter are around 3.75 mm, thus the Orbscan II is not recommended for that estimation (Kohnen et al., 2004). More recently, though, Keratograph 4-Vario topolyzer showed a strong correlation between its mesopic pupil results and scotopic pupil ones obtained with Procyon, while being more stable and having a higher repeatability than the last. (A. J. Kanellopoulos, 2017) Additionally, the Medmont corneal topographer can be used to measure pupil decentration, and a study found a photopic decentration of about 0.21 mm nasally and superiorly. (Tabernero et al., 2009)

Aberrometers are capable of obtaining pupillometric data under low light settings, showing a good clinical correlation with IR pupillometry for that setting. (Kohnen et al.,

2004) It was found no clinically relevant differences between the WASCA aberrometer and the Procyon pupillometer (Kohnen et al., 2004) but only statistically significant ones attributed to the reflection of the instrument's bright screen (Schmitz et al., 2003). Measures for low-mesopic pupils range from 5.5-6 mm. (Kohnen et al., 2004) The COAS aberrometer presented a mesopic decentration of about 0.23 mm nasal and superiorly, a mean maximum nasal shift of 0.12mm between 0,01 lux and 6100 lux, and a mean maximum absolute shift of 0.26 mm. (Mathur et al., 2014)

### 3.4 Pupil's impact in modern ophthalmology

Study of the entrance pupil became more relevant with the development of optic surgery with intraocular lens (IOL) implantation. Not only the pupil plays a considerable role in the design process of such devices, but individual variations in its parameters also influence the pre-operative choice of lens and postoperative vision quality (Tabernero et al., 2009) related to vision acuity, retinal image quality and other optical phenomena, altogether with other ocular parameters such as keratometry, axial length, lens thickness, selection and position of IOL, ACD (Ning et al., 2019) and WTW (Hashemi et al., 2015).

Literature suggests that pupil diameter correlates with Optical Quality on those patients, a phenomenon called Pupil Dependence. (Fernández et al., 2020a) As a result, subjects with larger scotopic pupils have lower post-surgical satisfaction with multifocal IOL (MIOL), lower contrast sensitivity under mesopic and scotopic conditions and experience optical phenomena such as glares, starbursts and halos when close to light sources (Salati et al., 2007), which may also be associated to decentration (especially if temporal) of the MIOL relatively to the pupillary axis (Fernández et al., 2018) and is also correlated with preoperative angle-kappa – the angle between pupillary and visual axis. (A. J. Kanellopoulos et al., 2015) There is clinical evidence that suggests that pseudoaccommodation, an ability some pseudophakic individuals report, is widely related to pupil diameter, as are near visual acuity and reading performance. (Fonseca et al., 2019)

### 3.5 Study of the pupil

As noted, the pupil plays a major role on vision quality especially when pseudophakic eyes are considered. Despite that fact, it is notorious its absence in the great majority of schematic models – working tools which are the basis of clinical evaluation and pupillometry. That absence might be influenced by the many imprecisions present in its study: with various sources presenting different results and information, it may be difficult to establish a general standard for the parameters of the pupil.
As a result, this work intends to study the biometric pupillary parameters of a group of patients of Hospital da Luz Lisboa, their correlation with other parameters and compare the results with the available data. This studies' intent can be summarized in six questions:

1. What is the mean pupil diameter (PD)?
2. Is there a difference in mean PD between right and left eyes?
3. Are PD and Anterior Chamber Depth (ACD) correlated?
4. Are PD and White-to-White distance (WTW) correlated?
5. How much is the pupil decentered in average?
6. Are PD and pupil decentration correlated?

# 4. Methodology

A retrospective study was done with the information of a group of patients, selected from the database of Hospital da Luz, Lisboa, which were to be submitted to a cataract surgical treatment. Those patients' eyes were measured pre-operatively with the Lenstar LS 900 (Haag-Streit, Koeniz, Switzerland).

The following exclusion criteria were applied: entries with missing measurements, entries that were repeated measurements of the same eye of one patient (where in such case, the last measurement was considered), and eyes that had already an IOL implanted. After application of exclusion criteria, a total of 1013 patients were obtained.

Since not every patient had both eyes measured, such sample corresponded to 1607 eyes: 763 right eyes (OD) and 844 left eyes (OS). It should be noted that gender was not available in this device's database, and only birthdate was available. As such, age at the date of the exam could not be calculated.

The device was operated according to the manufacturer's recommendations. Patients were told to rest their head in the chin rest and forehead band, and to hold the side handles. Distance from the measuring head to the eye was approximately 68mm. Patients were then instructed to stare at the red fixation light in the measuring lens during the measuring procedure. If a patient could not complete this task, he would be asked to fixate a remote object with the eye. Finally, the patient would be asked to blink before the measurement starts. The procedure was repeated until a satisfactory number of measurements was achieved. Phakic mode was chosen for every patient.

The Lenstar LS 900 performs Optical Low Coherence Reflectometry (OLCR) in monocularity and is capable of measuring anterior segment parameters. It measures Pupil Diameter (*PD*), Pupil barycenter (*Pupil decentration*), Anterior Chamber Depth (*ACD*) and White-to-White distance (*WTW*). Pupil barycenter is measured as the shift of the pupil centre relative to the corneal apex in X – *PCX* – and Y – *PCY* – coordinates. ACD is the sum of both central corneal thickness (CCT) and aqueous depth (AD), corresponding to the distance between the anterior surface of the cornea and the anterior surface of the lens. WTW is measured as the horizontal diameter of the iris, determined using the image of the iris and the eye radii obtained from keratometry. Absolute pupil decentration was calculated from each patient's PCX and PCY values using the Pythagorean theorem: *Absolute decentration* = *sqrt* ($PCX^2$ + $PCY^2$). For PCX and PCY, a positive value represents a nasal/superior shift of the pupil centre relatively to the corneal apex, and a negative value translates into a temporal/inferior shift.

The Lenstar LS 900 uses a white LED light source for A-Scan and central fixation at 820nm, for Keratometry at 950nm and for Positioning aid at 940nm. Room lighting conditions were assumed to be photopic but illumination at the eye level was not measured.

Statistical analysis was performed using IBM SPSS (IBM corporation) on the right eyes (OD) of the population, except when comparing eye sides. To test for differences between right and left eyes, an Unpaired samples t-test was used. When studying correlations between variables (ACD, WTW, Pupil Decentration and PD), Pearson Correlation was the statistical test used. When a significant correlation was found, a scatter plot with linear regression modelling was done. For t-tests, a *p-value* > 0.05 was considered significant, and for a Pearson's Correlation test, a Pearson coefficient > 0.150 or <-0.150 was considered sufficient to establish a correlation.

## 5. Results

A mean pupil diameter (PD) of 4.109 ± 0.532 mm (2.45-4.99) was obtained in the studied group for right eyes (*table 3*). For left eyes, a mean PD of 4.034 ± 0.542 mm was obtained. Those results were found to be significantly different from each other (p=0.005), which show a significant difference in PD between right and left eyes in this population, as shown in *Table 4*.

| | N | Minimum (mm) | Maximum (mm) | Mean (mm) | SD |
|---|---|---|---|---|---|
| Pupil Diameter | 763 | 2.45 | 4.99 | 4.1089 | 0.53214 |

Table 3 – Analysis of the Pupil Diameter (PD) of right eyes (OD).

| | N | Mean PD (mm) | Std. Deviation | Sig. (2-tailed) | 95% confidence Interval of the difference | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| OD | 763 | 4.1089 | 0.53214 | 0.005 | 0.02232 | 0.12759 |
| OS | 844 | 4.0339 | 0.54171 | | | |

Table 4 – Analysis and comparation of the Pupil Diameter (PD) of right (OD) and left eyes (OS). *Sig (2-tailed)* corresponds to the *2-tailed p-value* that is the result of a t-test.

Anterior chamber depth (ACD) and White-to-white distance (WTW) had mean values of 2.618 ± 0.387 mm and 11.919 ± 0.445 mm, respectively. Relatively to PD, correlation of those parameters was tested through a Pearson Correlation analysis. None of those parameters were found to have a significant correlation: for the relation between ACD/PD, a Pearson coefficient of 0.06 was found (*p*=0.1), and for WTW/PD, a Pearson coefficient of 0.087 was calculated (*p*=0.016). Results are shown in *Table 5*.

| | N | Mean (mm) | Std. Deviation | Pearson coefficient | *p* |
|---|---|---|---|---|---|
| ACD | 763 | 2.6176 | 0.38738 | 0.06 | 0.1 |
| WTW | 763 | 11.9189 | 0.44541 | 0.087 | 0.016 |

Table 5 – Analysis of Anterior Chamber depth (ACD) and White-to-white distance (WTW), and the correlation of each of them with Pupil Diameter. Pearson coefficients and p-values are the results of a Pearson's Correlation analysis.

Pupil decentration was studied through the coordinates of the pupil centre. In the present group, the pupil had a mean horizontal decentration – PCX – of 0.259 ± 0.165mm, showing a clear tendency towards the nasal side, and a vertical decentration – PCY – of -0.010 ± 0.153 mm, which represents a minimal shift towards the lower side of the referential. Absolute pupil decentration, or the distance from the corneal apex to the pupillary centre, was calculated for each patient through the application of the Pythagorean Theorem to PCX and PCY. For this parameter, a mean value of 0.312 ± 0.144mm was found.

| | N | Minimum (mm) | Maximum (mm) | Mean (mm) | Std. Deviation |
|---|---|---|---|---|---|
| Horizontal pupil decentration (PCX) | 763 | -0.26 | 0.92 | 0.2593 | 0.16526 |
| Vertical pupil decentration (PCY) | 763 | -0.53 | 0.72 | -0.0102 | 0.1533 |
| Absolute pupil decentration | 763 | 0.01 | 1 | 0.312 | 0.14404 |

Table 6 - Analysis of Horizontal, Vertical and Absolute pupil decentration. Horizontal decentration of the pupil (PCX) and Vertical decentration of the pupil (PCY) refer to the horizontal and vertical distances between corneal vertex and pupil center, respectively. Absolute decentration refers to the absolute distance between corneal vertex and pupil center.

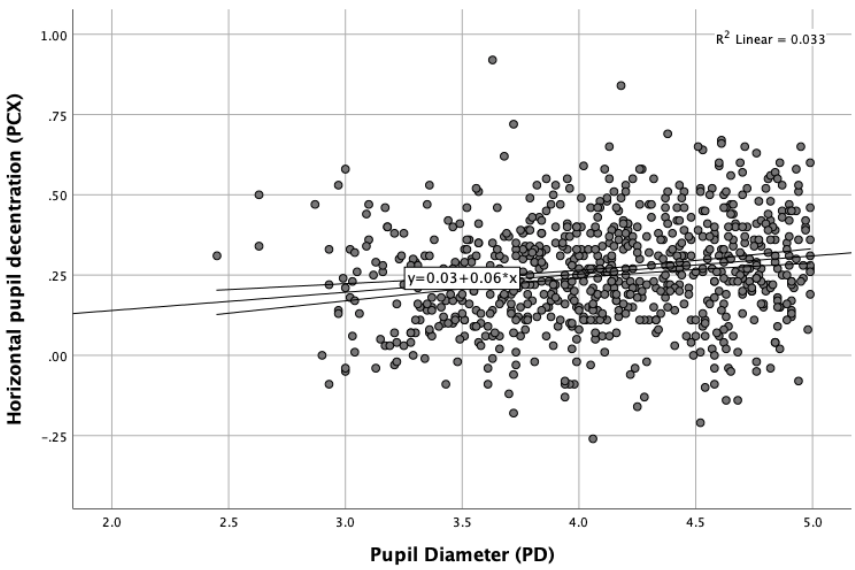
Correlation between PD and Horizontal, Vertical and Absolute pupil decentration was also studied. While PCY was not found to be significantly correlated with PD (Pearson coefficient=-0.022, p=0.542), both PCX (Pearson coefficient=0.183, p<0.001) and

Absolute pupil decentration (Pearson coefficient=0.174, p<0.001) were found to be weakly correlated with PD in a significant way.

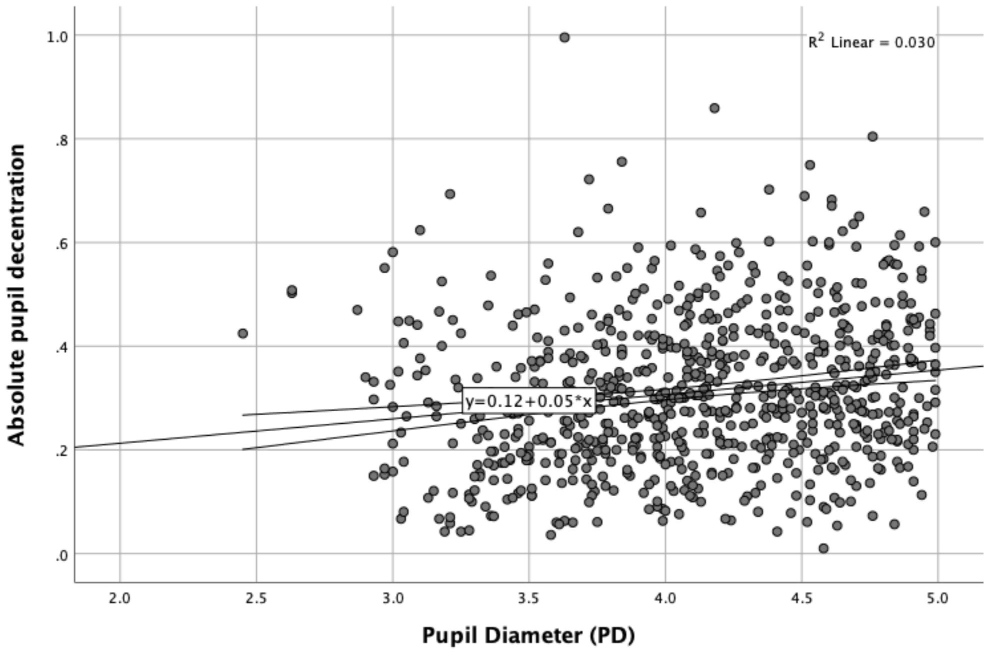
| | Mean (mm) | Std. Deviation | Pearson coefficient | *p* | *R* | *$R^2$* |
|---|---|---|---|---|---|---|
| Horizontal pupil decentration (PCX) | 0.2593 | 0.16526 | 0.183 | <0.001 | 0.06 | 0.033 |
| Vertical pupil decentration (PCY) | -0.0102 | 0.1533 | -0.022 | 0.542 | . | |
| Absolute pupil decentration | 0.312 | 0.14404 | 0.174 | <0.001 | 0.05 | 0.03 |

Table 7 – Correlation of Horizontal, Vertical and Absolute pupil decentration with Pupil Diameter (PD). Pearson coefficients and p-values were obtained with a Pearson's Correlation analysis between those parameters. R and $R^2$ were obtained through linear modelling.

The correlation between PD and PCX/Absolute pupil decentration was further studied. Regression lines that were drawn show that for the correlation between PD/PCX, R was 0.06, which means a nasal shift of the pupil centre of 0.06mm per 1mm of increase in PD. For the relation between PD/Absolute pupil decentration, R was 0.05, meaning an increase of 0.05mm in distance between the corneal vertex and the pupil centre per 1mm of increase in PD. The $R^2$ value, which represents the extent to which the regression line explains the presented results, was about 0.03 for both cases, suggesting that the regression model might be a poor fit to the current dataset, though.




Graph 1 – Correlation between Pupil Diameter (PD) and Horizontal pupil decentration (PCX). (Dispersion graph; values in millimeters)




Graph 2 - Correlation between Pupil Diameter (PD) and Absolute pupil decentration. (Dispersion graph; values in millimeters)

# 6. Discussion

## 6.1 Mean Pupil Diameter

In this study, the mean of the PD obtained (4.109 ± 0.532 mm) was in accordance with the findings of another work that used Lenstar to measure PD in photopic conditions. (Y. Wang, 2019) According to that study, as may be seen in *Table 1*, photopic PD was 4.18 ± 1.03 mm for a population that was <60 years old, 4.19 ± 1.05 mm for 60-70 years old patients, and 3.70 ± 1.04 mm in patients older than 70 years. Even though age at the time of examination could not be formally calculated, a mean age between 50.15 and 71.15 years for the population of this study is certain, taking into consideration that examinations were done between years 2000 (when the device was launched) and 2021 (when the database was extracted). Nonetheless, results regarding this information should not be extrapolated.

Another work presented a mean PD of 4.86 ± 0.70mm in photopic conditions (150 lux) (Koktekir et al., 2014), showing a higher value than this study's result. Such difference is probably due to a young population (mean age 27 years; minimum 20, maximum 40). Because of the senile myosis phenomenon, it is expectable that younger individuals have wider pupils than older ones. (Robl et al., 2009) Thus, such discrepancies may happen. However, this might also hint at possible inter-populational variations.

Additionally, the population sizes of the studies are very different, with *Koktekir et al.'s* and *Wang's* having much smaller population sizes than this study (N=763), which predisposes to less credible and reproductible results.

As to comparation with other devices, literature is not consensual as implicit in *Table 1*. Because many factors impact the biometrics of the pupil (including differences in measuring procedures of different devices), it is a very challenging work to compare results, and so pupil biometrics should be compared to other works which use similar equipment and methodologies.

### 6.2 Eye side

Results show a significant difference between OD and OS in the studied population, which was not an expectable outcome since PD is approximately equal in both eyes for the same subject/population. (Robl et al., 2009) However, only 594 of the 1013 subjects in the database had both eyes analysed, and 419 subjects had a single eye measured. As a result, OD and OS groups are only partially overlapping, making it possible that the groups presented different mean PD values. Also, the size of each of those groups is different, which might influence the results and their validity.

### 6.3 ACD and WTW

In the study's population, mean ACD was 2.618 ± 0.387 mm and mean WTW was 11.919 ± 0.445 mm. Compared to the manufacturer information and to the literature, these results show generically smaller mean values for ACD - 3.19mm in the manufacturer's manual, 2.93 ± 0.30mm in (O'Donnell et al., 2012), 3.04 ± 0.35mm in (Koktekir et al., 2014) - and for WTW - 12.27mm in the manufacturer's manual, 11.79 ± 0.06mm in

(Cakmak et al., 2012). In addition, no correlation was found between any of those two parameters with PD, which is not concordant with literature: *Cakmak et al.* found that WTW and ACD had a moderate correlation with mesopic pupil diameter.

In the first place, it should be noted that the population in our study is composed of patients with cataracts, generally older. In contrast, all the cited articles based their study on young, healthy populations. Since both WTW and ACD inversely correlate with age (Hashemi et al., 2015; Schuster et al., 2016), then our results may be in line with those findings. In addition, the study of *Cakmak et al*. evaluated the correlation of ACD/WTW in mesopic pupils, while our measurements were done in photopic conditions.

### 6.4 Pupil Decentration

In the horizontal axis, in average, pupil centre was clearly displaced nasally to the corneal vertex. These results are in line with the findings of previous works (Atchison & Smith, 2000; Iskander et al., 2004; Kaschke et al., 2014; Walsh, 1988; Wildenmann & Schaeffel, 2013) which suggest values of about 0.25-0.5mm for this parameter, even though pupil centre can be highly variable. Because pupil decentration is said to be inversely correlated with age and illumination, (Mathur et al., 2014) it would be expected that our results would be closer to the lower limit of the value interval, as happened. However, our population also had a high inter-individual variability as seen in Graph 1, a phenomenon highly related in previous works.

As for vertical decentration, the average displacement was close to a neutral value, even though it showed a minimal tendency towards an inferior displacement. Literature is indeed sparse in this aspect, and can be variable: even though it may be considered slightly superior or close to the centre (Atchison & Smith, 2000), some diverging results may be found among studies. (A. J. Kanellopoulos et al., 2015; Wildenmann & Schaeffel, 2013; Wyatt, 1995)

## 6.5 Pupil Diameter and Decentration

Results in Table 7 show that PCX and Absolute pupil decentration were both significantly correlated to PD. This correlation translates into nasal and absolute pupil centre shifts of 0.06mm and 0.05mm, respectively, per millimeter of increase in PD. Opposingly, vertical pupil centre shift was not found to be correlated with pupil dilation. In other works, temporal (about 0.02-0.04mm/mm of dilation) and inferior shifts of the pupil centre, and a decrease in absolute pupil decentration were generally reported with pupil dilation (Mathur et al., 2014; Walsh, 1988; Wildenmann & Schaeffel, 2013).

On one hand, in those studies, subjects were evaluated at various levels of illumination and the pupil was assessed under different light conditions for each patient. That was not the case of this study, where subjects were measured in stable light conditions. Therefore, results don’t translate into a reliable study of intra-individual response to light nor its impact in pupil decentration. In the other hand, some studies report high inter- and intra-individual shifts and even shifts in a nasal and/or superior direction with dilation (Wildenmann & Schaeffel, 2013), suggesting that this parameter is of high variability and difficult to accurately measure. Additionally, studies and devices may use different referential systems to evaluate pupil centration, sometimes, causing inconsistency of the results in literature. (Wildenmann & Schaeffel, 2013)

## 7. Conclusion

As the pupil becomes a more important structure due to its conditioning on post-surgical outcomes, this work intended to study its parameters, concretely Pupil Diameter and Decentration, their relationship to each other and to other parameters such as eye side, ACD and WTW. Because schematic eye models lack on incorporation of such parameters and variables - as studies are frequently contradictory - the aim of this work was to draw a parallel between other works and our population in terms of pupillometry. This could lead to a standardization of pupil biometrics, potentially translating into better outcomes in clinical practice.

Results show that mean Pupil Diameter was, as far as to our knowledge, grossly similar to other studies that used the same device (Lenstar LS 900), even though there was a significant difference in PD between right and left eyes. ACD and WTW were not correlated with PD, despite their mean values being considered normal according to other sources. Globally, findings in pupil centration were similar to the references‘. However, and despite correlations between Horizontal and Absolute decentrations with PD were found, they were inversely correlated to what would be expected. On its turn, vertical pupil decentration was not found to be correlated with PD.

Some limitations were found in the present study that could explain some of the results and should be addressed. To start with, exclusion criteria were sparse, only appliable to the dataset, and not to the selection of subjects themselves. More extensive criteria should have also been formulated that accounted for diseases and conditions that potentially have an impact on optical biometry (such as patients previously submitted to LASIK or other ophthalmologic surgical procedures) – however, with the available information, this was not possible. Secondly, there was a substantial difference in OD and OS group sizes and constitution because of exclusion of eye measurements, but not patients themselves. Such problem leads to a heterogeneity between the two samples and compromises results. It could have been avoided by excluding subjects if at least one of their measured parameters was missing. Furthermore, to correctly evaluate the

Pupil centre shift with variation of PD (i.e., myosis and mydriasis) at an individual level, each patient should be submitted to at least two measures in different light conditions. Results would, therefore, better represent the variables in study.

Because pupillometry consists of highly variable parameters, a special effort should also be made to maintain room conditions as constant as possible between measurements and patients, and a strict protocol should be followed, so that more reproducible results are obtained, and the risk of dispersing results (intra- and inter-individually) is reduced. Such conditions and methods should also be standardized literature-wise, so that future works can be more easily compared.

There are also influencing factors that are inherently present in pupillometry. Differences between measuring equipments and age of the studied individuals are some and they greatly influence results. Results should be compared with the outcomes of works which had similar demographic features and methodologies. Because of this, even though it is possible to draw parallels in pupillometry in gross terms, comparing results in more concrete settings with differently designed studies should be avoided. In the case of age, in future works, age at the time of examination for each patient should be analysed.

However, there is also the possibility that some inter-populational variability exists for the parameters of the eye and, in this case, of the pupil. As much as non-accounted for variables might be present, studies constantly report different values (to a bigger or smaller extent) even if they sometimes have similar designs and populations in terms of demographics. As a result, the possibility of population-established "normal" values for pupillometry should be further studied, which could help the development of population-adjusted models of the eye, possibly impacting post-surgical quality of vision in cataract surgery.

In conclusion, even though some of the results were similar to the ones found in the literature (mean Pupil Diameter, ACD, WTW and Pupil Decentration), there were limitating factors that restricted the extent of the agreement and even might have inversely impacted agreeability. Such factors should be addressed in future research projects intended to study similar parameters. In addition, comparing different sources, especially ones that used different devices or had significantly different demographics and methods, was found to be extremely hard as there are multiple confounding factors that impact the pupil. On the one side, this shows that an effort should be made to establish standard conditions for pupillometry at a research level. On the other side, it creates the possibility that different populations might have slight variations of the same parameter, opening doors to future works.

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