IMIOL

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Period report – Final report
Project duration – 2 Years

Project period –

01-10-2017 – 30-09-2019

PART A

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 713694.

Project Full Title	Imaging Techniques to Study and Improve the Performance of Intraocular Lenses
Host institution	Instituto de Óptica 'Daza de Valdés', Madrid, Spain
Scientist in charge	Susana Marcos
Start date of the project	01-10-2017
Duration of the project	2 years
Periodic report no.	2
Period covered by the report	01-10-2017 –30-09-2019
Project website address (if any)	

Declaration

I, Alberto de Castro, hereby declare that

- Both Part A and Part B of this Report and its related appendices have been approved by the Scientist in-charge, Susana Marcos and any other relevant party (for e.g. secondment academic/non-academic organisation).

- The contents of the publishable summary (Section 1 of Part A) do not contain any confidential data, and have been approved by the Scientist in Charge and any other relevant party ((for e.g. secondment academic/non-academic organisation) involved in the generation of the Results.

Signed,

Alberto de Castro

Madrid, 21-03-2020

1. Summary for publication

1.1 Summary of the context and overall objectives of the project

This section must be of suitable quality to enable direct publication by the MULTIPLY Management Team. It should be easy to read i.e. written in a language easily understandable by a broader public, thereby promoting the dissemination and supporting the exploitation of EU funded results. It should preferably not exceed 7480 characters (equivalent to two pages of a text document).

PLEASE NOTE – As this summary will be made publically available, this part must not contain any confidential data.

The summary for publication must be drafted as a "stand-alone" text. No references should be made to other parts of the report. References can be made only to publicly available information.

Beside the summary, diagrams or photographs illustrating and promoting the work of the project can be provided

During cataract surgery, the opaque crystalline lens is removed and replaced by an intraocular lens (IOL) whose power is selected to minimize the refractive error of the patient after surgery. While the selection of the power of the IOL to implant is an optical problem, it is not always solved using optics itself. Some of the first approaches proposed in the 1980s used paraxial optics to calculate the IOL power so that refractive error is minimized after the surgery. However, soon several methods that used the outcome of previous surgeries as data, and where the IOL power was calculated using formulas appeared. Nowadays, several generations of these formulas coexist and surgeons use one or the other depending on the characteristics of the eye. While the formulas are optimized with thousands of patients and can be very accurate for most of patients, they fail when the eye geometry is not within the normal range, or when the patient's cornea have had a previous eye surgery such as refractive surgery or even a previous cataract surgery. At present, more and more people in need of cataract surgery have undergone previous eye surgeries years before, such as refractive surgery, and there is a need for new methods that would prove accurate to select the best IOL for these patients. This project aims at building correct eye models to find the right power and choose between different IOL designs.

In the host research group there is a long term experience in measuring the shape of the optical surfaces of the anterior segment of the eye with Optical Coherence Tomography (OCT). While these images suffer from distortions because the rays refract at the interfaces between media, the host research group has proven that with correction algorithms it is possible to quantitative measure the shape of the optical surfaces of the eye. With this information a few studies have built personalized model eyes that show good correspondence with the experimental measurements of the wave front aberration of the eye. This would imply that optical models could be used to predict the optical quality before implanting the intraocular lens, but there are still some uncertainties about the refractive index of the crystalline lens and the position of the intraocular lens after surgery. The crystalline lens that is removed during cataract surgery is a biconvex lens with a gradient refractive index and a shape that changes with age and accommodation. If this distribution was known, we would be able to correct the images of the posterior surface of the lens and build correct optical models of the eye before surgery. There is also an uncertainty in the axial position of the IOL after surgery that prevent clinicians from irrefutably choosing the right IOL and researchers and optical designers from predicting to its full extent the impact of new designs in the post-op vision. The host institution developed algorithms to increase the accuracy in the determination of the IOL position that could be used to better predict the IOL power of the lens to be implanted and to increase the precision of the predictions on the optical quality of the eye after surgery.

During the first part of this research project, I have developed routines to use the information from three dimensional OCT images obtained from patients to build personalized pseudophakic eye models. These models use the pre-surgery corneal shape because the modifications to the cornea during surgery affect only the high order aberrations and not its power, and try different intraocular lenses from a catalogue to select the one that maximizes optical quality. All algorithms were programmed using MATLAB (www.mathworks.com). Input data are segmented ocular surfaces from OCT images corrected from optical distortion. I programmed MATALB script to fit the optical surface topography with Zernike polynomials and send the computer eye model information to an optical design program. The program application programming interface (API) available in the last version of the optical design program OpticStudio (www.zemax.com) was used to create these models automatically from MATLAB. From the models we were able to calculate several parameters to estimate visual quality.

Since the models are built automatically, the tool can be also used to study systematically the tolerance of several variables (for example, power) to changes in different parameters change. The algorithms developed are being used to study the impact of new intraocular lens designs.

The second part of the project focuses on the development of the new generation of intraocular lenses that will be able to change its power. The crystalline lens loses its ability to accommodate with age resulting in what is known as presbyopia, a condition that affects 100% of the people over an age of about 50. Current IOLs cannot modify their power but there are several designs of a deformable lens that, once implanted, would use the intact intraocular accommodative plant to change its power. This would allow restoring accommodation in presbyopic patients.

During cataract surgery, the crystalline lens is removed but the lens capsule is left inside the eye. An accommodative IOL designed in the host institution uses the force from ciliary muscle to change its power by attaching its haptics to the remaining lens capsule. The attachment is done with light through a process called photobonding. This process creates chemical bonds between the IOL haptic plastic material and the tissue promoted by an initiating agent activated by light. I have studied the possibility of using the haptics of the intraocular lens to deliver light to the edges of the haptics by exporting the 3D design of a piece to use it with a non-sequential ray tracing program. Models such as these will allow us to understand details about the photobonding process and to know how we need to deliver light to specific areas of the interface between the IOL and the capsule. Biomechanical models can inform us about the forces that the ciliary muscle can apply to the IOL and the use of these models is key in understanding how much the accommodative IOL will deform.

1.2 Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

During the first year of the project, I worked with other members of the research lab of the host institution in the development of a new imaging system based in Swept Source Optical Coherence Tomography (SSOCT) to be able to image the complete anterior segment of the eye, i.e. cornea and crystalline lens with a single measurement. In the lab, previous studies were carried out with an OCT with an insufficient axial range to capture the whole eye anterior segment. This difficulty was solved by capturing several images and registering them to compose an image with the full anterior segment. Alignment problems due to eye movements were the cause of some variability and one way to increase the precision in the measurement was to use a full anterior segment imaging system. Before my arrival, the research group had acquired equipment to set up a full anterior segment SSOCT. The laser source used in this imaging technology, the most expensive element of the imaging system, sweep through a frequency range with speeds in the order of the kHz. One interferogram per sweep is captured by a point detector and this allow to detect structures in depth in the sample. The axial range that these instruments can image depends on the bandwidth of the detector (more deep if more points are acquired) and ultimately, is limited by the sweep range and the instantaneous linewidth of the laser source that should be as thin as possible. An unforeseen risk that we had to solve during this first year is that the properties of the laser that was already present in the lab were not enough to image the full anterior segment of the eye. The host institution acquired a new swept source laser source with a smaller instantaneous linewidth that was used to fully image the anterior segment of the in vivo human eye.

OCT images were acquired in the lab using the previous experimental systems for which I have programmed image processing algorithms to build personalized model eyes. The programs can be quickly adapted to use surface data obtained with other imaging systems. The segmented surface elevation is fitted by Zernike polynomials and the Zernike coefficients data and the distance between surfaces is programmatically exported to OpticStudio so that a model eye is built automatically. The optical quality after selection of a particular IOL is studied in terms of the concentrations of the ray in the retina when collimated light enter eye, the MTF value at a certain spatial frequency, the area below the MTF or the area below the MTF weighted with the Contrast Sensitivity Function of the eye. Using these algorithms, we can now predict the visual outcome after the implantation of a certain IOL in a particular patient and we have several metrics to decide which IOL design and which IOL power is best for that patient.

During the second part of the project we have made an effort towards understanding the sources of error and increasing the precision of these models. In particular, we have worked on the study of how tilt and decentration of the intraocular lens affects the optical quality. This study is essential for optical designers because the accuracy in the positioning of the lens that can be achieved with current surgical methods determines the possibility of improvement with new designs. We have studied the possibility of implementing multifocal diffractive intraocular lenses in computer eye models. This is a topic of interest right now because with this technology chromatic aberration is different in the different foci, and with some designs even correction of the chromatic aberration can be achieved. We have also proposed, for the first time in the literature, a method that could be used to measure the gradient refractive index (GRIN) of the lens in vivo with OCT. This would allow not only a complete characterization of the optical properties of the eye, but also better measurements of the shape of the posterior surface of the eye, hence better estimation of the IOL position after surgery. Finally, we have studied the effect of eye movements in the measurement. Since OCT employs a raster scan to image the eye, eye movements can affect the measurement. A computer model of the cornea was used to study the measurement in the presence of eye movements. The average of all the measurements is always the model itself but we can only image a patient a few times. These simulations will not only allow us to determine the confidence interval expected from a number of measurements, we also plan to use them to guide the process of finding the best scanner pattern to determine the topography of the ocular surfaces.

1.3 Progress beyond the state of the art, expected results until the end of the project and potential impacts (including the socio-economic impact and the wider societal implications of the project so far)

The results of the project have provided the group and the scientific community with new tools essential to study the performance of intraocular lenses in the eye prior to surgery. We have developed computer eye models that will facilitate the selection of the best IOL to implant in a patient in a personalized way. We have devised a method to measure, for the first time, the refractive index of the crystalline lens with optical methods in vivo and we have studied the influence of misplacement of IOL inside the eye. In addition, we have studied the precision of the measurements so that, not only the result but also the confidence interval can be provided. The tools that we have develop will impact in the way in which we design novel intraocular lenses.

One of the objectives in the work was to apply the results to lead the design of accommodative intraocular lenses. The project was focused, not only in modelling the optics but also in advancing in the understanding of the transmission of forces from the ciliary muscle to the capsule of the crystalline lens to be able to predict the behaviour of accommodative IOLs in a given patient before surgery. We have worked on getting ready the tools to move computer eye models to the next level by exploiting as much as possible what can we learn from the optics. To design correctly the optics and the biomechanics of these new generation of IOLs we have built tools to be able to improve what was assumed before (GRIN, IOL position, etc) that will allow designing accommodative IOLs for presbyopic patients.

Specifically, the results have been essential in collaborative work with industry, and the following projects in particular:

- Funded collaborative project with PhysIOL (Liège, Belgium), where eye models are used to assess the optical quality with the PhysIOL Fine Vision Trifocal IOL and the Isofocal IOL (a lens design patented by the host institution and licensed to PhysIOL).
- Funded collaborative project with Alcon Research Labs, where eye models are used to assess the optical quality with the Extended Depth of Focus Vivity IOL.
- IMCUSTOMEYE Project, and Innovation Action H2020 Consortium, coordinated by the Host Institution, where Optical Coherence Tomography Imaging is used for CUSTOMized EYE diagnostics and surgical planning.