journal of the mechanical behavior of biomedical materials 124 (2021) 104793

Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Research paper

Experimental evaluation of the injection force exerted in intraocular lens delivery with syringe-type injectors

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ARTICLE INFO

Keywords:
Cataract surgery
Hydrophobic and hydrophilic acrylate
IOL material
IOL haptic design

ABSTRACT

The process of intraocular lens (IOL) delivery within the capsular bag during cataract surgery is crucial, as the integrity of the IOL, the injector and the ocular structures should be preserved at all times. This study aims to obtain the main parameters that affect the injection force exerted in the ejection of an intraocular lens (IOL) through syringe-type injectors. For that purpose, ejection tests were carried out in vitro, measuring the resistance force throughout the entire delivery process. The effect of IOL material, haptic design, IOL thickest area and ophthalmic viscosurgical device (OVD) was studied by ejecting seven IOLs with four syringe-type injectors of different sizes, 3.0, 2.2 and 1.8 mm. In all injectors, plate hydrophilic IOLs present the lowest resistance forces; hydrated C-loop hydrophobic IOLs present higher forces and the C-loop hydrophobic IOL in dry conditions presents the highest resistance forces. All IOLs could be properly delivered with an injector size of 2.2 mm, making injector sizes of 3.0 mm outdated. The injector size of 1.8 mm damaged several IOLs. IOL material and cartridge nozzle size were the most influential parameters in IOL delivery. IOL thickest area was also relevant but in a lesser extent whereas IOL haptic design was not as relevant.

1. Introduction

Since the implantation of the first intraocular lens (IOL) by Ridley (1952), the field of cataract surgery has been developing substantially. From the use of flexible materials with different haptic designs in the IOLs to the development of less invasive implantation devices, important advances have improved the outcome of the surgery (Rahimy et al., 2013; Cabeza-Gil et al., 2019; Remón et al., 2020; Ang et al., 2020). Nowadays, one of the main goals of cataract surgery is focused on the incisions, their size and location (Beltrame et al., 2002; Elkady et al., 2009), in order to reduce the risk of suffering post-surgery complications, like an infection from contamination (Nagaki et al., 2003), and assure a faster recovery (Dewey et al., 2014). This aim has promoted the development of new soft materials for the IOL, such as hydrophobic and hydrophilic acrylate, together with the availability of innovative surgical instruments as injectors and new foldable IOL designs (Kodjikian et al., 2006).

Incision damage has been studied to depend on injection speed and type (Ouchi, 2012; Allen et al., 2012). Currently, the most common injector types are syringe and screw. The latter allows a constant insertion speed, avoiding abrupt alterations in the delivery. However, its mechanism requires the use of both hands. In contrast, syringe-type injectors can be operated using only one hand, allowing surgeons to use the other hand to secure and stabilize the eye. The main limitation of this design is that the force applied by the IOL delivery system needs to be manually controlled and carefully balanced in order to minimize possible complications in the cornea of the patient, by damaging the IOL or the injection system in the delivery.

The main findings in literature focus on how the geometry of the injector affects the corneal incision (Kohnen and Klaproth, 2008; Nanavaty and Kubrak-Kisza, 2017; Arboleda et al., 2019; Haldipurkar et al., 2020). In terms of surgical outcomes, the insertion of the IOLs causes enlargement of all corneal incision wounds (Kohnen and Klaproth, 2008; Arboleda et al., 2019; Haldipurkar et al., 2020). Nevertheless, fast-speed IOL insertion, newer motorized injectors and new injector designs have been shown to decrease the amount of wound enlargement caused by IOL insertion (Ouchi, 2012; Allen et al., 2012; Khokhar et al., 2014; Tataru et al., 2015; Wang et al., 2016; Yamakawa et al., 2017). Their most significant differences are the size of the nozzle, the shape of the silicone cushion and the design of the lens cartridge, which has shown to influence IOL ejection (Kleinmann, 2005; Marcovich, 2006). Furthermore, Kleinmann and Kleinmann (2014) designed a finite element (FE) model for comparing stress induced on corneal incisions during IOL implantation. However, to the best of our knowledge, only two studies have evaluated the resistance force exerted

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https://doi.org/10.1016/j.jmbbm.2021.104793
Received 23 April 2021; Received in revised form 20 August 2021; Accepted 22 August 2021
Available online 30 August 2021
1751-6161/

by the IOL delivery system (Bozukova et al., 2013; Usui and Tanaka, 2015). Bozukova et al. (2013) reported the maximum force needed to inject 13 different IOLs in the ACCUJECT™ 2.2-1P syringe-type injector, whereas Usui and Tanaka (2015) evaluated several IOL deliveries using 5 different syringe-type injectors. This resistance force is an interesting in vitro marker, as high or unbalanced forces can lead to damage in the IOL and poor surgery outcome.

This study was aimed to analyze the effect of IOL material, haptic design and IOL thickest area, as well as the dimensions and shape of the syringe-type injection system, in the resistance force exerted in IOL delivery for cataract surgery. The influence of the ophthalmic viscosurgical device (OVD) (Bissen-Miyajima, 2008) was also studied by conducting tests with three different viscoelastic solutions.

2. Material & methods

2.1. Materials

The injection devices chosen for all the experiments of this study were the ACCUJECT™ 3.0-1P , 2.2-1P, VISCOJECT™-BIO 2.2 (Medicel, Switzerland) and BLUEMIXS®180 (Carl Zeiss Meditec AG, Germany), four syringe-type injectors shown in Fig. 1. Seven different IOLs were ejected in these injectors, see Fig. 2, and the resistance force exerted by the system was measured.

Three hydrophilic IOL plate designs were tested, AT LISA (Carl Zeiss Meditec AG, Germany), Y60 and LIOCAN (AJL Ophthalmic, Spain). The AT LISA and Y60 models are quite similar in many ways: their haptic design, overall diameter and thickest area, see Fig. 2. The LIOCAN model shares the same shape as Y60 but with a bigger overall diameter, 14.25 mm. Four hydrophobic IOLs were analyzed: a hydrophobic double C-loop POD F GT (PhysIOL, Beaver-Visitec International, USA), which has an overall diameter of 11.40 mm and has the lowest thickest area of all IOLs under investigation, 0.65 mm; and three different hydrophobic C-loop IOLs, two IOL prototypes that were designed in a previous work (Cabeza-Gil et al., 2020), hereinafter referred to as model #C and #D, and the AIALA model (AJL Ophthalmic, Spain), see Fig. 2. All three C-loop IOLs have different designs of the haptics, but they share the same overall diameter of 13.00 mm. Moreover, the AIALA model has a lower thickest area than models #C and #D, 0.83 mm against 1.13 mm. A priori, model #C is considered a flexible C-loop design whilst the other two are considered stiffer designs, according to their behavior in the standardized compression test ISO 11979-3 (Cabeza-Gil et al., 2019, 2020).

The optical power of all human IOLs tested was +22.0 diopters (D) while the LIOCAN, a dog-intended IOL, was +41.0 D. The optic thickness of the IOLs or its thickest area was measured with CellScale MicroTester, see Supplemental Data file for further knowledge on the technique used. All IOLs were kept submerged in a saline solution for at least 72 h before the experiments to assure they were tested in a hydrated state. Additionally, model #D was analyzed in a dry state, i.e., not having been kept submerged before the tests, as a comparison of the material behavior with and without water content. This was performed as several ophthalmology companies offer the IOL preloaded in the injector and not submerged in a saline solution.

The thickest area of the IOL is expected to have a large influence on the force exerted by the injector due to the high compression stress to which the IOL is subjected to when passing through the lens cartridge and the nozzle. For this reason, seven different AT LISA models with an optical power between 0.0 and 27.0 D, which implies a range of thickest areas from 0.29 mm to 1.23 mm, were analyzed in the BLUEMIXS®180 injector, see Table 1, the one recommended for this IOL.

In all tests, the injector was filled with an OVD, as in clinical interventions. In order to observe the influence of this viscoelastic solution, three different OVDs, AJL VISC 1.4%, AJL VISC 2.0% and AJL VISC 3.0% (AJL Ophthalmic, Spain)—percentages referring to the amount of sodium hyaluronate they contain—were tested with model #D IOL in the ACCUJECT™ 2.2-1P injector in dry conditions.

2.2. Experimental procedure

The tests consisted in a controlled displacement of the loading pusher of the injector, replicating the IOL injection by the ophthalmologist, while the force needed in the ejection was recorded. The loading pusher was displaced the total length of the loading pusher to assure the ejection of the IOL, i.e., 42.5 mm for injectors ACCUJECT™ 2.2-1P, 3.0-1P and BLUEMIXS®180 and 52.5 mm for injector VISCOJECT™-BIO 2.2, at a constant velocity of 4 mm/s, as supposed for clinical values (Allen et al., 2012). The IOLs were placed into their reference configuration, without bending the IOL haptics as shown in Fig. 3. A video of an IOL delivery in each injector is uploaded as Supplemental Data to help the reader understand the process of the experiments.

The resistance force exerted by the IOL delivery system was measured and recorded using an Instron 5548 Electroplus Microtester with a 50 N full-scale load cell, see Fig. 3, for all injectors under investigation. In the specific cases where 50 N were not enough to push the IOL through the nozzle, which happened only with BLUEMIXS®180 injector, a 250 N full-scale load cell was used. Finally, IOL resistance force to injection along the length of the injector was processed with MATLAB 2020a (MathWorks, USA). To compare all results, an ANOVA analysis, considering a $p_{value} < 0.05$ as significant, was performed.

All experiments were conducted at a temperature of 23.5±1 °C and a relative humidity of 28%. This setting is based on the conditions in the operating room. A minimum of three tests were conducted for each testing condition.

2.3. Study design

The stages followed in this study are here described. Firstly, the effect on the resistance force in IOL delivery of the composition of the OVD was evaluated testing three different OVDs, AJL VISC 1.4%, AJL VISC 2.0% and AJL VISC 3.0%, with injector ACCUJECT™ 2.2-1P and model #D in dry conditions.

Secondly, the effect of the IOL and the size of the injector was analyzed. To do so, every IOL under investigation was ejected in all four injectors and the resistance force of the delivery was recorded. Fig. 2 shows all the IOLs that were ejected and Fig. 1 shows all the injectors used in the study. All tests were carried out using AJL VISC 1.4%. In order to isolate the effect of the IOL, control cases of all injectors were previously performed. These tests consisted in the ejection of the system without any IOL, allowing to observe the forces exerted intrinsically by the injectors. These tests were conducted for 2.50 mm more than the ejection tests, at the same constant speed of 4 mm/s, to monitor the force exerted by the injector itself, which is that of the silicone cushion passing through the cartridge.

Thirdly, in order to compare the effect of the material exclusively, hydrophobic and hydrophilic acrylate, two lenses without the haptics (only the spherical optic part) with the same optical power, +22.0 D, and therefore thickest area, but different materials were analyzed in the ACCUJECT™ 2.2-1P injector. In this test, the effect of the haptic geometry of the IOL is subtracted. Thus, it can also serve as control test for the effect of the haptics in the delivery system.

Finally, the effect of the thickest area of the IOL, which is highly correlated with IOL optical power, was analyzed. For that purpose, all AT LISA IOLs described in Table 1 were tested in the BLUEMIXS®180 injector.

3. Results

For a better understanding of the IOL delivery process, Fig. 4 shows an example curve of the force exerted by the IOL delivery system to describe the most important regions throughout the delivery process. As example, the resistance force of the Y60 IOL ejected by the ACCUJECT™ 2.2-1P syringe-type injector is shown. The shape of this graph has been assured throughout the research to be representative of any IOL ejected

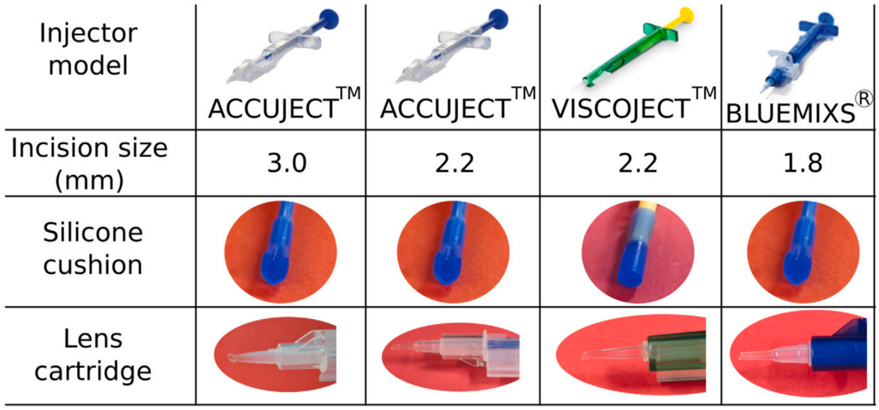

Fig. 1. The syringe-type injectors ACCUJECT™ 3.0-1P, ACCUJECT™ 2.2-1P, VISCOJECT™-BIO 2.2 and BLUEMIXS®180 and their main characteristics are shown. All injectors share the same silicone cushion, except for that of VISCOJECT™-BIO 2.2, which has a rounder shape. The shape of the silicone cushion is the same as the shape of the nozzle.

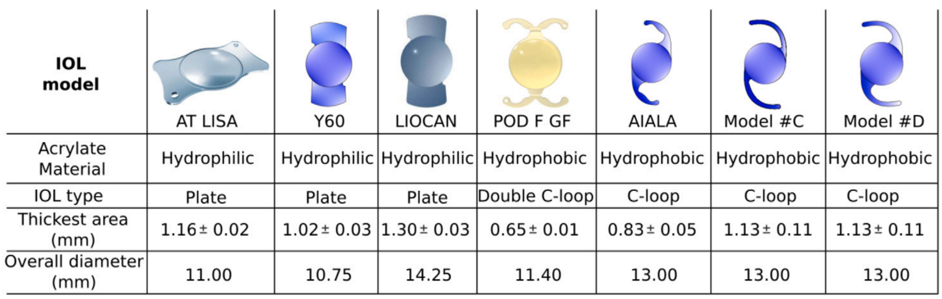

Fig. 2. All the IOL models analyzed in the study. The material, the haptic design and the overall diameter of each IOL are shown. Moreover, the thickest area, which is the maximum optic thickness, was measured since it is expected to be a relevant factor in the resistance force in the IOL delivery system. The optic diameter of all IOLs under investigation is 6.00 mm, except for the LIOCAN model, which is 6.50 mm.

Table 1
Diopters and thickest area (mm) of the different AT LISA IOLs tested in the BLUEMIXS®180 injector to evaluate the influence of the thickest area in ejection force.

AT LISA Power (D)	+0.0	+3.5	+8.0	+12.5	+18.0	+22.0	+27.0
Thickest area (mm)	0.29 ± 0.02	0.48 ± 0.02	0.61 ± 0.02	0.74 ± 0.02	0.98 ± 0.02	1.16 ± 0.02	1.27 ± 0.02

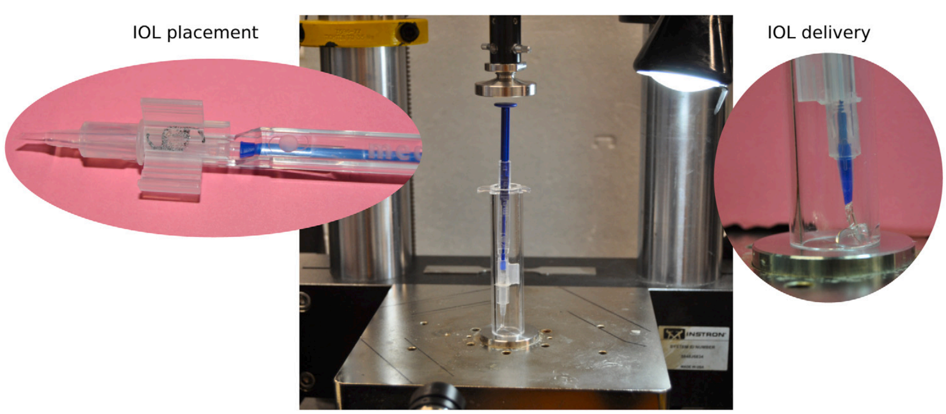

Fig. 3. IOL delivery system using an Instron 5548 Electroplus Microtester. A methacrylate tube was designed to place and fix the injector during IOL delivery. Figure shows the placement of the IOL on the left and the process of delivery on the right.

in a syringe-type injector. Four key regions can be highlighted in the graph. Firstly, a peak force that appears approximately 9 mm after starting to push the injector corresponds to the initial contact of the loading pusher with the IOL. Subsequently, the IOL starts being dragged and the applied force increases as the IOL and silicone cushion are inserted into the lens cartridge. This occurs while the displacement of the loading pusher is between 15 and 30 mm. Once they are in, the force applied decreases gradually, as there are no abrupt changes in the cross-sectional area of the nozzle. At around 30 mm of displacement of the loading pusher, the IOL reaches the tip of the injector, the narrowest part of the nozzle, and for the next 8 mm the force significantly increases as the IOL is driven out. This is the part of the IOL delivery where the resistance force is the highest (not counting the subsequent silicone cushion delivery) and thus, this is the force that will be compared among all cases. It is also the most important part of the delivery, as it is mostly at this moment when the IOL can be

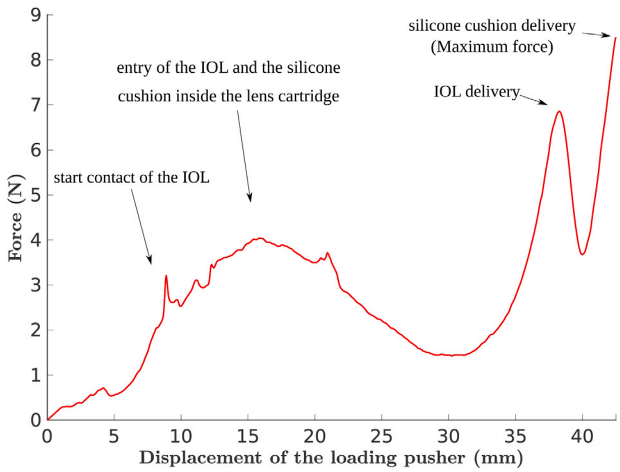

Fig. 4. Description of the IOL delivery process. Resistance force of the Y60 IOL through the ACCUJECT™ 2.2-1P injector. All syringe-type injectors under investigation follow the same pattern in the resistance force exerted.

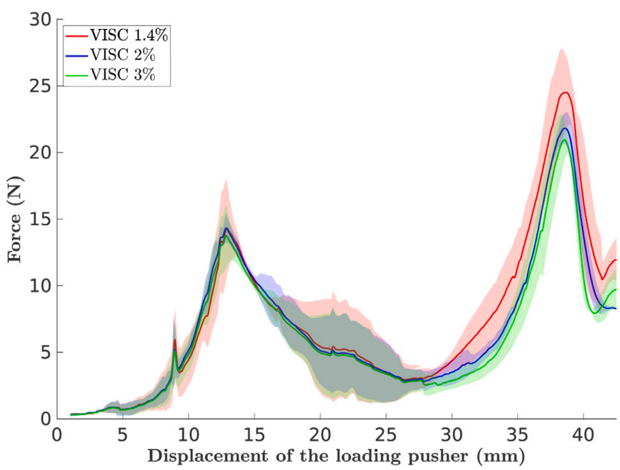

Fig. 5. Study of the effect of OVD composition in IOL delivery (model #D in dry conditions) by means of the resistance force using three different sodium hyaluronate concentrations, AJL visc 1.4% (red), AJL visc 2% (blue) and AJL visc 3% (green). All cases were reproduced three times (n = 3).

damaged or erratically delivered. The process of IOL delivery would already be finished by this point. However, for this example graph, the following displacement of the silicone cushion through the tip and its eventual ejection are shown. It can be noted that the ejection force rises considerably, even more than for the IOL delivery, as the cushion is wider and less lubricated. In the following graphs, except for the control cases, the delivery of the cushion has been removed as it has no clinical interest.

3.1. Effect of OVD

The three different OVDs object of this study were compared by means of ejecting model #D in dry conditions with ACCUJECT™ 2.2-1P injector, see Fig. 5. It seems that the higher the sodium hyaluronate concentration, the lower the force exerted by the IOL delivery system. However, there is no statistically significant difference in the maximum resistance force ($p_{value} > 0.05$) among the different viscoelastic solutions. From these results, the remaining tests were decided to be carried out with the AJL VISC 1.4%.

3.2. Effect of IOL delivery and injector size

Before testing the lenses on both injectors, a control assay, i.e., without any IOL, was performed to evaluate the resistance force exerted by each injector itself, see Fig. 6A. The maximum force obtained at the end of the pusher displacement and the resistance force when the IOL would be driven out – at around 30 mm as commented above – are shown in Table 2.

The comparison between the forces exerted by the different IOLs under investigation for the ACCUJECT™ 3.0-1P is presented in Fig. 6B and Table 3. All cases can be differentiated into 4 groups, regarding the force exerted by the ejection of the IOL, that match the differences in IOL material and IOL thickest area: model #D (dry), which unsurprisingly presented the highest force exerted, 15.78 ± 2.00 N; models #D (submerged) and #C, two C-loop hydrophobic designs, presented an average of force 7.19 and 7.76 N; the models AIALA and POD F GF, hydrophobic designs with a lower thickest area, presented a slightly lower average force than models #D (submerged) and #C, 4.82 and 4.84 N; and the hydrophilic plate designs, AT LISA, Y60 and LIOCAN, presented the lowest average force of 3.51, 3.71 and 2.68 N, respectively. For graphical purposes and due to their similar behavior with models #D and AT LISA, respectively, models #C and Y60 are not plotted in Fig. 6. Their graphs can be observed in the Supplemental Data file.

Fig. 6C and D show the force exerted by the IOLs under investigation when ejected by the injector ACCUJECT™ 2.2-1P and VISCOJECT™-BIO 2.2. Again, the same trend referring to the difference in behavior according to IOL material and IOL thickest area was observed. The maximum forces and their corresponding deviations for each IOL are gathered in Table 3.

Fig. 6E shows the force exerted by model #D (submerged), POD F GF and AT LISA when ejected by the BLUEMIXS®180. The other IOLs are not included as they were macroscopically damaged in the delivery process. The same trend as in the other injectors is obtained. However, the average forces are notably higher. Model #D (submerged) presented the highest force, 78.29 ± 14.67 N, followed by the POD F GF IOL, with 36.78 ± 1.96 N and finally by the AT LISA IOL, 25.88 ± 2.02 N The resistance force in the IOL delivery process for the damaged IOLs is presented in the Supplemental Data file.

3.3. Effect of IOL material: delivery of the optic part

In order to verify the influence of the material, the hydrophobic and hydrophilic acrylic material under in vivo conditions (hydrated) were compared in the ACCUJECT™ 2.2-1P injector. The haptics were carefully removed from the IOLs to test only the optic of +22.0 diopters and same diameter (6 mm), subtracting the effect of the geometry. Fig. 7A shows the resistance force for the two optics with different materials. The maximum resistance force for the hydrophobic acrylate is considerably higher, 14.29 ± 2.47 N, compared to the maximum resistance force for the hydrophilic acrylate (HEMA), 5.83 ± 1.83 N.

3.4. Effect of IOL thickest area

Lastly, the influence of the thickest area of the IOLs was analyzed by means of testing AT LISA IOLs with an optical power range between 0.0 and 27.0 D in the BLUEMIXS®180 injector, see Fig. 7B. For graphical purposes, some IOLs have not been plotted, see Supplemental Data file. The IOL barely exerted resistance force up to an IOL optical power of 8.0 D, which corresponds to a thickest area of 0.61 mm, see Table 1. With this IOL, the maximum force was 17.83 ± 2.93 N. A similar resistance force was obtained for the IOL with an optical power of 12.5 D and 0.74 mm of thickest area. The following significant change is for the IOL of 18.0 D, 0.98 mm of thickest area, with a maximum force of 22.74 ± 1.93 N. Finally, a similar resistance force was obtained for the IOLs with 22.0 and 27.0 D, 1.16 and 1.27 mm in thickest area respectively, of 25.82 ± 3.14 N

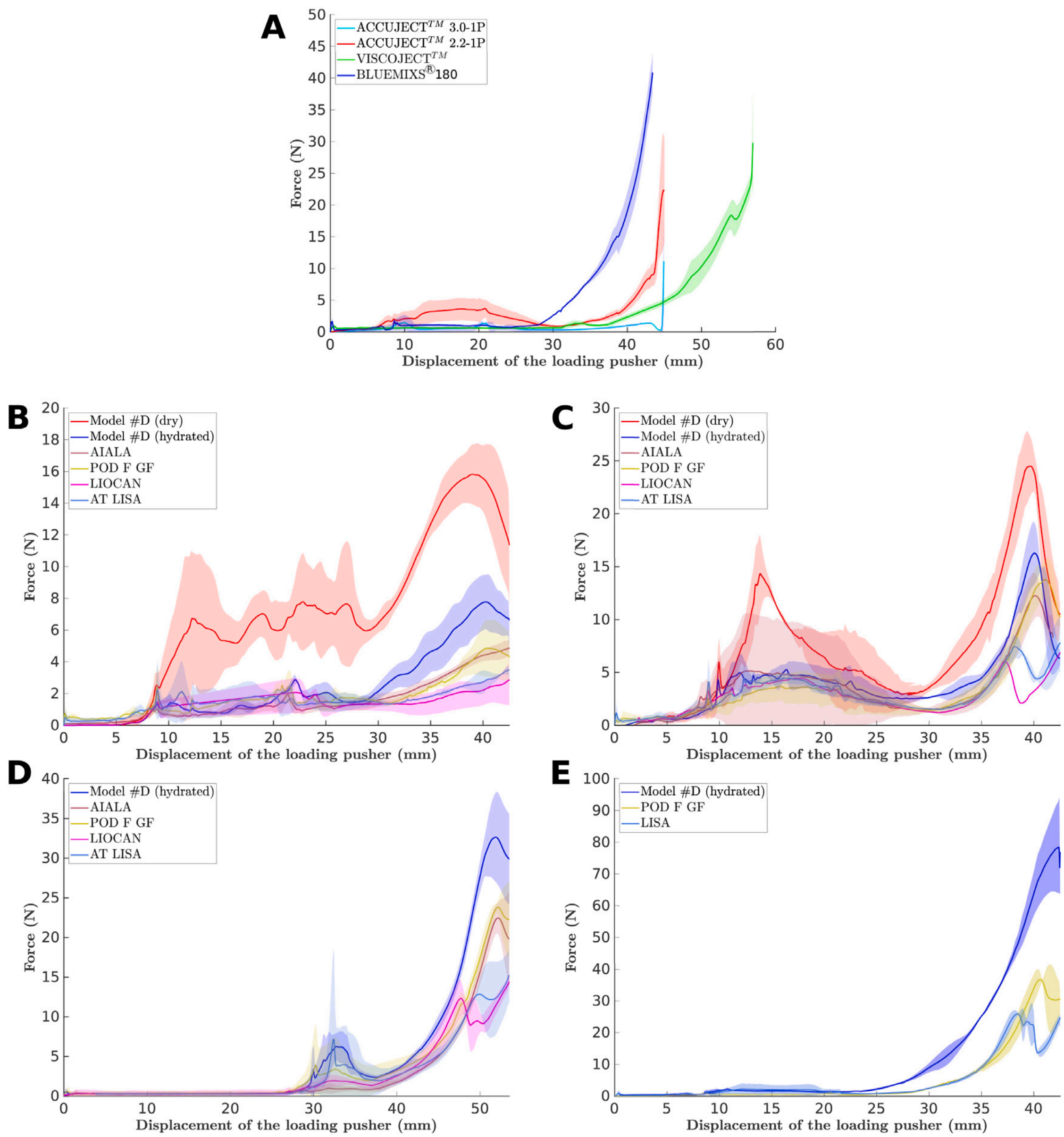

Fig. 6. A. Resistance force (N) of the four syringe-type injectors under investigation, the ACCUJECT™ 3.0-1P and 2.2-1P, the VISCOJECT™ and the BLUEMIXS®180, without the ejection of an IOL (n = 5 for all cases). IOLs delivery in the ACCUJECT™ 3.0-1P injector B., in the ACCUJECT™ 2.2-1P injector, C. in the VISCOJECT™ 2.2 injector, D., and in the BLUEMIXS®180, E., for the different IOLs analyzed: model #D dry (n = 6) and hydrated (n = 5), model #C (n = 5), AIALA (n = 5), AT LISA (n = 5), Y60 (n = 5) and LIOCAN (n = 6). Some videos of the IOL delivery process for each injector under investigation are uploaded as Supplemental Data.

Table 2
Maximum force (N) exerted by the injector itself and the resistance force of each injector when the IOL would be driven out for the four syringe-type injectors under investigation.

	ACCUJECT™ 3.0-1P	ACCUJECT™ 2.2-1P	VISCOJECT™	BLUEMIXS®180
Maximum force	11.16 ± 7.16	22.24 ± 8.18	29.24 ± 7.45	40.49 ± 3.62
Contributed force in IOL delivery	0.85 ± 0.11	2.95 ± 0.58	9.20 ± 2.63	14.71 ± 1.86

4. Discussion

The resistance force exerted by an IOL injection system is an interesting in vitro marker for comparing the mechanical effect of material, geometry and injection device in the delivery of the IOL. It can give an insight in the adequacy of certain conditions, considering that high resistance forces are undesirable as they can damage the IOL or the delivery system during implantation, as well as complicate a controlled and balanced ejection. Therefore, in this study, the force needed to deliver IOLs with different conditions and in different injectors was obtained and compared, in order to evaluate the effect of geometry, optical power (related to the IOL thickest area) and material of the IOL, as well as injector size, in the delivery.

This study has obtained clear evidence of the influence of IOL material, nozzle diameter of the injector and IOL thickest area in the IOL delivery process. The importance of a proper hydration of the IOLs has also been proven by testing the same C-loop hydrophobic IOL, model #D, being or not hydrated before the tests. When the IOL was tested dry, the force needed to eject it was notably higher and thus, the chances of IOL damaging increased significantly, see Fig. 6,

Table 3
Maximum force (N) applied for each IOL and injector under investigation. The force expressed in the Table is the peak force when the IOL is driven out.

	ACCUJECT™ 3.0-1P	ACCUJECT™ 2.2-1P	VISCOJECT™-BIO 2.2	BLUEMIXS®180
Model #D (dry)	15.78 ± 2.00	24.48 ± 3.19	Damaged	–
Model #D (submerged)	7.76 ± 1.74	16.26 ± 3.01	32.89 ± 5.49	78.29 ± 14.67
Model #C	7.19 ± 1.44	15.55 ± 1.55	34.38 ± 3.02	–
AIALA	4.82 ± 0.53	12.25 ± 2.05	22.45 ± 1.97	Damaged
POD F GF	4.84 ± 1.76	13.79 ± 1.81	23.82 ± 1.01	36.78 ± 1.96
AT LISA	3.51 ± 0.27	7.42 ± 1.00	12.78 ± 0.96	25.88 ± 2.02
Y60	3.71 ± 1.25	6.52 ± 0.95	14.03 ± 4.14	Damaged
LIOCAN	2.68 ± 1.22	6.00 ± 0.91	12.26 ± 2.46	Damaged

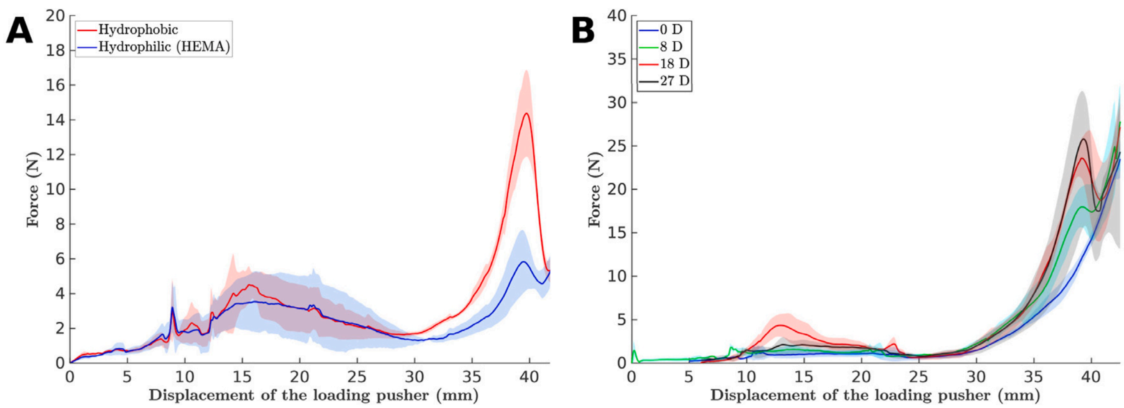

Fig. 7. A. Comparative between the delivery of the optic part of the IOL (+22.0 D, without the haptics) for hydrophobic and hydrophilic acrylate. All cases were reproduced three times (n = 3). B. Resistance force for several AT LISA IOLs with a different optical power range [0.0 – 27.0 D], which is related to IOL thickest area (n = 5 for all tests conducted).

which in fact happened with some injectors, see Table 3. The resistance forces obtained could be differentiated into 4 groups, depending on the state or type of material of the IOLs and the IOL thickest area: model #D, hydrophobic acrylate in dry state, which presented the highest resistance force; models #D and #C; POD F GF and AIALA IOLs, all hydrophobic acrylate in hydrated state; and AT LISA, Y60 and LIOCAN, all hydrophilic acrylate plate designs in hydrated state, which presented the lowest resistance forces. The same trend was confirmed for all injectors under investigation, ACCUJECT™ 2.2-1P, 3.0-1P, VISCOJECT™-BIO 2.2 and BLUEMIXS®180, see Fig. 6. These behaviors lead to the conclusion that the hydrophobic acrylate has different mechanical properties in the dry and hydrated state. Further material tests can be carried out to confirm this conclusion. Additionally, the effect of IOL material was verified testing the same optics, one made of hydrophobic and the other of hydrophilic acrylate. These tests confirmed the high effect of the material in the resistance force, as the hydrophobic optic produced a force of 14.29 N, more than twice as much as the hydrophilic one, which resulted in 5.83 N. These results were similar to the forces obtained in the tests of the IOLs with the same material and optics, models #C and #D submerged and Y60, respectively.

Therefore, it could be said that haptic design barely influences the force exerted, see Fig. 6, and Fig. 7A. This can be explained considering that the force required to push the IOL through the cartridge depends on the relationship between the diameter of the cartridge nozzle and the volume of the IOL in its thickest area. Since the haptics are not a part of the thickest area of the IOL, this explains why the IOL haptic has no relevant importance in the determination of the force required to push the IOL. This trend was also confirmed in the similarity of the resistance force exerted by models #D and #C, two different C-loop hydrophobic models, and the different plate hydrophilic designs, AT LISA and Y60, see Supplemental Data file.

As a clear verification of the influence of the thickest area of the IOLs, model AT LISA with different optical powers, and thus different thickest area measurements, was tested in injector BLUEMIXS®180. With these tests, the high correlation between the thickest area and the resistance force was verified, see Fig. 7B.

In this study, few IOLs were damaged in the tests, all happening in injector BLUEMIXS®180, which has the lowest nozzle size, 1.8 mm, and model #D (dry) in injector VISCOJECT™-BIO 2.2. Only models #D (hydrated), POD F GF and AT LISA were suitable to be tested correctly in the BLUEMIXS®180 injector, see Table 3. The rest of the IOLs were damaged in the delivery process with this injector. Surprisingly, the Y60 IOL, similar to AT LISA, was damaged in this injector whilst AT LISA was not. It is likely that the hydrophilic material of both lenses was not completely the same. In screening tests, which were not included in the study, some IOLs were damaged when they were misplaced in the lens cartridge. IOLs with no apparent breakage were checked in an optical microscope to observe any internal damage. It was not observed in any case.

The present study has also shown that the injector size of 3.0 mm is outdated and that even IOLs such as LIOCAN, a dog-purpose IOL, could be implanted in injectors of 2.2 mm. Moreover, observing the resistance force exerted by model #D in dry state, it is recommended for IOL manufacturers to preload the IOL in a saline solution.

The importance of the injector in the resistance force of the system can be checked when comparing the different results in Fig. 6 and Table 3. For injector BLUEMIXS®180, the resistance forces are higher as the diameter of the tip is smaller, resulting in a higher force to push the IOL through the nozzle. This is less desirable. However, a smaller nozzle implies a smaller incision size in the cornea (Arboleda et al., 2019; Haldipurkar et al., 2020; Oshika and Wolfe, 2019). Therefore, a compromise should be reached between the incision size and the proper IOL delivery. The relevance of the injector was also shown in the study of Usui and Tanaka (2015). In their case, the values of force range from 2 to 20 N for injector with a nozzle diameter higher than 2.2 mm, similar to the results obtained in our tests.

In this study, the same syringe-type injector as Bozukova et al. (2013), ACCUJECT™ 2.2-1P, was used. The resistance forces obtained for IOL ejection in this study are similar to what Bozukova et al.

obtained. However, the test method was different, as they used a loading–unloading cycle. The maximum resistance force in the control assay – the injection without any IOL – of Bozukova et al. was of 13 N against the 22.24 N obtained in this study for a displacement of the pusher of 45 mm. If the pusher in this study had been displaced only 1 mm less, the maximum resistance force would be of around 13 N. Therefore, the results can be assumed comparable.

One of the limitations of the study was that the tests were conducted in an air filled chamber instead of a fluid filled chamber that would mimic natural environment. Usui and Tanaka (2015) performed these tests in a porcine eye and in a plastic dish and they obtained that the forces in the plastic dish were slightly lower. Another limitation might be the few trials conducted per sample that could have influenced the OVD conclusion. Moreover, further investigations could study the effect of injector material, as more flexible nozzles are expected to enlarge with IOL ejection and therefore require less injection force.

This study has added some light to the effect of IOL characteristics in the delivery. The importance of a well preserved and hydrated IOL prior to use has been demonstrated. Furthermore, the minor effect of the composition of the viscoelastic solution was shown. Finally, the material of the IOL, the injector size and the IOL thickest area were key factors in the resistance force exerted by the system. When comparing to literature, the importance of the delivery device was made clear. Nevertheless, a compromise between the resistance force and the incision size must be met when selecting the adequate injector.

5. Conclusions

The shape of the resistance force curves throughout the entire ejection process of an IOL with a syringe-type injector is explained in this work. The IOL material is key in the IOL delivery, being the hydrophilic acrylate the one that produces smaller forces. Moreover, hydrophobic IOLs are recommended to be hydrated before implantation as dry IOLs present higher resistance forces and thus higher probability of damage. Injector sizes of 3.0 mm are outdated. No hydrated IOL was apparently damaged with an injector size of 2.2 mm.

CRediT authorship contribution statement

I. Cabeza-Gil: Conceptualization, Methodology, Resources, Formal analysis, Investigation, Writing – original draft. **I. Ríos-Ruiz:** Methodology, Validation, Formal analysis, Investigation, Writing – review & editing. **B. Calvo:** Conceptualization, Validation, Resources, Supervision, Project administration, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors gratefully acknowledge research support from the Spanish Ministerio de Ciencia, Innovacion y Universidades (Grant DPI2017-84047-R) and the Department of Industry and Innovation (Government of Aragon) through the research group Grant T24-20R (cofinanciado con Feder 2014-2020: Construyendo Europa desde Aragon). Part of the work was performed by the ICTS "NANBIOSIS" specifically by the Tissue & Scaffold Characterization Unit (U13), of the CIBER in Bioengineering, Biomaterials & Nanomedicine (CIBER-BBN at the University of Zaragoza). CIBER Actions are financed by the Instituto de Salud Carlos III with assistance from the European Regional Development Fund. I. Cabeza-Gil and I. Ríos-Ruiz were supported by Spanish Ministerio de Ciencia, Innovacion y Universidades, through grant PRE2018-084021, and Government of Aragon, order IIU/1408/2018, respectively.

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.jmbbm.2021.104793.

References

Allen, D., Habib, M., Steel, D., 2012. Final incision size after implantation of a hydrophobic acrylic aspheric intraocular lens: New motorized injector versus standard manual injector. J. Cataract. Refract. Surg. 38 (2), 249–255. http://dx.doi.org/10.1016/j.jcrs.2011.08.038.

Ang, M., Gatinel, D., Reinstein, D.Z., Mertens, E., del Barrio, J.L.A., Alió, J.L., 2020. Refractive surgery beyond 2020. Eye http://dx.doi.org/10.1038/s41433-020-1096-5.

Arboleda, A., Arrieta, E., Aguilar, M., Sotolongo, K., Nankivil, D., Parel, J., 2019. Variations in intraocular lens injector dimensions and corneal incision architecture after cataract surgery. J. Cataract. Refract. Surg. 45 (5), 656–661. http://dx.doi.org/10.1016/j.jcrs.2018.10.047.

Beltrame, G., Salvetat, M., Driussi, G., Chizzolini, M., 2002. Effect of incision size and site on corneal endothelial changes in cataract surgery. J. Cataract. Refract. Surg. 28 (1), 118–125. http://dx.doi.org/10.1016/s0886-3350(01)00983-x.

Bissen-Miyajima, H., 2008. Ophthalmic viscosurgical devices. Curr. Opin. Ophthalmol. 19 (1), 50–54. http://dx.doi.org/10.1097/icu.0b013e3282f14db0.

Bozukova, D., Pagnoulle, C., Jérôme, C., 2013. Biomechanical and optical properties of 2 new hydrophobic platforms for intraocular lenses. J. Cataract. Refract. Surg. 39 (9), 1404–1414. http://dx.doi.org/10.1016/j.jcrs.2013.01.050.

Cabeza-Gil, I., Ariza-Gracia, M.A., Remón, L., Calvo, B., 2019. Systematic study on the biomechanical stability of c-loop intraocular lenses: Approach to an optimal design of the haptics.. Ann. Biomed. Eng. 48 (4), 1127–1136. http://dx.doi.org/10.1007/s10439-019-02432-9.

Cabeza-Gil, I., Pérez-Gracia, J., Remón, L., Calvo, B., 2020. Effect of haptic geometry in C-loop intraocular lenses on optical quality. J. Mech. Behav. Biomed. Mater. 104165. http://dx.doi.org/10.1016/j.jmbbm.2020.104165.

Dewey, S., Beiko, G., Braga-Mele, R., Nixon, D., Raviv, T., Rosenthal, K., 2014. Microincisions in cataract surgery. J. Cataract. Refract. Surg. 40 (9), 1549–1557. http://dx.doi.org/10.1016/j.jcrs.2014.07.006.

Elkady, B., nero, D.P., Alió, J., 2009. Corneal incision quality: Microincision cataract surgery versus microcoaxial phacoemulsification. J. Cataract. Refract. Surg. 35 (3), 466–474. http://dx.doi.org/10.1016/j.jcrs.2008.11.047.

Haldipurkar, S., Shetty, V., Haldipurkar, T., Dhamankar, R., Sehdev, N., Khatib, Z., Nagvekar, P., Mhatre, P., Setia, M., 2020. Incision size changes after cataract surgery with intraocular lens implantation. J. Cataract. Refract. Surg. 46 (2), 222–227. http://dx.doi.org/10.1097/j.jcrs.0000000000000014.

Khokhar, S., Sharma, R., Patil, B., Aron, N., Gupta, S., 2014. Comparison of new motorized injector vs manual injector for implantation of foldable intraocular lenses on wound integrity: an ASOCT study. Eye 28 (10), 1174–1178. http://dx.doi.org/10.1038/eye.2014.162.

Kleinmann, G., 2005. Linear deposits on the surfaces of intraocular lenses implanted through a hexagonal cartridge which mimic scratches/cracks on the lenses. Br. J. Ophthalmol. 89 (11), 1474–1477. http://dx.doi.org/10.1136/bjo.2005.071738.

Kleinmann, G., Kleinmann, I., 2014. Intraocular lens injector–induced stress on the corneal incisions during lens implantation. Am. J. Ophthalmol. 158 (1), 185–191.e1. http://dx.doi.org/10.1016/j.ajo.2014.03.001.

Kodjikian, L., Beby, F., Rabilloud, M., Bruslea, D., Halphen, I., Fleury, J., Grange, J.-D., Garweg, J.G., 2006. Influence of intraocular lens material on the development of acute endophthalmitis after cataract surgery? Eye 22 (2), 184–193. http://dx.doi.org/10.1038/sj.eye.6702544.

Kohnen, T., Klaproth, O., 2008. Incision sizes before and after implantation of SN60wf intraocular lenses using the monarch injector system with c and d cartridges. J. Cataract. Refract. Surg. 34 (10), 1748–1753. http://dx.doi.org/10.1016/j.jcrs.2008.06.031.

Marcovich, A.L., 2006. The course of surface deposits on a hydrophilic acrylic intraocular lens after implantation through a hexagonal cartridge. Br. J. Ophthalmol. 90 (10), 1249–1251. http://dx.doi.org/10.1136/bjo.2006.097857.

Nagaki, Y., Hayasaka, S., Kadoi, C., Matsumoto, M., Yanagisawa, S., Watanabe, K., Watanabe, K., Hayasaka, Y., Ikeda, N., Sato, S., Kataoka, Y., Togashi, M., Abe, T., 2003. Bacterial endophthalmitis after small-incision cataract surgery. J. Cataract. Refract. Surg. 29 (1), 20–26. http://dx.doi.org/10.1016/s0886-3350(02)01483-9.

Nanavaty, M., Kubrak-Kisza, M., 2017. Evaluation of preloaded intraocular lens injection systems: Ex vivo study. J. Cataract. Refract. Surg. 43 (4), 558–563. http://dx.doi.org/10.1016/j.jcrs.2017.02.019.

Oshika, T., Wolfe, P., 2019. In vitro comparison of delivery performance of 4 preloaded intraocular lens injector systems for corneal and sclerocorneal incisions. J. Cataract. Refract. Surg. 45 (6), 840–846. http://dx.doi.org/10.1016/j.jcrs.2018.10.050.

Ouchi, M., 2012. Effect of intraocular lens insertion speed on surgical wound structure. J. Cataract. Refract. Surg. 38 (10), 1771–1776. http://dx.doi.org/10.1016/j.jcrs.2012.06.031.

Rahimy, E., Wilson, J., Tsao, T.-C., Schwartz, S., Hubschman, J.-P., 2013. Robot-assisted intraocular surgery: development of the IRISS and feasibility studies in an animal model. Eye 27 (8), 972–978. http://dx.doi.org/10.1038/eye.2013.105.

Remón, L., Cabeza-Gil, I., Calvo, B., Poyales, F., Garzón, N., 2020. Biomechanical stability of three intraocular lenses with different haptic designs: In silico and in vivo evaluation.. J. Refract. Surg. 36 (9), 617–624. http://dx.doi.org/10.3928/1081597x-20200713-02.

Ridley, H., 1952. Intra-ocular acrylic lenses : A recent development in the surgery of cataract. Br. J. Ophthalmol. 36 (3), 113–122. http://dx.doi.org/10.1136/bjo.36.3.113.

Tataru, C.P., Dogaroiu, A.C., Mihai, C., 2015. Modified injector for optimal insertion of standard ctrs in lax zonules. Eur. J. Ophthalmol. 26 (1), 98–100. http://dx.doi.org/10.5301/ejo.5000613.

Usui, M., Tanaka, T., 2015. Resistance force for intraocular lens insertion through lens cartridges and syringe-type injectors. J. Cataract. Refract. Surg. 41 (8), 1745–1751. http://dx.doi.org/10.1016/j.jcrs.2015.03.018.

Wang, L., Wolfe, P., Chernosky, A., Paliwal, S., Tjia, K., Lane, S., 2016. In vitro delivery performance assessment of a new preloaded intraocular lens delivery system. J. Cataract. Refract. Surg. 42 (12), 1814–1820. http://dx.doi.org/10.1016/j.jcrs.2016.10.014.

Yamakawa, M., Kusaka, M., Yamada, S., Akimoto, M., 2017. Remnant extraction by using an intraocular lens injector with essential flow. Eur. J. Ophthalmol. 27 (4), 509–511. http://dx.doi.org/10.5301/ejo.5000962.