Technology and needs for tomorrow's treatment of cataract

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ABSTRACT

Cataract surgery is considered to be the most successful surgery worldwide. However, new developments are ongoing either to improve the surgical stress or to improve the surgical outcome. While restoration of the transparency and optical parameters of the eye were initially the first goals, the need to improve the quality of sight (QOS) and to restore accommodation became evident during the last decades.

By introducing the bag-in-the-lens (BIL) intraocular lens (IOL) and technique of implantation (US Patent 6,027,531) in 2000, PCO was no longer a matter of concern. Clinical studies conducted between 2000 and 2004 proved the efficacy of this new IOL with respect to PCO control, but showed additional advantages like surgeon-controlled centration and rotational stability.

Surgeon-controlled IOL centration based on the alignment of the first and third Purkinje reflexes is one method to promote IOL centration but future tracking devices will probably enhance the precision by which IOL centration along the line of sight can be achieved.

Optimal alignment is a major issue if toric correction and compensation of the spherical aberrations is intended to be incorporated into the IOL optic.

IOL optics with toric correction to compensate for regular astigmatism are in development now, but toric correction for irregular astigmatism remains extremely challenging for the manufacturers.

Improving the quality of the image by compensating for the spherical aberrations is the next step on our research programme.

The BIL offers some opportunities to optimize postoperative accommodation by introducing the capsular accommodation ring.

KEYWORDS

ACCC, BIL, ECCE, IOL, IOL centration, line of sight, PCCC, PCO, quality of sight (QOS), ring caliper, spherical aberrations, toric IOL, tracking.

INTRODUCTION

The history of modern cataract surgery started in 1949 when Sir Harold Ridley performed his first intraocular (IOL) implantation after having removed the natural crystalline lens.[1]

The insertion of an IOL into the human eye after intracapsular cataract extraction (ICCE) or extracapsular cataract extraction (ECCE) has become a standard procedure nowadays. The site of implantation can be angle-supported, iris-supported, sulcus-fixated or in-the-bag implantation as it is most commonly performed nowadays.

The most common complication of the lens-in-the-bag (LIB) implantation, however, is the occurance of after cataract or secondary cataract with time.[1]

Secondary cataract is caused by the proliferation and transformation of the LECs, left behind in the equator of the lens capsule, after uneventful ECCE. Because these cell deposits are preferentially located at the level of the posterior

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capsule, the term "posterior capsule opacification" (PCO) has been given to this major complication.

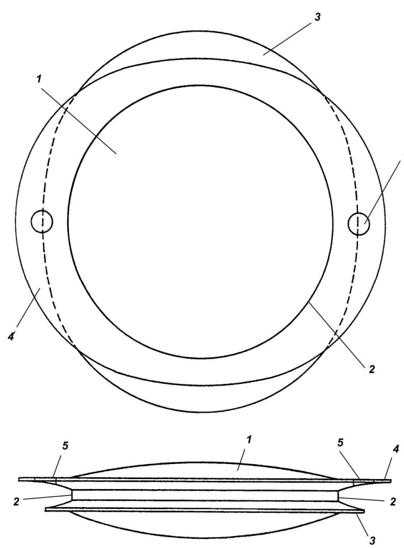
Many techniques have been advocated to prevent PCO, the major cause of visual loss after cataract surgery. These include special IOL materials and designs,[2-7] adhesive lens coating,[8] the use of chemical substances with the IOL,[9-10] physical removal of remaining proliferative cells within the lens bag,[11] physical techniques to destroy LECs,[12] the use of antibodies against LECs,[13] implantation of a capsular tension ring,[14] and removal of the central part of the posterior capsule or posterior continuous curvilinear capsulorhexis (PCCC).[15-19] These methods have substantially reduced the prevalence of PCO but have not eradicated it, especially in compromised eyes such as those of pediatric, uveitis, and diabetic patients.[20]

At present, the only efficient treatment for established PCO is surgically induced rupture of the opaque posterior capsule (i.e. capsulotomy) using a capsulotomy needle or a Q-switched neodymium:YAG (Nd:YAG) laser.[21] These secondary capsulotomies, however, increase the post cataract surgery complication rate to nearly the same rate as the now mostly abandoned ICCE procedure. Complications of a Nd:YAG capsulotomy, including retinal detachment, glaucoma, cystoid macular edema, and IOL pitting, have been widely described.[1-22]

The surgical removal of the central part of the posterior capsule, immediately before IOL implantation, did not prevent further cell proliferation[17-19] as expected. The reason is that LECs do not need the support of the posterior capsule to proliferate and reclose the PCCC opening.[23] We therefore propose a new type of IOL that is supported by both the anterior and posterior capsules, called the bag-in-the-lens (BIL) implantation technique. This lens could also be called the twin-capsulorhexis IOL to stress the crucial role of both the anterior and posterior capsulorhexis for proper IOL fixation.

1/ THE FIRST CLINICAL RESULTS WITH BIL IMPLANTATION

The biconvex IOL (Morcher) (Fig. 1) consists of a central optic surrounded by two haptics, comprising anterior and posterior peripheral flanges (Fig. 1). The anterior flange is oval and is perpendicularly oriented to the oval posterior



flange. The suggested shape and orientation of both flanges are designed to prevent tilting of the IOL once it is properly positioned in the eye.

Fig. 1. *Top*: Drawing of the bag-in-the-lens IOL. The central optic is surrounded by the haptics. The 2 oval-shaped haptics are oriented perpendicularly for lens stability. *Bottom*: Side view showing the characteristic groove into which both lens capsules will settle (1 = optic, 2 = groove, 3 = posterior haptic, 4 = anterior haptic, 5 = orientation mark)

The IOL is placed in and supported by the anterior and posterior lens capsules, after having opened both capsules with identical calibrated CCCs of approximately 4.5 to 5.0 mm. The capsules are placed in the IOL's groove, hence the term bag-in-the-lens technique (Fig. 2 A) in contrast with the lens-in-the-bag technique where the IOL, comprising the optic and the haptic, is fixed within the capsular bag (Fig. 2 B).

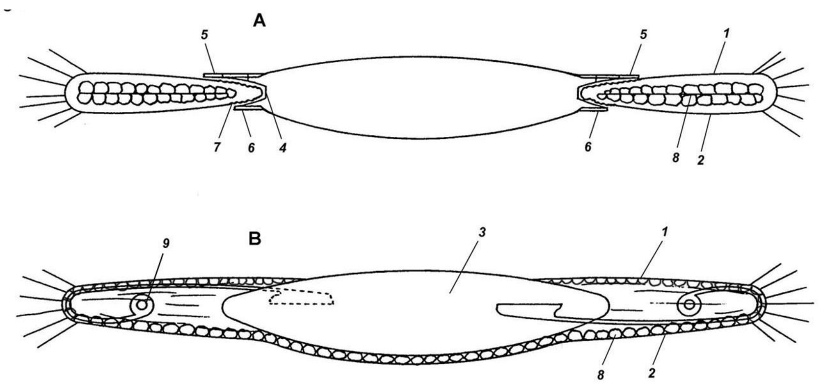


Fig. 2. *A*: Drawing showing the bag-in-the-lens positioning of the IOL. The LECs are captured in the remaining peripheral capsular bag.
B: Conventional lens-in-the-bag positioning. The LECs are on the anterior capsule, in the equatorial region, and on the posterior capsule (1 = anterior capsule, 2 = posterior capsule, 3 = IOL in place, 4 = lens groove into which both anterior and posterior capsule rims are inserted, 5 = anterior haptic, 6 = posterior haptic, 7 = wrinkles in anterior and posterior capsules caused by stretching of both capsulorhexis openings around the IOL, 8 = LECs).

The IOL is a foldable hydrophylic polyHEMA (acrylic) copolymer with approximately 24 % water content.

Before implantation in humans, the prototype of the BIL was implanted in the capsular bag model of Liu et al.[25] and put in culture for 4 weeks. Using the phase contrast microscope we demonstrated that LEC growth was indeed limited to the space between the anterior and posterior capsule and that neither could LECs be found on the anterior or posterior surface of the capsule, nor on the surface of the lens optic. This was consistently encountered in those bags where the anterior and posterior capsular openings were identical. However, in the case where both capsulorhexes did not match, LEC proliferation did occur.[26] When implanted in rabbits, the same results were found as in the in vitro model: no LEC proliferation besides the expected proliferation at the level of the capsular equator, provided both capsulorhexes were slightly smaller than the diameter of the lens optic (Fig. 3).[27] These exceptionally good experimental results were found five months after implantation in rabbits and stimulated us to find the solution for the perfect calibration technique of the anterior and posterior capsulorhexis in order to facilitate the surgical procedure in humans.

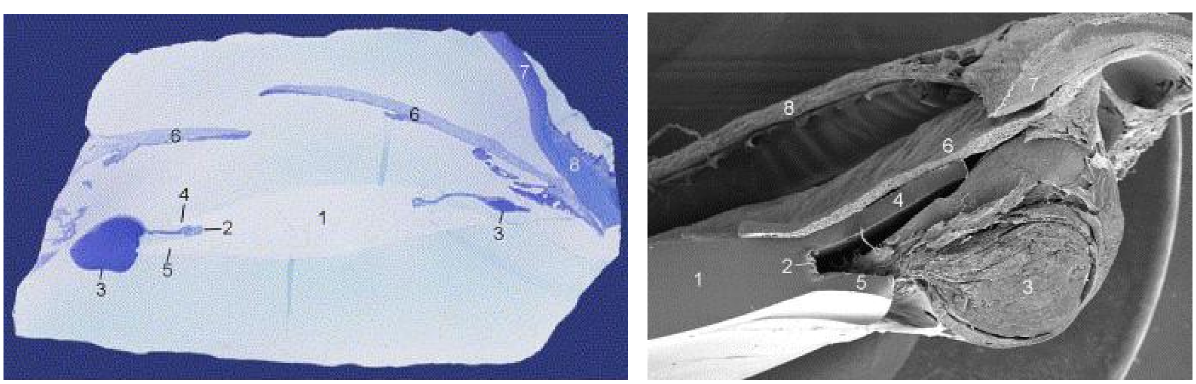


Fig. 3. Light (*left*) and scanning electron (*right*) micrographs of rabbit eyes 2 months after successful implantation of the BIL-IOL. The micrographs show that the capsules are inserted in the groove (2) of the IOL (1). A Soemmering's ring is formed at the periphery (3) (4 = anterior haptic, 5 = posterior haptic, 6 = iris, 7 = cornea, 8 = sclera).

2/ THE RING-SHAPED CALIPER TO OPTIMIZE SIZING AND CENTRATION OF THE ANTERIOR CAPSULORHEXIS

It is not easy to perform a perfectly sized anterior capsulorhexis using the free-hand method. The anterior capsulorhexis obtained will be continuous but not always curvilinear.

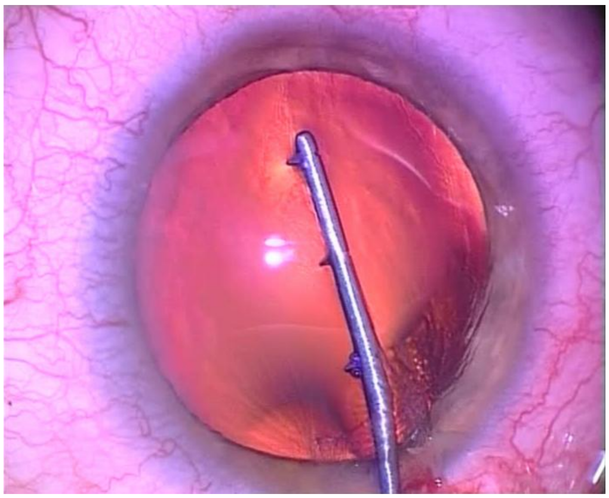


Fig. 4. Stick-shaped caliper with 3 points to make collinear marks on the anterior capsule surface.

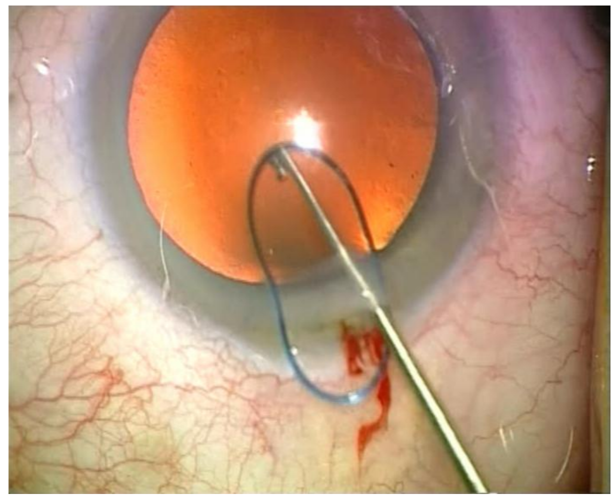


Fig. 5. Insertion of the flexible poly(methyl methacrylate) ring caliper into the anterior chamber using a lens manipulator

We first designed a metallic stick caliper (models 9-675 and 9-675-1, Duckworth and Kent, UK)[28] to apply 3 linearly arranged points at 2.25 mm from one another (Fig. 4). If performed slowly, it is possible to realise a curvilinear, centered and sized anterior capsulorhexis but the success rate will not be 100 %. In order to optimize the success rate, a PMMA ring caliper was developed (patent pending: PCT/IB2006/002835) (Fig. 5). Once implanted, it is easy to tear the anterior capsule following the internal border of the ring (Fig. 6).[28]

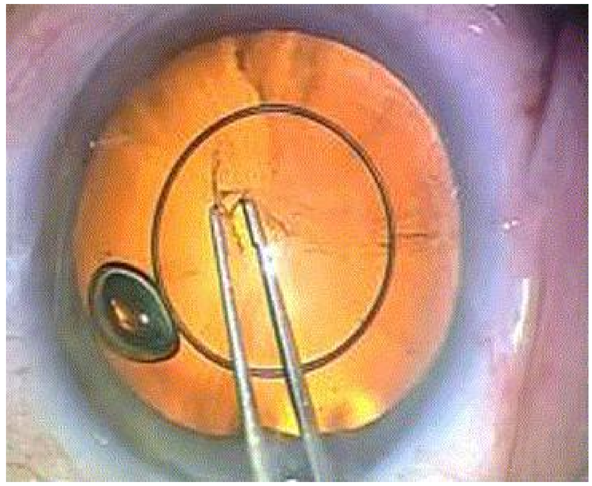


Fig. 6. Tearing of the anterior capsule along the ring caliper.

3/ EARLY AND LONG-TERM CLINICAL RESULTS WITH THE BIL

In a prospective study of 60 eyes implanted with the BIL-IOL by three different surgeons, the one year follow-up showed no reproliferation of the LECs at the level of the visual axis. In absence of the posterior capsule the term PCO to describe secondary cataract due to reproliferation of LECs in the visual axis, is inadequate and replaced by visual axis reproliferation (VAR).

We found 0 % VAR one year after BIL implantation, moderate intercapsular LEC growth at the capsular equator and a Soemmering at the merging of the anterior and posterior capsule within the lens groove (Fig. 7).[24]

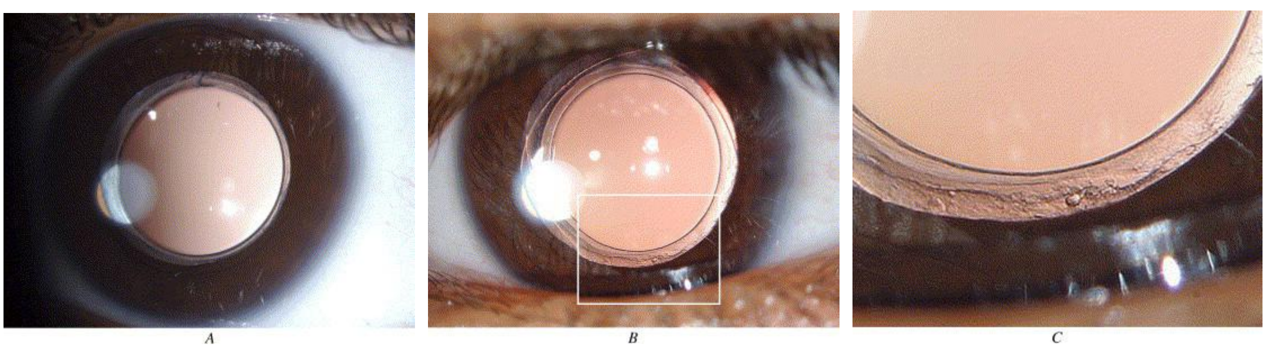


Fig. 7. A bag-in-the-lens IOL in a 4-year-old girl (A) and a 5-year-old boy (B) 5 years and 3 years after implantation, respectively. The visual axis is clear in both eyes. Mild LEC growth between the 2 lens capsules is visible at the level of the groove. *C*: magnification of boxed area in B.

One hundred eyes implanted with the BIL-IOL, having a follow-up of 17 to 72 months, were compared to 100 eyes of the same age and follow-up but implanted with the LIB-IOL manufactured out of the same biomaterial as the BIL.

Our conclusion was that none of the 100 eyes implanted with the BIL-IOL presented VAR while 20 eyes out of the LIB IOL series needed a Nd:YAG laser capsulotomy because of secondary cataract.[29]

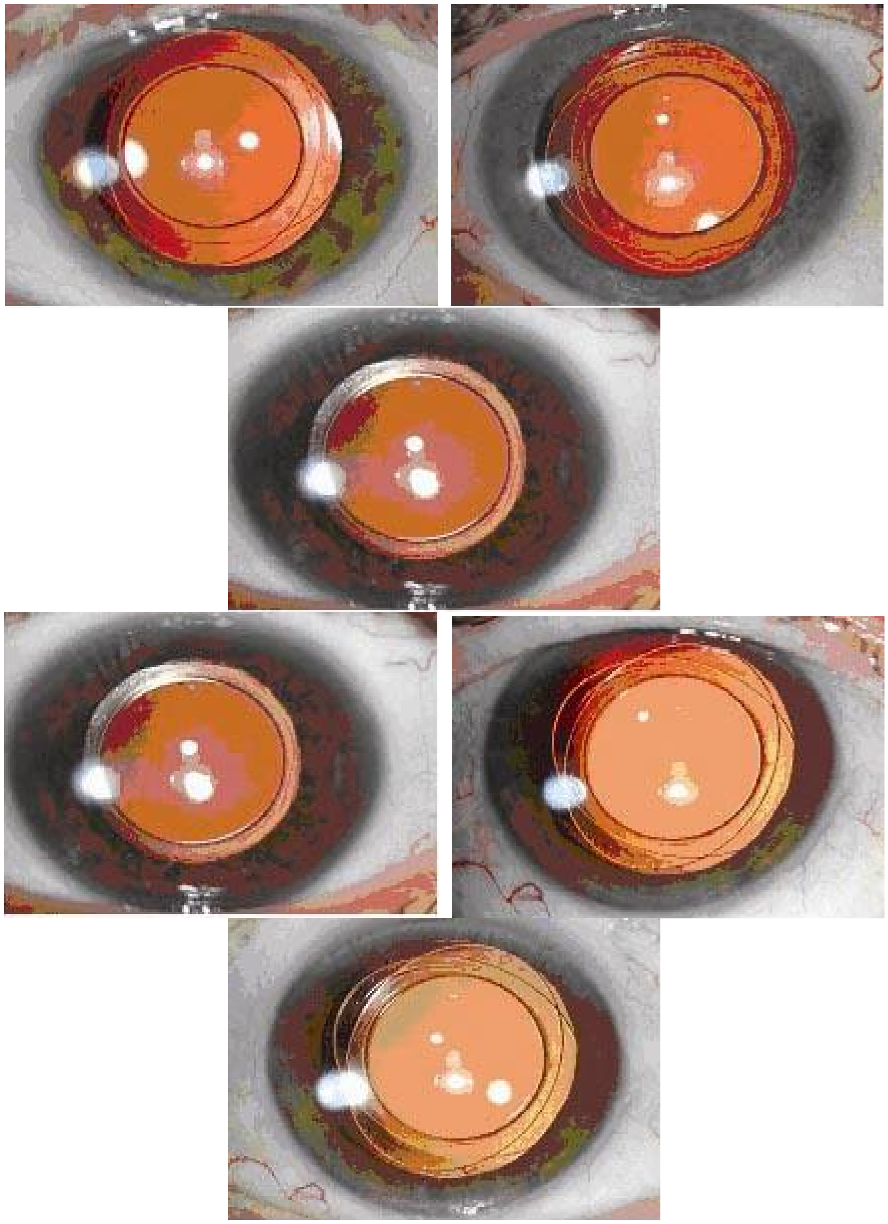


Fig. 8. Postoperative results after BIL implantation. *Top left*: 6 months follow-up. *Top middle:* 12 months follow-up. *Top right:* 18 months follow-up. *Bottom left*: 24 months follow-up. *Bottom middle*: 30 months follow-up. *Bottom right*: 36 months follow-up

The possibility of a secondary cataract ever developing can be completely eliminated when using the BIL-IOL and implantation technique (Fig. 8).

4/ HOW TO IMPROVE QUALITY OF SIGHT USING THE BIL IOL?

We need to focus our attention on two different aspects:
1. Optimal IOL centration
2. Restoration of accommodation

4.1. In a prospective clinical study of 182 eyes, the geometrical centre of the BIL IOL was compared to the geometrical centre of the pupil and of the limbus after implantation over time (5 weeks, 6 months and one year) (Fig. 9). The mean decentration of the BIL with respect to the pupil was 0.256 mm at an axis of –5.2° (nasal side). Postoperative follow-up did not significantly influence decentration, suggesting a stable positioning of the BIL over time, which is independent of the capsular healing process as is the case for the LIB-IOLs. (Fig. 10) (Table 1).

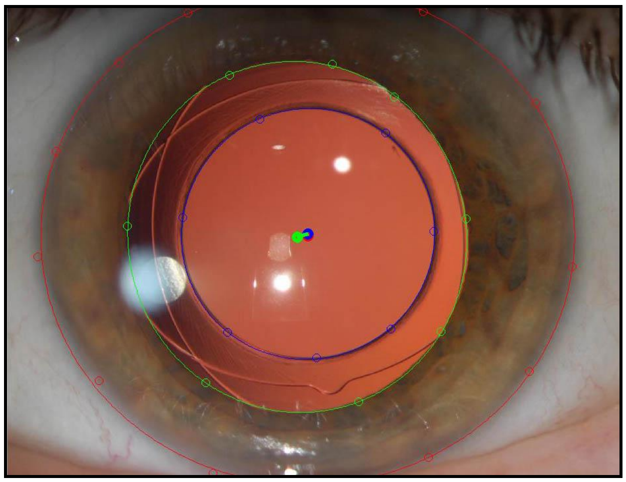


Fig. 9. The blue ellipse follows the contours of the IOL optic, the green ellipse follows the border of the pupil and the red ellipse follows the border of the limbus. The shift between the geometrical centres (IOL-pupil and IOL-limbus) is calculated.

Fig. 10. Decentration of the BIL 5 weeks postoperatively with respect to the geometrical centre of the dilated pupil, plotted on a Cartesian coordinate system. The resulting oblique value is expressed in degrees. The mean decentration is shown in red. In both eyes the positive values on the X-axis point nasally in the eye.

N = 15 eyes	5 weeks	6 months	12 months or more	GLM repeated measures
Decentration w.r.t. pupil: Mean ± SD (mm)	0.256 ± 0.107	0.246 ± 0.132	0.223 ± 0.115	F(2,28)= 1.03*
Decentration w.r.t. limbus: Mean ± SD (mm)	0.293 ± 0.174	0.290 ± 0.171	0.285 ± 0.175	F(2,28)= 0.04*

* No significant difference between decentration at 5 weeks, 6 months, 12 months or more

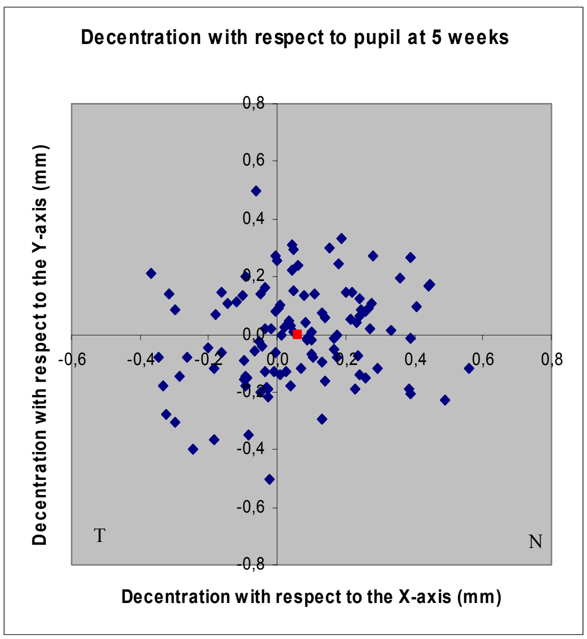


Table 1. 5 weeks, 6 months and 1 year or more of follow-up of the IOL decentration in relation to the pupil versus the limbus (15 eyes with consecutive measurements)

It should be emphasized that the BIL-IOL is the only IOL currently on the market allowing surgeon-controlled IOL centration (Fig. 2).

However, the question can be raised whether IOL centration based on the alignment of the first and third Purkinje reflexes, as observed under the microscope during surgery, is sufficient to obtain a perfect centration of the IOL along the line of sight. The answer is probably no. The solution needs further investigation. First, the line of sight needs to be defined peroperatively and second, it would be ideal to open the anterior capsule by laser under control of a tracking system, taking the ring-shaped caliper as reference. This would be a more accurate approach for optimal BIL-IOL centration.

Centration of the IOL is very important once toric correction or compensation of the spherical aberrations is intended to be incorporated in the IOL optic. Most of the current devices developed to measure the corneal astigmatism or the optical aberrations of the eye use the line of sight as reference. It would therefore be optimal to use this line of sight for IOL centration. Collaboration with the industry is necessary at this point.

4.2. Another issue needing intense collaboration with the industry is how to restore accommodation. Before incorporating multifocality in the IOL optic, which will never give an optimal quality of sight due to reduced contrast sensitivity and micro-aberrations, it is imperative to first have perfect centration, optimal compensation of the spherical aberrations and restoration of the tensile strength of the zonular fibers at the level of the capsular equator. This issue has never been approached up till now. When looking carefully at Fig. 2, the BIL-IOL does not exert any pressure on the periphery of the capsular bag. In addition, the postoperative images clearly show the transparency of the peripheral capsular bag and that it continues to remain so over time. This brought us to the idea to restore the angle of the capsular equator by inserting an accommodative ring manufactured out of a material having a Young's modulus comparable to that of the capsular bag. By restoring the peripheral capsular angulation, the transfer of the energy, exerted by the zonular fibers on the capsular bag would be restored. If the capsular accommodative ring has a Young modulus similar to that of the peripheral capsule, the antero-posterior movement of the capsular bag BIL-IOL complex will be optimalized. Once this is achieved, the missing accommodative amplitude, if any, can be corrected by means of variable refractive index optics or the like.

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