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Master in Photonics

## MASTER THESIS WORK

## AGREEMENT OF 4 PUPILLOMETERS UNDER 3 DIFFERENT ILLUMINATION CONDITIONS

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# Agreement of 4 pupillometers under 3 different illumination conditions

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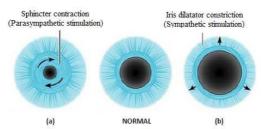
Abstract. Pupil diameter is an important parameter to be taken into account for numerous processes, such as in refractive surgery where the size of the ablation zone is partially determined by the pupil size in certain illumination conditions. In this work, four commercial pupillometers are tested: NeurOptics VIP-200 (Neuroptics), PowerRef II (Plusoptix), WAM-5500 (Grand Seiko) and EVA prototype (Davalor Salut). In order to carry on the study, the pupil diameter of 40 right eyes of 40 patients was measured under 3 different illumination conditions (±SD): 0.047±0.012 lx, 0.8± 0.3 lx and 20.33±0.577 lx. The pupil diameter was measured in crescent order of illumination, starting with the lowest level (low-mesopic), then a mid-level (mid-mesopic) and finally the highest one (high-mesopic). The order of the four instruments for each patient was randomly chosen. For each instrument and illumination condition, two measurements were taken. A descriptive analysis was first computed in order to see pupil diameter size values, obtaining as a largest value 6.76250±0.924506 mm and as a lowest one 4.70750±0.854367 mm. Also, ANOVA and Bland & Altman tests were carried on. In low-mesopic level, WAM-5500 had the best confidence limits (0,635 - 0,324 mm) and PowerRef II the best mean difference (0,277 mm). EVA prototype showed the best mean differences and confidence limits in the other two levels with 0,036 mm mean difference and 0,331 - 0,258 mm of confidence limits (mid-mesopic) and 0,233 mm mean difference and 0,004 - 0,471 mm confidence limits (high-mesopic) according to ANOVA Post-Hoc analysis and Bland & Altman graphs. Therefore, PowerRef II and WAM-5500 showed better performance than EVA prototype in the low-mesopic level while EVA prototype showed a better one in the other two illumination levels, mid-mesopic and high-mesopic.

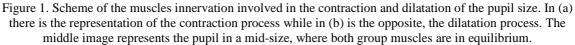
#### 1. Introduction

The eye can be described as a simple optical system, formed by two lenses (cornea and crystalline), the pupil and the retina. Both the lenses and the pupil play key roles into the image formation process. Improving the image quality on the retina turns into better quality of vision for the subject. The pupil is the dark circular opening in the center of the iris, where its size can be modified from a small aperture of around 2 mm to a big one of around 8 mm of diameter<sup>1</sup>. This aperture restricts the amount of light entering the optical system avoiding saturation of the photoreceptor cells located into the layers of the retina as in any other digital system. It also plays a key role on the image quality because it prevents that light going through the periphery of the cornea enters the system. In other words, aberrations are affected by the pupil size<sup>2,3</sup>. However there is a trade-off so, large pupils will affect image quality through aberrations but small pupils will also affect it with diffraction. This pupil size also plays a role in the depth of field, the greater the pupil size the less the depth of field<sup>4</sup>.

An important aspect of the pupil is how it works. Its performance is controlled by two principal muscle groups, one is the sphincter or constrictor and the other is the iris dilatator. Both muscle groups are controlled by the autonomic nervous system or neurovegetative<sup>5</sup>. Two main processes can be carried out, the mydriasis where pupil diameter increases and the missis where the diameter

decreases. In the mydriasis process, the principal muscle working is the iris dilatator, which is innervated by the sympathetic nervous system. On the other hand, in the miosis process the muscle involved is the sphincter, which is mostly innervated by the parasympathetic nervous system<sup>5,6</sup> (Figure 1).





At the end, the pupil size is determined not by the action of one or the other muscle groups but with a joint action of all of them.

The pupil is an important part of the eye and it plays key roles in many aspects. In LASIK surgery, its diameter value under certain illumination conditions is a parameter taken into account for the calculation of the ablation diameter. Therefore, obtaining its value with precision is fundamental for good surgery results. Pupil also is a key in the process called triad proximal, where accommodation, convergence/divergence and pupil size are bounded. Then, it is deeply related with accommodation processes, where more accommodation results in decreasing pupil size and the other way around.

In neurologic processes there is also change of the pupil size. Because the innervation of the pupil is well-known, some nerve issues can be found through pupil dysfunctions. Alterations on symmetry, reactivity to light and many others are directly related with neurologic problems<sup>7</sup>. Moreover, cognitive processes also affect the pupil size, like for instance state of mind.

At this point, the importance of the pupil size and its measurement and evaluation has been exposed. When measuring the pupil, two main situations are evaluated, static (where basically the aim is to compare pupil sizes) and dynamic (where the aim is to study the reaction of pupil in size and in comparison with the other pupil when some stimulus are provided)<sup>8</sup>.

An important fact to remember is that the pupil is not a motionless system and therefore its diameter does not remain constant in time even if there are no stimulus or changes in the illumination, and numerous factors can affect directly or indirectly its size, for example micro-fluctuations, the previously mentioned triad proximal, cognitive alterations, response to accommodation and so on<sup>9-10</sup>.

There are objective and subjective methods for the measurement of the pupil size, which is called pupillometry. A very common subjective method used still these days is the direct comparison of the pupil size with a chart containing different pupil diameters with known values<sup>10</sup> (Figure 2).

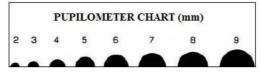


Figure 2. Pupillometer chart with known values of different diameters<sup>7</sup>.

Nevertheless, nowadays objective measurements are on the lead. The basis of these objective methods is the direct illumination of the pupil with infrared light (IR) for the further recording with

a camera working on a spectrum range which includes IR. Thanks to the non-sensitivity of the eye to the IR, these methods do not affect the real pupil size. Moreover, these techniques enable to work with dynamic changes of the pupil, and with resolutions up to hundredths of a millimetre. The differences between the various devices working with this principle are the algorithms used to recognise the circle of the pupil; however this topic is beyond the objectives of this article. Objective methods have better resolution, better performance, are able to work under dynamic circumstances and the result do not depend on the observer; nevertheless, they are much more expensive than conventional subjective ones.

There are many devices which are able to measure pupil size diameter and some of them have been validated in other studies. The pupillometer which has shown high good performance and can be considered as gold standard is the Neuroptics<sup>11-13</sup> and it focus on the evaluation of pupil diameter size. Other devices have also been demonstrated to show good results, even though they not only measure the pupil but also the refraction of the eye and are commonly used for this last objective: PowerRef II and WAM-5500. Finally, a new instrument is being examined in this work, which among many other applications, it measures pupil size diameter, EVA prototype.

The goal of this study is then, not to analyse the different algorithms configuration but to compare the results of pupil diameter obtained with four commercial devices. The aim is also not to determine which instrument is better because it may vary for different usages, but to see which of them have better agreement.

#### 2. Methods

#### 2.1. Subjects

This observational, descriptive and transversal study was conducted on fifty right eyes of fifty healthy subjects recruited from the staff and students of the GAIA and CD6 facilities (UPC) (Terrassa, Spain). All subjects were older than eighteen and signed a document of acknowledgment before the realization of the experiment, which followed the tenets of the Declaration of Helsinki<sup>14</sup>. Yet there was no limit on refraction, ametropic patients were encouraged to come with contact lenses if possible and so did the majority of them. Exclusion criteria were: history of ocular pathology, any difference between pupils or any alteration in at least one of them, opacification of the intraocular media, to have undergone any ocular surgery and to be under any treatment which may affect pupils. Forty right eyes were finally included in the study with a mean $\pm$ standard deviation (SD) in age of 26.98 $\pm$ 7.89 years (from 20 to 59 years).

#### 2.2. Instrumentation

Four devices were used in this survey: WAM-5500, PowerRef II, Neuroptics, and EVA prototype.

NeurOptics VIP-200 (Neuroptics) is a pupillometer based on IR illumination in order to determine the pupil diameter size with an autocalibration process and autofocus<sup>15,16</sup>. Moreover it takes into account the vertex distance. It has a LCD screen which acts as a display and also is used for the focusing of the eye (Figure 3). Fourteen images are taken within one second and for a period of three seconds. The collected data includes maximum and minimum size of the pupil, latency, contraction and dilatation velocities and others<sup>16,17</sup>. It is often used as a gold standard device in pupil size measurement works.

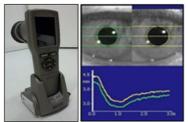


Figure 3. On the left image, NeurOptics VIP-200. On the right image, the device screen display.

The Grand Seiko WAM-5500 (Grand Seiko Ltd. Japan) (Figure 4) is an autorefractor working in the IR spectrum and with binocular open field of view. It gives both values of refraction and keratometry and pupil diameter size. It projects an IR ring into the subject's retina and its reflection is registered with a CCD camera for numerous meridian values. It has been demonstrated its capability for measuring refraction without the participation of accommodation, which would result in false refractive measurements and it is widely used in accommodation measurements<sup>18,19</sup>.



Figure 4. On the left, Grand Seiko WAM-5500. On the right, the display screen.

PowerRef II (Plusoptix Inc. Germany) is an automatic refractor of open field of view based on the photorefraction principle, which is able to register both monocular and binocular measures (Figure 5). Its main use is focused on refraction, used in some cases for those non cooperative patients with subjective methods. However it also shows pupil diameter size value, interpupilar distance and the eye position all simultaneously with a refreshing frequency of 25  $Hz^{20-22}$ . It has been very useful for screening<sup>22</sup>.



Figure 5. Left picture, PowerRef II. On the left part, on the top of the tripod, the IR camera. On the right, the computer with the PowerRef II owns software. Right picture, display of the software.

EVA prototype (Eye Vision Analyzer, Davalor Salut,SL, Spain) is a device based on a binocular virtual reality system with the capability of reproduce many different optometric exams. One of those procedures is a continuous registration of eye movements and the pupil thanks to a circle of IR LEDs which are continuously sending information of that. It is an experimental device comprising two microdisplays with two electro-optical lenses and with two pupil cameras (Figure 6).

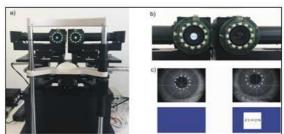


Figure 6. EVA prototype. In a), the mount of the device. On b), the two electro-optic lenses with its IR illumination (LEDs). On c), the display shown by the software.

#### 2.3. Illumination Levels

Three illumination levels were studied: low-mesopic, mid-mesopic and high-mesopic. The study of these three levels and their values has been chosen according to the existing literature<sup>23,24</sup>. In the low-mesopic condition the illumination was of  $0.047\pm0.012$  lx, in the mid-mesopic  $0.8\pm0.3$  lx and in the high-mesopic  $20.33\pm0.577$  lx.

#### 2.4. Examination Protocol

Firstly, in order to discard subjects with anomalous pupil functions, a pupil examination was carried out measuring the reactivity with direct response, consensual response and alternant evaluation.

After that, some questions were asked to the patient in relation with the inclusion/exclusion criteria previously commented. The patient then was blindfolded for five minutes with dark adaptation purposes. During these five minutes, the room was set with low-mesopic light conditions (0.05 lx). Next, the blindfold was removed and the measures of the pupil diameter size were performed, with random order of the devices. For every pupil diameter size measurement, the candidate was instructed to open the eyes and asked to close them afterwards. For three of the four instruments (PowerRef II, EVA prototype and WAM-5500) the patient wore a patch on its left eye, except for the Neuroptics device, in which its working procedure implies covering the eye under study and so it also recreated the patch as in the other situations.

After that, the room condition was set to mid-mesopic illumination condition (0.9 lx) and the patient was asked to stay 1 minute with opened eyes under these conditions for illumination adaptation. Next, the measurements were taken in the same order as before.

Finally, the room was set with high-mesopic illumination condition (22 lx) and the same procedure as in mid-mesopic case was followed.

In three out of four cases (Neuroptics, WAM-5500 and PowerRef II), the patient was asked to look to a red dot on the wall, which was at five meters distance of every device. In the EVA prototype the red dot was virtually created as long as this is a virtual reality system.

All the four devices were placed in the same room in order to minimize illumination differences among them (Figure 7).

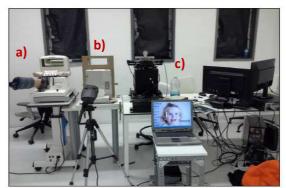


Figure 7. Image of the measurement room, where a) is the WAM-5500 device, b) is the PowerRef II and Neuroptics device and finally c) is the EVA prototype one.

#### 2.5. Pupillometry Data

In this study data of pupil size in mm is recorded, two measurements for each device for each illumination condition. Therefore, for each subject there are a total of twenty-four measures to be analysed. As previously pointed out, these measurements are distributed as follows: for the WAM-5500 device, two measurements in the low-mesopic), two more in the mid-mesopic and two more in the high-mesopic.

#### 2.6. Statistical analysis

The statistical analysis was done using the software SPSS Statistics version 20 (IBM Corp., USA) for Windows and the Microsoft Office Excel 2007 (Microsoft Corp. USA). In all cases a 95% confidence interval was considered.

First of all, a descriptive analysis is made for each illumination condition, where the sample (n) is n=34 for the low-mesopic, n=40 for the mid-mesopic and n=40 for the high-mesopic. The reason of n=34 in the low-mesopic illumination level is because some pupil sizes were unable to be obtained due to its large value (for WAM-5500 and for PowerRef II), therefore they had to be considered out of this particular level. This descriptive analysis is computed with means, standard deviation (SD) and 95% confidence interval calculated as 1.96\*SD. For each case the power analysis was computed through Glimmpse software, obtaining the following statistical powers: 0.993 for the low-mesopic, 1.0 for the mid-mesopic and 1.0 for the high-mesopic. Hence, the number of the sample in each case is sufficient.

After that, ANOVA analysis was carried on, where the values of F and P (Greenhouse-Geiser) are computed and it will be done with Post-Hoc (Bonferroni) analysis.

Finally, Bland & Altman analytic method will be presented. This analysis is used to compare two methods of measurement for the same variable, which should result in good correlation if both have agreement. Nonetheless having high correlation does not directly imply a high agreement level. On the abscissa axis it is represented the average of the tow measurements while in the ordinate one the difference between them is shown. The adjustment will be lineal ( $\mathbb{R}^2$ ) as it is common procedure in the studies of the visual field.

#### 3. Results

First of all, descriptive analysis is presented. Due to extension limitations on this article, the most representative results are shown. Neuroptics values were determined as the most representative ones among the four devices used in this survey for the three illumination conditions, and their values are gathered in Table 1 showing means, standard deviation (SD) and 95% of confidence limit (CL).

Descriptive Analysis								
Illumination	Mean (mm)	SD (mm)	95% CL LOW	95% CL UPP				
Low-Mesopic	6,67	.91	6.37	6.96				
Mid-mesopic	5,26	,84	4,99	5,53				
High-mesopic	4,70	,85	4,43	4,98				

Table 1. Neuroptics descriptive analysis as representative for all the instruments. Mean values, standard deviation (SD) and the lower and upper confidence limits (CL LOW and CL UPP respectively) are shown.

Next, The ANOVA analysis indicates the mean differences between groups, the confidence limits (upper and lower) for each comparison, and the statistically significance of each case (pointed out with a "\*"). Post-Hoc analysis was computed to look for differences between any instruments against Neuroptics. Also, Bonferroni correction was applied in order to be able of multiple comparison analysis. All results are put together in Table 2.

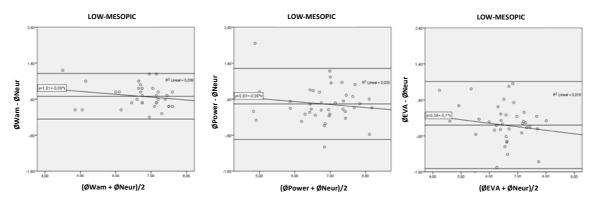
Low-mesopic pair Comparison. F(df=2.161, error=71.316)=24.999		95% confidence limit for difference		ANOVA	
		Mean differences	Lower Limit	Upper Limit	( <i>p</i> )
Neuroptics	WAM-5500	-,479*	-,635	-,324	,000

	PowerRef II	-,277*	-,526	-,028	,023
	EVA Prototype		-,031	,589	,099
Mid-mesopic pair Comparison. F(df=2.501, error=97.520)=43,614			95% confidence limit for difference		ANOVA
		Mean differences	Lower Limit	Upper Limit	<i>(p)</i>
Neuroptics	WAM-5500	-,825*	-1,052	-,598	,000
	PowerRef II	-,695*	-,938	-,452	,000
	EVA Prototype	-,036	-,331	,258	1,000
High-mesopic pair Comparison. F(df=3, error=117)=40.158			95% confidence limit for difference		ANOVA
		Mean differences	Lower Limit	Upper Limit	<i>(p)</i>
Neuroptics	WAM-5500	-,378*	-,623	-,133	,001
	PowerRef II	-,606*	-,843	-,368	,000
	EVA Prototype	,233	-,004	,471	,056

 Table 2. ANOVA results with Post-Hoc Bonferroni analysis for each instrument against Neuroptics and for the three illumination conditions.

Finally, the Bland & Altman (B&A) analysis is made. There is always a comparison of on device against the Neuroptics one for the same illumination condition as Neuroptics is considered a gold standard<sup>15,16</sup>, for instance WAM vs Neuroptics both in low-mesopic. On the top of each graph there is the illumination condition (keep in mind it is comparing with Neuroptics always). In the ordinate coordinates, there is the difference between pupil diameter values of the instrument under study and NeurOptics. In the abscissa coordinate, there is the sum of pupil diameter values of the two instruments and divided by two. In each graph, there are two continuous parallel lines which represent the confidence limits (upper and lower limits). There can be found the point distribution also. Finally, there is the trendline with its correlation factor ( $\mathbb{R}^2$ ), where the higher this factor is the more concordance there will be and thus a systematic error could be present. On the contrary, low  $\mathbb{R}^2$  factors indicate low correlation and discard this systematic error. All the results are found in Figure 8.



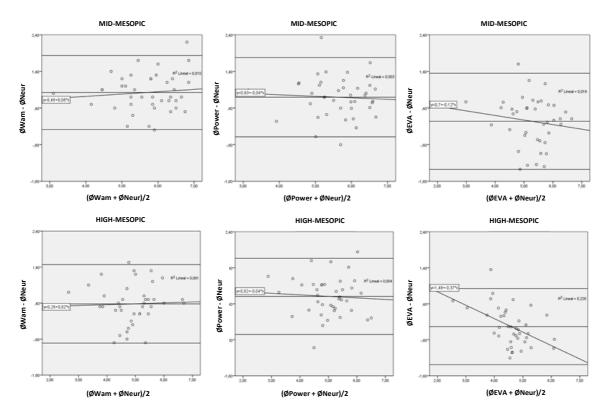


Figure 8. Representation of the different cases against the Neuroptics device results applying B&A analysis. In all cases the adjustment is lineal ( $R^2$ ). All graphs are in the same scale.

#### 4. Discussion

In the present study the agreement between four instruments regarding pupil diameter size has been carried out. First of all, looking at the descriptive results, it can be seen that the results have a concordance with the theory which says that more light relates with lower pupil diameter size and the contrary, lower light relates with larger pupil diameter sizes. The highest value of pupil diameter is 6.76250±0.924506 mm (low-mesopic) and the lowest one 4.70750±0.854367 mm (highmesopic), table 1. Table 2 highlights differences among instruments with ANOVA analysis. Devices WAM-5500 and PowerRef II show bigger pupils in relation to Neuroptics for all three illumination levels whereas EVA prototype shows closer pupil sizes in comparison to Neuroptics. An evidence of that are the mean differences values. A possible explanation of this is that both PowerRef II and WAM-5500 measure with an open field view while EVA prototype is a virtual scene and there could be some accommodation which leads to smaller pupil sizes. Only in the lowmesopic level the mean difference is lower for PowerRef II instead of EVA prototype. In relation to the confidence limits, also the low-mesopic level shows WAM-5500 as the one with the narrowest interval while in the other two illumination conditions EVA shows better results. Therefore, EVA prototype gives pupil sizes closer to the Neuroptics ones in two illumination levels (mid-mesopic and high-mesopic), but in the low-mesopic one WAM-5500 has more precision while PowerReff II would have less error (mean difference).

Bland and Altman graphs are in the same scale, hence a direct comparison for each illumination level can be done. As in the previous analysis, for the low-mesopic level PowerRef II show a lower Bias than the other ones while WAM-5500 shows narrower concordance limits. For the mid-mesopic condition, EVA prototype has the lower Bias and the concordance limits are very similar between WAM-5500 and PowerRef II and a bit more apart on the EVA device. In the high-mesopic level EVA prototype has the best bias and the narrowest concordance limits. The result is then, EVA prototype shows closer pupil sizes to Neuroptics in comparison with PowerRef II and WAM-

5500 for the high-mesopic and mid-mesopic levels but not in the low-mesopic one, where there is more likeness with PowerReff II and WAM-5500.

#### 5. Conclusions

Pupil diameter size is an important tool for many different aspects, from LASIK surgery to cognitive responses. In an effort to maximize the precision for its measurement, objective devices are being distributed on the market. It is important to see if the different instruments show a real value of the pupil size under different illumination conditions so that misleading is evaded. With the measurements carried out in this study, the agreement between 4 instruments has been studied, considering Neuroptics as a gold standard. EVA prototype has a high agreement with it for the high-mesopic and mid-mesopic illumination levels, where the mean difference is under 0.5 mm of pupil size and therefore it is not clinical significant. The two other instruments, PowerRef II and WAM-5500 show worse performance for the tow previously mentioned illumination levels, even leading to clinical significant differences in some cases. For the low-mesopic condition, EVA prototype show worse results than PowerRef II and WAM-5500, however there are no clinical significant values for pupil diameter size mean differences when compared with Neuroptics. Summing up, EVA prototype has shown a good performance in the high-mesopic and mid-mesopic levels (also in low-mesopic but not as good as in others) while PowerRef II and WAM-5500 show some clinical significant differences in certain cases and not a performance as good as EVA device. Therefore, EVA prototype shows the best agreement with Neuroptics among the other two.

#### 6. References

- 1. Puell Marín MC. Óptica Fisiológica. El sistema óptico del ojo y la visión binocular. E. Prints. 2006. 307 p.
- 2. Wang Y, Zhao K. Changes of higher order aberration with various pupil sizes in the myopic eye. Journal of refractive surgery 2002; V2 pp 269-274.
- 3. Campbell F W, Gubisch R W. Optical quality of the human eye. J Physiol 1996; 186 pp 558-578.
- 4. Hecht E. Optics. Fourth Edi. Editorial Addison-Wesley; 2002.
- 5. Atchison D, Smith G. Optics of the Human Eye. Butterworth-Heinemann. 2000;259.
- 6. Nowak W, Żarowska A, Szul-Pietrzak E, Misiuk-Hojło M. System and measurement method for binocular pupillometry to study pupil size variability. Biomed Eng Online [Internet]. 2014;13:69. [citat el 27 de Maig del 2015] Available from: <u>http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4057653&tool=pmcentrez&r</u> endertype=abstract
- Vázquez Castro J. Exploración ocular en Atención Primaria. Semer Med Fam [Internet]. Elsevier; 2002;28(5):265–74. [citat el 27 de Maig del 2015] Available from: <u>http://linkinghub.elsevier.com/retrieve/pii/S1138359302740677</u>
- 8. Leon-sarmiento FE, Prada DG, Gutiérrez C. Pupila, pupilometría ypupilografía.
- Bergamin O, Kardon RH. Latency of the pupil light reflex. Sample rate, stimulus intensity, and variation in normal subjects. Investig Ophthalmol Vis Sci. 2003;44(4):1546–54.
- 10. Laeng B, Sirois S, Gredeback G. Pupillometry. A Window to the Preconscious? Perspect Psychol Sci. 2012;7(1):18–27.
- 11. Schallberg M, Bangre V, Steuhl K-P, Kremmer S, Selbach JM. Comparison of the Colvard, Procyon, and Neuroptics pupillometers for measuring pupil diameter under low ambient illumination. J Refract Surg 2009; In press.

- 12. Bradley J C, Bentley K C, Mughal A I, Brown S M. Clinical performance of a handheld digital infrared monocular pupillometer for measurement of the dark-adapted pupil diameter. J Cataract Refract Surg 2010; 36:277-281.
- 13. Brown S M, Bradley J C. Comparison of 2 monocular pupillometers and an autorefractor for measurement of the dark-adapted pupil diameter. J Cataract Surg 2011; 37:660-664.
- World Medical Association. WMA Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. [Internet]. 2013 [cited 2014 May 5]. p. 1–8. Available from: http://www.wma.net/en/60about/index.html
- Brown SM, Bradley JC. Comparison of 2 monocular pupillometers and an autorefractor for measurement of the dark-adapted pupil diameter. J Cataract Refract Surg [Internet]. ASCRS and ESCRS; 2011;37(4):660–4. [citat el 29 de Maig del 2015] Available from: http://dx.doi.org/10.1016/j.jcrs.2010.10.059
- 16. Bradley JC, Bentley KC, Mughal AI, Bodhireddy H, Brown SM. Dark-adapted pupil diameter as a function of age measured with the NeurOptics pupillometer. J Refract Surg. 2011;27:202–7.
- 17. Martínez-Ricarte F, Castro a., Poca M a., Sahuquillo J, Expósito L, Arribas M, et al. Pupilometría por infrarrojos. Descripción y fundamentos de la técnica y su aplicación en la monitorización no invasiva del paciente neurocrítico. Neurologia. 2013;28(1):41–51.
- 18. Lopez C, Fuente D, Sanchez-cano A, Segura F, Pinilla I. Comparison of Anterior Segment Measurements Obtained by Three Different Devices in Healthy Eyes. Hindawi Publishing Corporation; 2014;8.
- Lin Z, Vasudevan B, Zhang YC, Qiao LY, Liang YB, Wang NL, et al. Reproducibility of nearwork-induced transient myopia measurements using the WAM-5500 autorefractor in its dynamic mode. Graefe's Arch Clin Exp Ophthalmol. 2012;250:1477–83.
- 20. Allen PM, Mcoptom H, Optom HRBS. Repeatability and Validity of the PowerRefractor and the Nidek AR600-A in an Adult Population with Healthy Eyes. 80(3):245–51.
- 21. Hunt OA, Wolffsohn JS, Gilmartin B. Evaluation of the measurement of refractive error by the PowerRefractor: a remote, continuous and binocular measurement system of oculomotor function. Br J Ophthalmol. 2003;87:1504–8.
- Abrahamsson M, Ohlsson J, Björndahl M, Abrahamsson H. Clinical evaluation of an eccentric infrared photorefractor: The PowerRefractor. Acta Ophthalmol Scand. 2003;81:605–10
- 23. Bootsman S, Tahzib N, Eggink F, De Brabander J, Nuijts R. Comparison of two pupillometers in determining pupil size for refractive surgery. Acta Ophthalmol. Scand. 2007; 85:324-328.
- 24. Rosen E S, Gore C L, Taylor D, Chitkara D, Howes F, Kowalewski E. Use of a digital infrared pupillometer to assess patient suitability for refractive surgery. J Cataract Refract Surg 2002; 28:1433-1438.

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