ISSN: 2573-9573

Review Article

Journal of Ophthalmology & Clinical Research

Cosmetic Laser Iridoplasty

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Submitted: 27 Aug 2018; **Accepted**: 03 Aug 2018; **Published**: 10 Sep 2018

Introduction

Ocular cosmetic alterations have been treated conservatively so far with contact lenses and aesthetic prostheses, and through different types of surgical interventions.

Usually, the causes of ocular cosmetic problems are due to congenital origin or secondary to drug iatrogenesis, metabolic diseases, accidental trauma or ophthalmologic surgeries.

The deformities, irregularities, defects (coloboma) or total absences of the iris (anhiridia) have been treated with intraocular implants of the brand Ophtec, Morcher or Dr Schmidt.

To solve the cases of congenital or acquired corneal opacities, contact lenses and prostheses have been used, or even keratopigmentation.

Regarding the pigmentary disorders of the iris, such as heterochromia, mono or bilateral, partial or complete, and nevus, single or multiple, there has been no safe, effective and permanent solution other than cosmetic contact lenses.

Given that the safety and effectiveness of contact lenses is very high, any surgical solution that puts visual health at risk should be evaluated with great care.

Up to now, the surgical techniques proposed to treat pigmentary iris problems have been mainly two: the cosmetic intraocular lenses (Newiris, Brightocular) and corneal tattoo techniques (Neoris, Corneal Eye Tattoo).

According to our point of view these two techniques should not be indicated due to reasons of safety and aesthetic result. Regarding intraocular lenses, they provoke a clear conflict of space in the anterior chamber, which causes glaucoma, uveitis and irreversible endothelial damage [1-10]. Due to these serious complications, the implants must be usually removed after a few months [11-13]. In relation to keratopigmentation, cases of corneal complications have also been described, but cosmetic problems are more evident. The biological dye introduced into the cornea progressively disappears by diffusion over time, so the color fades, and on the other hand, the best result obtained never improves that of cosmetic contact lenses, so its realization is meaningless.

In both cases, the effect is always artificial, “robot eye”, with fixed pupils that do not react to light, weird synthetic colors, and functional limitations of the visual field, together with photophobia and glare.

New Proposal: Cosmetic Laser Iridoplasty

After a few years of basic research and evaluation of possible alternatives, in 2012 we began the technological development and clinical studies of the solution with laser application. A priori offered two clear advantages over the previous possibilities, greater security because it is not a surgical intervention, and naturalness of the result, by obtaining biological tissue colors of the patient and by not altering the functionality of the pupil, which continues to react to light and darkness in a normal way [14,15]. Thus, visual aberrations and limitations of the peripheral visual field are not caused. The premises of the project were defined but should be demonstrated over the following years. Several phases were planned: First security phase: 2012-2014 Second phase of effectiveness and predictability: 2014-2016 Third phase of technological improvement: 2017-2018 Fourth phase of technical sophistication: 2019-2020.

Fortunately, our premises were confirmed over time and, not without big effort, we were able to solve the problems we encountered on the road and achieve a state close to the excellence of the original technique. This is the summary of the last 7 years of scientific, clinical and technological progress, similar to that performed in the past with cataract surgery (intracapsular, extracapsular, intraocular lenses, phacoemulsification, femtolaser) or refractive surgery (radial keratotomy, PRK, Lasik, Intralasik, Smile).

First Phase of 2012-2014

Of course, safety was the first requirement to advance the clinical trial. Only 6 cases were treated in 2012 in order to assess the results obtained in the medium term as well as the complications generated.

The New eyes laser used was version 1G and several sessions were programmed for each procedure. Although the cosmetic results were fast and spectacular from the beginning, the technique was a bit aggressive, proportional to the amount of pigment in each eye. Cases with little pigmentation and clear type were very easy to treat, while dark eyes were more difficult.

In the first phase of safety, clinical studies of visual acuity (chart recovery curve), eye pressure (Goldman recovery curve), camerular angle and trabeculum (by Goldman gonioscopy), anatomical structure of the iris by means of OCT (Zeiss optical coherence tomography) and corneal endothelium (with Konan specular microscopy) were established.

Regarding vision and eye pressure, we found directly proportional evolution curves, the increase in pressure observed after laser application was related to the transient decrease in vision. Both parameters returned to normal quickly depending on the duration of the laser session and the type of pigmented iris (Figures 1 and 2). After one or two hours both the vision and the eye pressure returned to normal values, and after twenty-four hours they were totally physiological. During twelve months, there was no decrease in visual acuity or secondary elevations of ocular pressure.

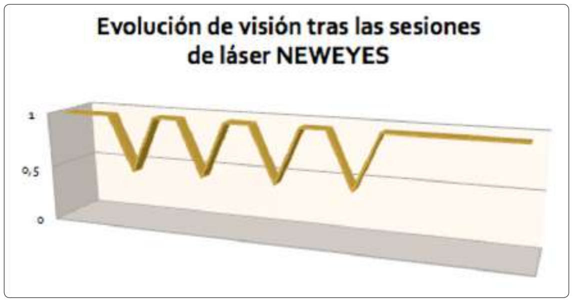

Figure 1: Recovery curve line of vision after each laser sesion

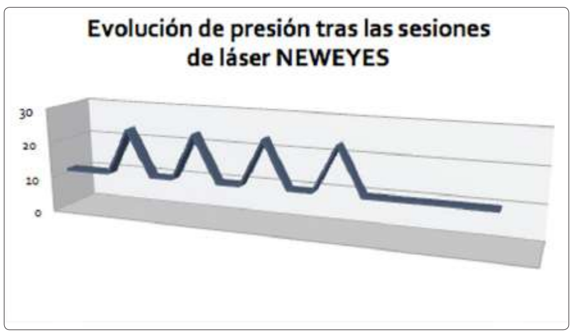

Figure 2: Recovery curve line of intraocular pressure after each laser sesion

The trabeculum and camerular angle was explored by Goldman lens gonioscopy, and the findings showed a transitory increase in the camerular pigmentation but only in the lower quadrant (from five to seven hours), due to the postural treatment prescribed to the patients to maintain the head raised during the first five hours after each laser session. After twelve months no increase in angle pigmentation was observed in the upper (270 degrees), and a progressive pigmentary clearance of the lower third (90 degrees) was observed (Figure 3).

Figure 3: Subtle pigment dispersion in lower camerular angle

The anatomical structure of the iris was studied "in vivo" with optical coherence tomography (OCT), using the anterior segment tomograph Visante by Zeiss, in its analysis mode of the camerular angle and wide field view to observe the entire anterior chamber. The resolution level of the OCT is not enough to analyze the inside of the Schlemm channel and its possible secondary block. Removal of the anterior pigmented layer of the iris was observed without stroma or posterior epithelium damage, which confirmed the limited effect of the laser on the surface of the iris and the preservation of its anatomical and functional structure (Figures 4 and 5). We never observed angular blockage by debris. The series of specular microscopy with the Konan model showed no repercussion of the laser on the cells of the corneal endothelium. No differences were detected between before and after applications in terms of density, heterogeneity and hexagonality values (Figures 6 and 7). After two years of treatment in a small number of patients, the safety of the procedure was demonstrated and aesthetic results were surprising from the beginning (Figures 8 and 9).

Figure 4: Removal of anterior pigmented iris layer with no stroma or posterior layer damage

Figure 5: Partial removal of pigmented iris Surface with no deeper action

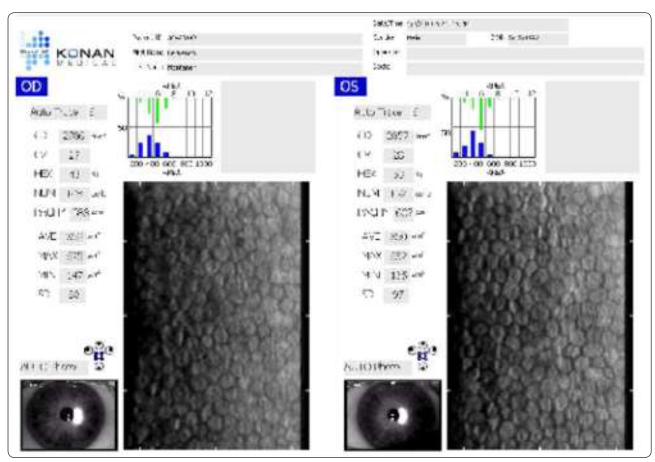

Figure 6: Konan specular microspocy analysis of corneal endothelium just after laser sesion. No variation was observed between before and after studies

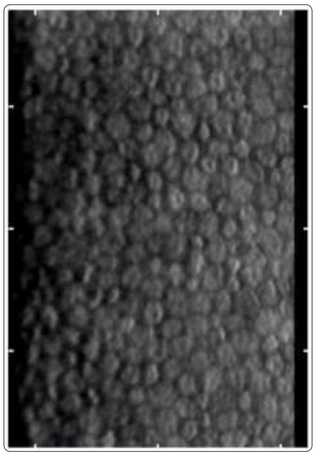

Figure 7: Density, heterogeneity and hexagonality values were similar between before and after studies

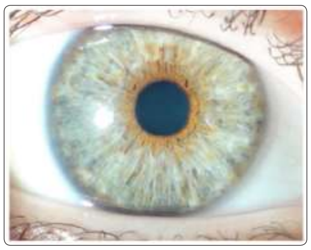

Figure 8: Regular cosmetic outcome from a level 3 pigmented eye. A typical turquoise color, light mixed green and blue, with a very thing pupil ring of original brown melanin by security reason (no laser damage to lens)

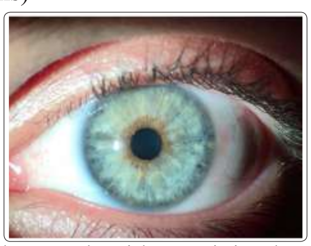

Figure 9: Bright blue result with so minimal pupil brown ring

Second Phase 2014-2016

The objectives of the second stage of development were to provide a new classification of iris pigmentation, to ensure the predictability of the result, to investigate the effectiveness of new lasers and to test specific medications to eliminate the undesired effects of the technique. Undoubtedly it is essential to advance in any investigation to have a tool that allows us to evaluate cases, both before treatment and afterwards. It was totally necessary to work with a classification, the first described on the level of iridian pigmentation (Figure 10). Thus we could group the eyes in four degrees according to their type of melanin, in order to predict the result of the laser and plan well the necessary sessions. Once the treatment schedule is concluded, we can better check its effectiveness thanks to the classification. To address the challenge of achieving good predictability of laser iridoplasty, we first had to clarify the scientific bases that determine the color of the eyes. The fundamental law is genetic and it is the Theory of the two genes, green and blue (Figure 11).

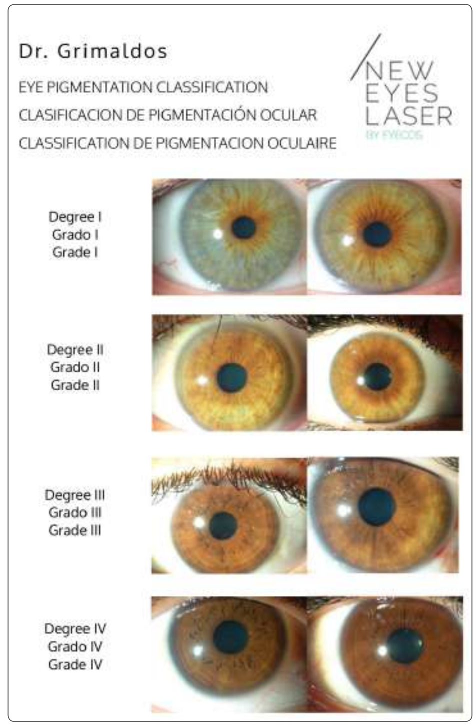

Figure 10: Grimaldos Iris Pigment Classification. Levels one (very light eye) to four (very dark brown)

BB bb	Brown
BB Gb	Brown
BB GG	Brown
Bb bb	Brown
Bb Gb	Brown
Bb GG	Brown
bb GG	Green
bb Gb	Green
bb bb	Blue

Figure 11: Theory of the two genes fo reye color. Allele combination chart. B: Brown, G: Green, B: Blue

The first thing to notice about this table is that when there is a B, the eyes turn brown. So B is dominant over G and b. In addition to that, when there is a G (but not B), the eyes turn green. Then, G is dominant over b. Some of these details must seem a bit strange. First, there are two distinct genes, but B of one gene is dominant over G of the other gene. The other strange thing is that the recessive form of both genes is blue. These two things are related. The eye color corresponds to the amount of melanin pigment in the eye. Not anywhere in the eye, but in a special place, the stroma of the iris. A lot of melanin in this part of the eye results in brown eyes and less melanin results in green eyes. Little melanin or the absence of melanin in the stroma of the iris results in blue eyes. This is the reason why the brown color is dominant over the green color. Version B of OCA2 tells the eyes to produce a lot of melanin. The G version of the gey gene tells the eye to produce some melanin. What happens if both genes are present? A lot of melanin is produced and this results in brown eyes. The fact that the recessive form of both genes is blue makes sense. The recessive form of both genes does not work and that is why it is recessive. An OCA2 gene without function is equal to a gene without function, melanin does not occur in the stroma. The absence of melanin in the stroma results in blue eyes. Now we can understand why brown is dominant over green. And why blue is recessive to both. The EYCL1 gene on chromosome 19 is responsible for the green and blue color of the eyes. On chromosome 15 is the EYCL2 that is responsible for the brown color. Also in chromosome 15 is the EYCL3 that causes pigmentation of skin and hair, and whose mutations cause different forms of albinism.

Based on the Theory of the two genes we first develop a software and then a mobile application to calculate the result of the laser iridoplasty taking into account the personal features with those of the parents: eye, skin and hair color (Figure 12). However, we found cases of ignorance of the ancestors, in which the use of the Predictor program was not reliable. So we carried out research with prestigious geneticists who developed a special probe that located the genes responsible for eye color and their different melanin production capacities. The biochip test is a non-invasive method that is performed from a sample obtained by buccal swabbing and that increases reliability in the prediction based on objective data (DNA analysis) and not only based on statistical predictions, as is usually done habitually. The genes that were studied were the HERC2, TYR, OCA2 and SLC24A4, closely related to the pigment levels of the retina. HERC2 is a neighboring gene of OCA2 that regulates the expression of the latter and determines to a large extent the pigmentation levels of the human iris. Certain variants in these genes determine for example the blue color of the eye. TYR is the gene that codes for tyrosinase, one of the enzymes that regulate melanin levels. Finally, the SLC24A4 gene is involved in the specific metabolic mechanisms of the retina. For the analysis of these five genes, the DNA of the buccal samples is purified. The fragments of interest located within the genes mentioned above are amplified by PCR and are subsequently studied by direct sequencing or analysis of fragments with the technology established for this purpose. As a result, specific genotypes are obtained for each person in the five genes studied, allowing the prediction of levels of iris pigmentation in each individual (Figures 13 and 14).

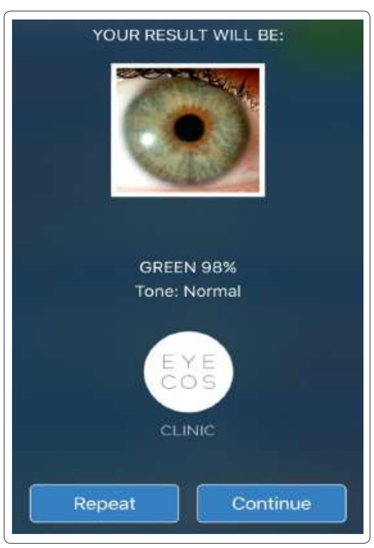

Figure 12: Scientific result by Eyecos App Predictor for a level 3 pigmented eye. A normal tone green outcome will be expected at 98% probability. Photo shows a real patient example

Figure 13: Genetic biochip box to ensure prediction based on DNA analysis. This test only needs to process a sample of saliva obtained by mouth scraping

INFORME:
DETERMINACIÓN GENÉTICA DEL NIVEL DE PIGMENTACIÓN DEL IRIS

CÓDIGO DE MUESTRA: GR11
FECHA DE ANÁLISIS: 02. – 16.6.2016

MÉTODO DE ANÁLISIS: A partir de la muestra de células bucales obtenida mediante raspado con hisopo, se obtiene el material genético (ADN) para análisis mediante PCR. Posteriormente se analiza cada uno de los fragmentos obtenidos mediante las técnicas de secuenciación directa y/o restricción.
El análisis cubre los siguientes polimorfismos genéticos (SNPs) en 4 genes relacionados con el nivel de pigmentación y el color del iris:

HERC2	SLC24A2	HERC2	OCA2	OCA2	TYR
rs12913832	rs12896399	rs1129038	rs1800407	rs1800401	rs1126809
AG	GG	AG	AG	CC	GG

CONCENTRACIÓN DE PIGIMENTO: MEDIA-BAJA

Los genes analizados dan información sobre 6 tonalidades de color del iris.
El gráfico representa la distribución genética y la probabilidad de correspondencia con las diferentes tonalidades que permiten predecir su color de ojos.

CAPACIDAD REGENERATIVA DEL PIGMENTO: probablemente MEDIA-BAJA

CONSIDERACIONES SOBRE LA TÉCNICA
- La coloración del iris sigue un patrón multifactorial, por tanto, existen múltiples genes, unos conocidos y otros no, para su determinación. Por tanto, todo test diseñado para determinar la concentración del pigmento del iris, incluyendo el presente, sólo tendría un valor relativo y de probabilidad.
- El color de los ojos está determinado por la cantidad y distribución de la melanina en el iris. Los ojos marrones contienen más melanina que los ojos verdes, mientras que los ojos azules tienen muy poca.
- Este test analiza 4 genes que han sido vinculados con la determinación de la concentración del pigmento del iris que, si bien no son todos los que participan en este proceso, sí son algunos de los más representativos en población caucásica. En este sentido, su valor predictivo es relativo, siendo más certero en la identificación del color marrón versus no marrón (fiabilidad >95% en este sentido).

Fecha: 27.6.2016

Fdo. Dr. J.I.Lao (COMB 41722)

Figure 14: Typical genetic report for a patient. Main eye color genes are studied to offer most accurate prediction

Two years after the start of the clinical trials, we found an unexpected adverse effect, which was the repigmentation of the iris. Due to it, after six to twelve months after treatment may appear a gradual darkening of the color obtained initially, due to the production of scar tissue and new melanin. The fact was related proportionally with the degree of initial pigmentation and with genetic factors inherited from the parents. New sessions of laser 1G only solved the problem in part, so we started two new lines of research: histological and pharmacological studies. First, we analyzed a series of corpse eyes with different degrees of pigmentation, together with specialized anatomopathologists. The main conclusions we reached were the following (Figures 15, 16 and 17): 1-Eumelanin is brown and yellow pheomelanin. Eumelanin is concentrated in the posterior epithelium and is mixed in both the stroma and the anterior epithelium. 2-There is a maximum concentration of melanin in the peripupillary area and upper quadrant. 3-The 65.9% of iris cells are melanocytes, and their percentage is the same in blue, green and brown eyes. 4-The difference in color is due to the type of melanin and the thickness of the granules. 5-A more extensive classification of the Grimaldos one could be divided histologically into nine grades: One=Light blue, Two=Dark blue, Three=Blue with brown ring, Four=Green, Five=Green with brown ring, Six=Brown central with peripheral green, Seven=Brown with some green, Eight=Full light brown, and Nine=Full dark brown. 6-Prostaglandins increase the thickness of melanin granules in the anterior epithelium.

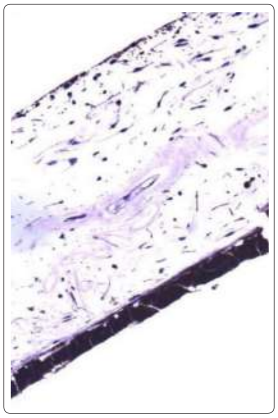

Figure 15: Histological sample of a low pigmented iris. Eumelanin (dark pigment) is highly concentrated and at thick posterior epithelium, while a very thin layer is showed at surface (anterior epithelium). In the middle, large stroma has few scattered granules of melanin

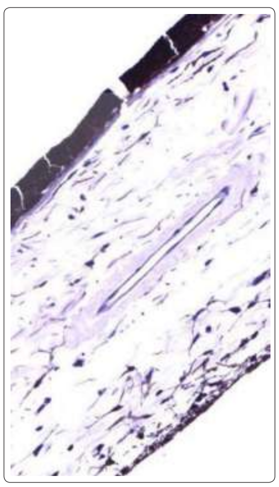

Figure 16: Every eye, even blue ones, show a thick and dark posterior epithelium layer in order to light protection. Stroma contains many functional structures such as blood vessels, muscles (pupil sphincter and dilator) and collagen fibers

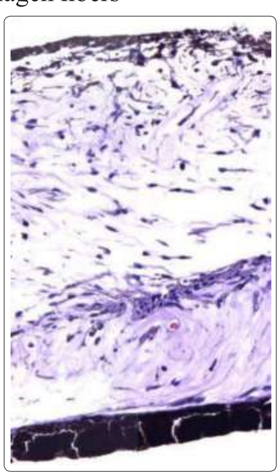

Figure 17: Typical level 4 pigmented eye showing a dark posterior and anterior epithelium, and also a high density of stroma melanin granules

The second histological study we conducted was to analyze the effects on the iris of corpse eyes of four different laser wavelengths. We tried to find out what kind of laser could avoid the pernicious effect of repigmentation, safeguarding the integrity of the anatomical and functional structure of the iris. Thanks to these works we introduced the 2G version of the Neweyes laser, which we used for a time in combination with the 1G. With the 2G laser, the possibility of reactive scar mechanisms after laser application was eliminated (Figure 18 and 19). At the same time, we began the pharmacological studies with researchers from prestigious laboratories of substances that facilitated the elimination of the pigment and inhibited the production of secondary melanin. The two main molecules that were useful are sodium heparin and alpha arbutin both at low concentration. Heparin helped us as a coadjuvant in cleaning the residual cellular debris of the anterior chamber and increasing the brightness of the final color. However, alpha arbutin showed a relatively low level of effectiveness in the reduction of reactive melanin (Figure 20 and 21). Topical prostaglandins, commonly used in the form of anti-glaucoma eye drops or serum to enhance the growth of the eyelashes have been shown to greatly increase the production of iris melanin. In a few months they are able to change a blue eye (Grade 1) into a dark brown (Grade 4), even irreversibly. On the other hand, in the second phase of research, we formulated a specific medical protocol to neutralize the transient elevations of ocular pressure and the episodes of inflammation and transient iritis fugaz (Figure 22). It has also been necessary to have special pharmacological protocols for cases of asthma (contraindicated blockers), intolerance to non-steroidal anti-inflammatory drugs (only eye drops without tablets), hypersensitivity to medications, etc. With the aim of being able to perform remote diagnostics (tele check up), we also began to develop photographic techniques that can be easily used by patients to obtain quality photos of the eyes, good focus, centered and lighting (Figure 23 and 24).

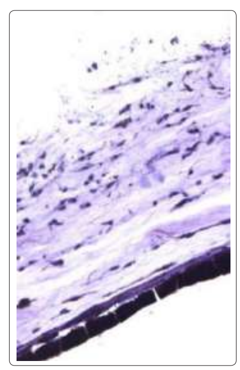

Figure 18: Removal of anterior pigmented epithelium with no stroma or posterior layer damage

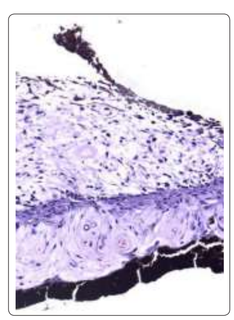

Figure 19: Partial removal of anterior pigmented epithelium by Neweyes laser

Figure 20: Low concentrated heparine eye drop (Hyloparin®) used to facilitate clearance pigment debris out the eye

Figure 21: Low concentrated Alpha Arbutin eye drop used to reduce melanin production after laser application but its effect was minimal with time

Figure 22: Apraclonidine 0.50% eye drop is indicated just before and after laser sessions to avoid eye pressure raises. Same medical protocol is usually followed to perform laser trabecuplasty procedures

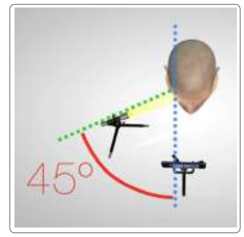

Figure 23: Special photo technique to take good eye photos by yourself. Light source should be directed with an angle of 45 degrees to avoid reflections and get a fine result

Figure 24: Current smartphones have high quality cameras and can be used with a tripod

Finally, we developed the first version of the IRÎZ Scanner, which thanks to specific software, was able to evaluate the degree of pigmentation and perform colorimetry, pachymetry and two dimensions topography studies. The most important parameters offered by the first iridian Scanner were the physiodynamics tools, which would then be optimized with the second version of the IRÎZ Analyzer.

Third Phase 2017-2018

New Mobile Apps

Two new mobile applications have greatly facilitated the daily work of the Eyecos Clinic in Barcelona. In the first place, Eye Selpfie has made it possible for the first time that a patient can take pictures of their eyes without the help of anyone and with high image quality, good focus, perfect centered and adequate lighting (Figures 25 and 26). The Eye Selfie App has finally made it possible to perform a remote diagnosis and effective follow-up (Figure 27). And second, the new App Simulator 3D is capable of generating three dimensional models of the patient's original eyes and simulations of the results predicted by the App Predictor (Figure 28). App Sim 3D can also simulate the effect of ambient lighting on the appearance of eye color. In low light the black pupil dilates and the intensity of color decreases proportionally (Figure 29). Finally this App can simulate the effect of the distance observation on the appearance of the eyes (Figure 30).

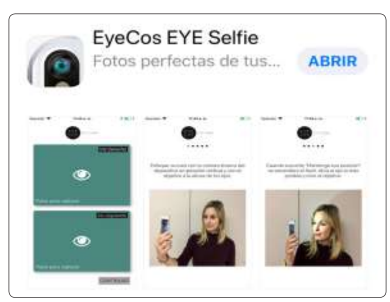

Figure 25: Eye Cos Eye Selfie App. Amazing way to take by yourself and automatically perfect HQ eye photos (good focus, centered

and adequate lighting). Both eyes are registered and saved on the smartphone. In order to check up, these two pictures can be easily submitted to the doctor by email and a quick medical report is received by email too

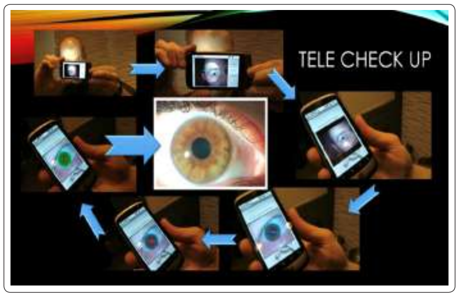

Figure 26: Automatic mode to take perfect eye photos by EyeCos Eye Selfie App

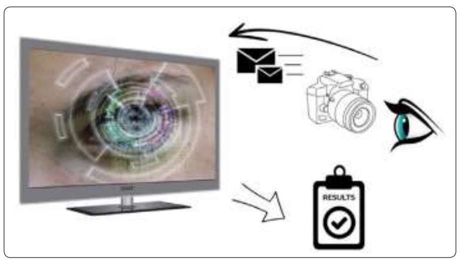

Figure 27: Both eyes pictures are sent to the doctor. After a detailed study by Grimaldos Iris Software, a quick medical report is received by email (remote check up and follow up)

Figure 28: Eye Cos 3D Simulator App generates automatically three dimension eye models to see final outcome. Once App Predictor calculation has be done, the patient can compare laser cosmetic effect, before and after procedure

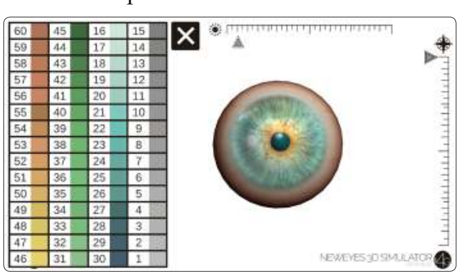

Figure 29: EyeCos 3D Simulator offers a dynamic simulation to understand how changes pupil size with different light levels

Figure 30: Sim 3D App has also a tool to check distance effect on eye color. A proportional relationship between far-near observation and brightness is so evident

New Software Version of IRÎZ Summary

The Iris Analysis Software, Grimaldos Summary, was perfected to a large extent at the level of graphics, maps and parameter quantification thanks to new algorithms and new colorimetric, pachymetric, densitometric and topographic scales (Figure 31). With them it has been possible to standardize the explorations, an essential milestone for the scientific advance of the technique. In addition, the second version of the IRÎZ Summary has made possible so many improvements as dynamic pupilometry, follow up in time, comparison between patients and partial studies of halves and quadrants. But the biggest challenge was to unravel the laws that govern the dynamic physiology of aqueous humor in situations of overload. To do this we perform anatomical, physiological and physical studies of bio reology, with the help of mathematicians specialized in fluid dynamics.

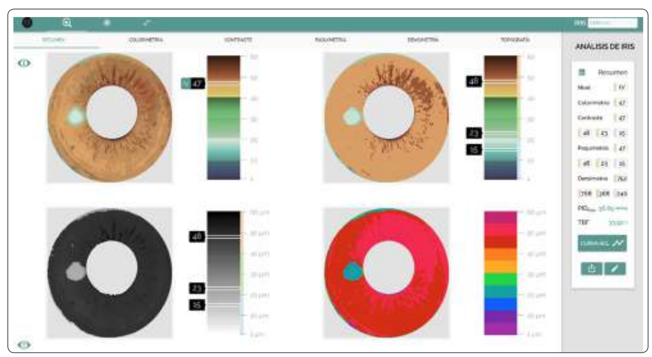

Figure 31: Grimaldos Iris Summary, is a reference standard about a quantitative iris study. This advanced software offers graphic maps of colorimetry, color contrast, pachymetry, densitometry and 3D topography. Dynamic fluids parameters are also calculated in order to warrant safety levels. Finally, dynamic pupillometry, follow up and partial evaluations, even between different patients, are available

New Eye Pressure Formula (IOP)

The classic Goldman eye pressure formula was not enough to predict the behavior of the ocular drainage system after the application of the Neweyes laser. Therefore, we had to describe a new IOP equation (Grimaldos Formula), which will contemplate all the variables involved in hydrodynamic stress situations in the anterior chamber (Figure 32). It is a regression equation and not theoretical, in the style of the SRK formula for the calculation of the dioptric power of the intraocular lenses to implant in cataract surgeries.

Figure 32: Grimaldos eye pressure formula. A new equation that takes into account the density of aqueous humor in overload stress

New Version of the Scanner with OCT and HD Photography

The second version of the IRÎZ Scanner incorporates great advantages, such as a new software for capturing high quality images and its processing with the Grimaldos Summary Software, also a wide-field optical coherence tomography (OCT) module and a high precision pneumatic tonometer and tonographer (Figures 33 and 34).

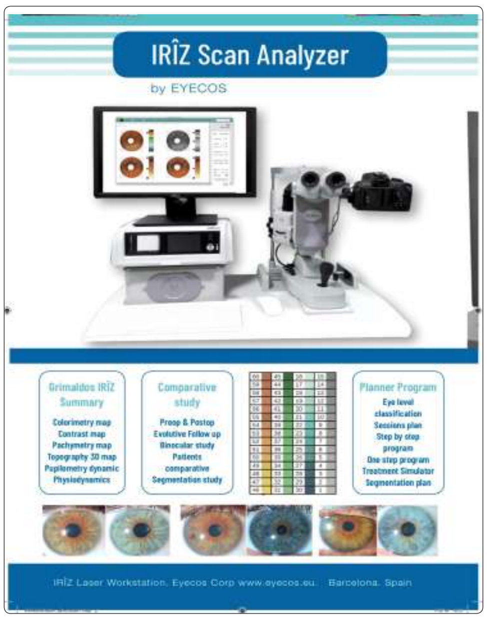

Figure 33: New IRÎZ Scanner version, with an improved capture system of HQ images, a pneumatic tonometer and tonographer and an OCT module

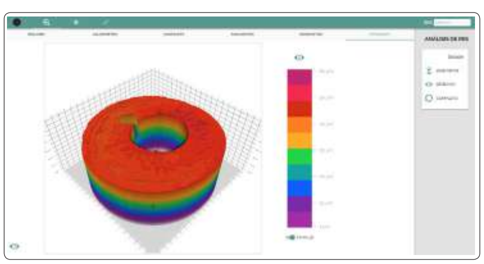

Figure 34: Three dimension iris color topography. A dynamic tool enables us to check any tissue angle

New 3G and 4G Laser Versions

A very special collaboration with a team of leading laser engineers has enabled the incorporation of two new generations of Neweyes laser, 3G and 4G. The 3G is the natural evolution of 2G one but with a different wavelength, which makes it minimally aggressive and selective of the iridian stroma tissue. The 3G laser has made possible the single sessions for the whole iris without any acute complications. On the other hand, the 4G laser is a device that combines the effects of the original 1G with those of 3G. This double action mechanism produces a direct cleaning of the melanin and at the same time avoids late repigmentation by definitive destruction of the melanocytes (Figures 35 and 36).

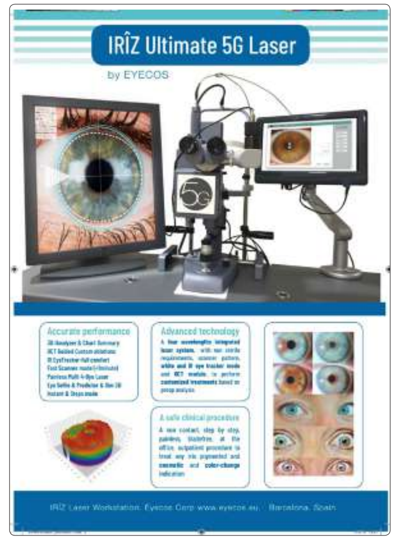

Figure 35: New 5G Neweyes laser version. An integral multiple laser system. Other remarkable improvements have been updated, as a big color screen, scanner patterns, and planner program screen and eye tracker

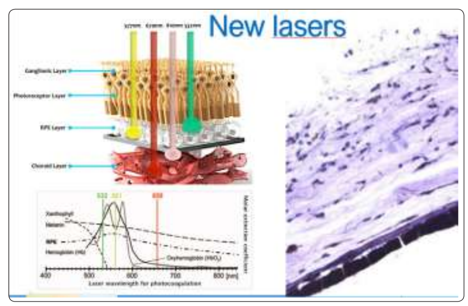

Figure 36: Different laser wavelengths must be tested on corpse eyes in order to know any specific tissue effect. This basic research is mandatory to check new laser options

New Eye Tracker Module

The ultimate 5G version of the new eyes laser refers to an integral system consisting of three-four different lasers. It also incorporates multiple scanner patterns and a passive eye tracker with visible light (not infrared) (Figure 37).

Figure 37: Large color screen to check iris treatment and manage any sudden movement by eye tracking

New Planner Program

The purpose of the IRÎZ Workstation is the routine realization of customized laser iridoplasties. As there are no two identical irises, personalized treatments are mandatory. The differences are in the degree of pigmentation, type of melanin, thickness, topographic irregularity, pupillary function and cicatricial capacity. On the other hand, heterochromia spots must be accurately mapped in order to eliminate them accurately.

After obtaining a meticulous analysis of the iris with the IRÎZ Scanner and the Grimaldos Summary Software, we have to introduce these data in the Planner Program to generate the specific treatment guideline, with number of sessions and specific parameters to be used in each case (laser type, energy) (Figure 38).

Figure 38: Accesory screen to manage Planner Program

Excellence of the Technique

After seven years of hard research and development we can affirm that we have achieved the challenges that we set ourselves in 2012 (Figure 39-50) and we can enunciate the following definitions:

Clinical Definition

"Laser cosmetic iridoplasty is a non-contact, step by step, painless, bladefree, at the office & outpatient procedure".

Technical Definition

"LCI is an integral multiple laser system, with non-sterile requirement, scanner patterns, eye tracker & OCT module to perform Custom Treatments".

Figure 39: Final cosmetic outcome of a monocular heterochromia secondary to an old and traumatic caratact surgery. Treated eye moved from a brown level 3 to a natural light blue, similar to contralateral eye

Figure 40: A typical case of congenital heterochromia. Left eye turned from brown to green, as right one

Figure 41: Another example of congenital heterochromia before laser treatment. Right eye is blue and left brown

Figure 42: Same Figure 41 patient after procedure. Left eye turned from brown to blue, as right one

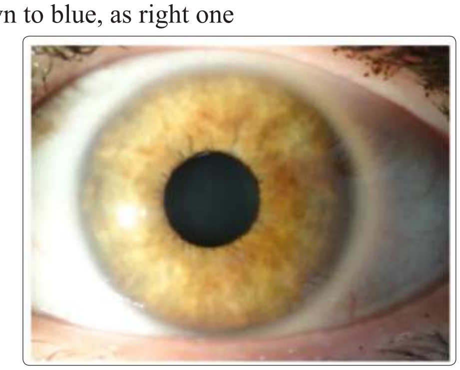

Figure 43: Left eye of 41 Figure patient before laser treatment

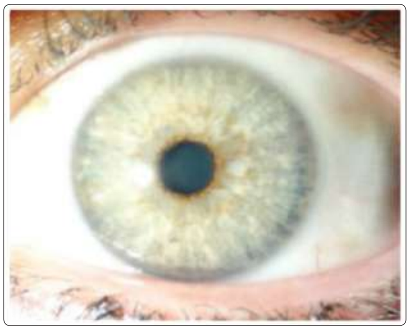

Figure 44: Left eye of 42 Figure patient after procedure

Figure 45: A case of multinevus before laser

Figure 46: Same 45 Figure patient after treatment

Figure 47: Detailed and magnified imaged of laser effect. Original brown in the middle and new blue color at periphery

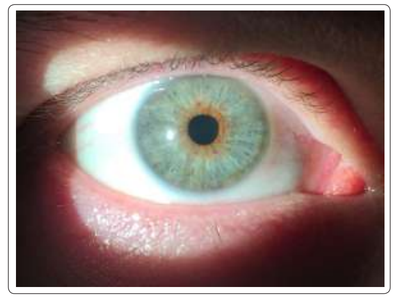

Figure 48: Bright blue outcome. Minimal reamining melanin close the pupil

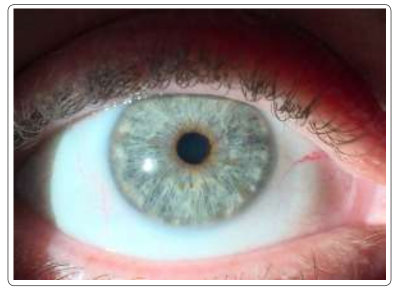

Figure 49: Fully clean eye with pigment absence

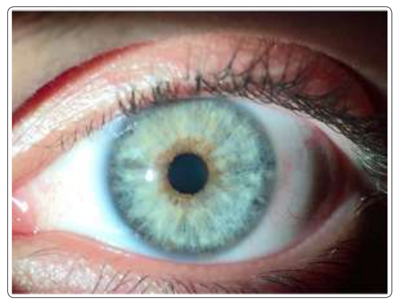

Figure 50: Very bright blue outcome from a level 3 pigmented eye

Rigid Admission Criteria for Candidates

General

-Over 18 years old and healthy -No psychiatry history -No drugs or hormones addiction -No selfimmune diseases.

Ocular

-No glaucoma history -Eye pressure under 15mmHg -No uveitis or iritis history -No high refractive errors -Not levels IV. Better pigment levels: I, II and III.

Fourth Phase of 2019-2020

New IRÎX Version of the Scanner and New Eyes Laser

We are already working on the new generation of IRÎX Scanner, with more precise and faster measurements of the iris parameters, and on the new "magic" laser IRÎX EXLICER/INLICER, which will make it possible for us to state an awesome definition of laser iridoplasty: "Bilateral technique, in a single step, with immediate and permanent aesthetic effect, without patient discomfort or side effects in the short, medium and long term".

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