Analytical tools for customized design of monofocal intraocular lenses

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Abstract: We propose a complete methodology to develop custom monofocal Intraocular Lens (IOL) designs and evaluate their performance on-axis based on an analytical formulation. The analytical formulation was based on Gaussian and primary aberration theory applied to custom (individual biometric data) and realistic (multilayer cornea and thick IOL) pseudoaphakic eye models. Gradient-based optimization algorithms were performed to search for optimal designs. Using two parameters, the best design was obtained by directly minimizing the wavefront variance. We showed, in a case example, that custom designs achieved better final performance than generic IOL designs. Tolerances analysis allowed an evaluation of the implications of the manufacturing errors of the different parameters.

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OCIS codes: (220.3620) Lens design; (220.4830) Optical systems design; (330.4460) Ophthalmic optics

References and links
Cataract surgery is a surgical procedure where the cataractous crystalline lens is removed and replaced by an artificial lens called intraocular lens (IOL). IOL design is the procedure used to select the optical design parameters of the lens (surface shapes, thicknesses and material) in order to achieve an optimal image quality. In monofocal designs, the main goal is to achieve
emmetropia, and in the most recent designs to minimize rotationally symmetric aberrations (e.g. by using conic surfaces).

In addition, other optical criteria must be considered, such as a reduction of internal reflections [1, 2] or to avert aniseikonia in monocular implants [2, 3]. The dimensions and flexibility are also important for the optical performance, since small corneal incisions could prevent the induction of corneal aberrations [4, 5]. Besides optical considerations, non-optical factors can impose additional constraints. For example, certain lens-in-the-bag designs providing pressure on the capsular bag could help in preventing posterior capsular opacification [6]. All together, it can be said that IOL design is a constraint optimization problem.

Monofocal IOL designs are usually based on homogeneous refractive index materials and spherical or aspherical surfaces. To optimize on-axis performance, the standard design procedures proposed in the literature involve a two-steps protocol [2, 7]: 1) First, to evaluate the optimal shape factor (combination of radii of curvature) to optimize the paraxial focus, considering or not additional constraints. 2) Second, to minimize the spherical aberration aspherizing one of the IOL surfaces. In this protocol it is implicitly assumed that the best on-axis image quality is achieved by sequentially minimizing paraxial focus (using radius) and spherical aberration (using asphericities). Cataract surgeons select the IOL to implant only considering the paraxial power of the lens (using standard formulae for intraocular lens power calculation) [8]. However, the spherical aberration interacts with the defocus paraxial term generating an effective optical power that can differ significantly from the paraxial power. Preussner [9, 10] considered the effect of the interaction of spherical aberration with paraxial power in intraocular lens power calculations using ray tracing computations. However a numerical ray tracing procedure is a blind design technique in the sense that it does not provide a relation between the design target and the design parameters. Explicit equations of the effective optical power in a pseudoaphakic eye model as a function of the IOL design parameters would provide a broader IOL design tool, specifically to search for customized designs.

Several works in the 80s and 90s [2, 11, 12, 13, 14, 15] proved the strength of using the theory of primary aberrations (astigmatism, spherical aberration, coma, field of curvature and distortion) in ophthalmic lens design. Primary aberration equations are also useful to analyze optical off-axis performance [16, 17]. Most of pseudoaphakic eye models assume generic simple schematic eye models. On one hand the cornea is modelled with a single surface or sometimes with two surfaces [18]. More realistic models consider the tear film layer and a multilayer structure of the cornea [18]. We propose a pseudoaphakic eye with as many customized parameters as possible. Some basic parameters are usually measured before IOL implantation: eye axial length, anterior chamber depth, anterior corneal keratometry, etc. Other parameters, such as refractive indices have to be assumed constant across eyes. Intraocular lenses are typically assumed to be thin lenses [12, 19]. In this study, we model the IOL as a thick lens.

Conventionally the analysis of optical performance of IOL designs using pseudoaphakic eye models is performed for a single wavelength; typically 550 nm (peak of the of the human spectral sensitivity in photopic vision) [6]. Atchison [20] computed polychromatic MTFs, but he only performed a posteriori analysis of designs optimized for a single specific wavelength. Recently Dai [21] used a polychromatic point spread function (with seven different wavelengths) in an optimization procedure but assumed a single surface eye model. To include polychromatic analysis, we introduced a dispersion formula for the refractive index of the different media in the eye model.

In practice, IOL designs are restricted by the accuracy in the knowledge of various parameters: the final location of the IOL (specially axial location), although IOL tilts and decentrations may be also important [22, 23, 24, 25], the post-cataract corneal shape or the axial length of the eye. Nowadays, monofocal IOL design is limited to use rotationally symmetric IOL surfaces.
Such designs cannot compensate for the asymmetries in the corneal shape or tilts and decentrations. Anyhow, analytical expressions allow a straightforward analysis of the optical uncertainties of the design parameters.

In the present manuscript we present a unified and complete IOL design procedure. The procedure is based on using the analytical expressions derived from Gaussian optics and primary order aberration theory applied to a pseudoaphakic eye model. Combining paraxial focus and spherical aberration formulae we construct a merit function where the target is the so-called equivalent defocus of the wavefront variance [26]. We propose to use optimization routines, based on the gradient (and Hessian) evaluation of the merit function, in order to search for the optimal IOL designs. A tolerance analysis, maximum allowed perturbations of the design parameters to maintain a certain optical quality, will be also performed. The main goal of this manuscript is not to propose new specific designs but to present a set of procedures, using an analytical framework (not based on ray-tracing), to search for realistic and optimal designs under different circumstances.

2. Methods

2.1. Pseudoaphakic eye model

We used a pseudoaphakic eye model defined as a set of concentric surfaces (represented by conics) and separated by homogeneous media with associated dispersion formulae. We used a multilayer corneal model based on three layers: tear film, epithelium and stroma [18]). In order to simplify the analytical expressions, we assumed a homogeneous refractive index, instead of a gradient index stromal layer. The refractive indices of the different ocular media were modelled using Cauchy dispersion formulas, proposed by Atchison and Smith [27]. For the tear film we used the same dispersion than the aqueous humour, and for the corneal epithelium and stroma we used the generic dispersion equation proposed for the cornea [27]. Our model also considered the pupil size as a parameter, which can be customized to the patient. In most examples we used a constant pupil radius of 2 mm, obtained from Winn et al.s [28] study on pupil sizes as a function of age, as an average value for normal luminance levels (44 cd/m-2 and 220 cd/m-2) and ages around 70 (typical of post-cataract eyes).

Table 1 summarizes the parameters of our pseudoaphakic eye model. Customized parameters (variable among patients) are denoted by C.

2.2. Defocus and spherical aberration from paraxial and primary aberration theory

We applied ray-matrix theory to derive an explicit equation of the paraxial power of the pseudoaphakic eye model as function of the radii of curvature, thickness and refractive indices. The global ray-matrix of the eye model was computed as follows:

$$M_t = R_1 * T_1 * R_2 * T_2 * R_3 * T_3 * R_4 * T_4 * R_5 * T_5 * R_6 * T_6,$$

where R were refraction ray-matrices and T translation ray-matrices [18]. R1 is the refraction in the air-tear interface, R2 is the refraction in the tear-epithelium interface, R3 is the refraction in the epithelium-stroma interface, R4 is the refraction in the stroma-aqueous interface, R5 is the refraction in aqueous-IOL interface and R6 is the refraction in IOL-vitreous interface. T1 is the translation in tear medium, T2 is the translation in epithelium medium, T3 is the translation in stroma medium, T4 is the translation in aqueous medium, T5 is the translation in IOL medium and T6 is the translation in vitreous medium. All the paraxial properties of the eye model (location of cardinal points) are contained in Mt. From Mt we computed the location of the paraxial image plane (Ro) and the retinal plane (Re) with respect to the image principal plane. From Ro and Re we derived an explicit expression for the Taylor paraxial defocus term.
Table 1. Parameters of a generic pseudoaphakic eye model. C denotes a custom parameter. R denotes the apical radius. Q denotes the asphericity (or deformation factor) defined by the conic explicit formula: $Y^2 = 2Rz - (1 + Q)z^2$. $n(\lambda)_a$, $n(\lambda)_c$, and $n(\lambda)_v$ denote the refractive index dispersion formulae for the aqueous, vitreous and corneal media derived by Atchison et al[26]. I1: Air-Tear. I2: Tear-Epithelium. I3: Epithelium-Stroma. I4: Stroma-Aqueous. I5: Aqueous-IOL. I6: IOL-Vitreous

<table>
<thead>
<tr>
<th>Interface</th>
<th>I1</th>
<th>I2</th>
<th>I3</th>
<th>I4</th>
<th>I5</th>
<th>I6</th>
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<tbody>
<tr>
<td>R (mm)</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>6.4[18]</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Q</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>-0.38[18]</td>
<td>C</td>
<td>C</td>
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</table>

<table>
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<tr>
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<th>Tear</th>
<th>Epithelium</th>
<th>Stroma</th>
<th>Aqueous</th>
<th>IOL</th>
<th>Vitreous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central thickness (mm)</td>
<td>0.004[18]</td>
<td>0.0537[18]</td>
<td>0.473[18]</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Refractive index</td>
<td>$n(\lambda)_a$</td>
<td>$n(\lambda)_c$</td>
<td>$n(\lambda)_c$</td>
<td>$n(\lambda)_a$</td>
<td>C</td>
<td>$n(\lambda)_v$</td>
</tr>
</tbody>
</table>

using a previously derived equation (equation 8 in Smith et al. [29]).

$$W_{20} = f(R_i, ti, \lambda),$$

(2)

where $f$ stands for a function of the radii of curvature ($R_i$), thicknesses ($ti$) and wavelength ($\lambda$). The explicit form of $f$ is not given because it has an excessively large algebraic length. We used the primary spherical aberration contribution of a conic surface derived by Schwarzschild [30]. Following the addition theorem [30], we computed the spherical aberration of the whole eye as the sum of all the surface contributions.

$$W_{40} = g(P, R_i, Q_i, ti, \lambda),$$

(3)

where $g$ stands for a function of radii of curvature ($R_i$), asphericities ($Q_i$), thicknesses ($ti$), pupil radius ($P$) and wavelength ($\lambda$). The explicit form of $g$ is not given because it has an excessively large algebraic length. However, this formula evaluates the spherical aberration with respect to the paraxial image plane, whereas the spherical aberration must be computed with respect to the retinal plane. To correct this shift-plane effect we applied an equation recently derived by Smith et al. [29] (equation 10 in Smith et al. [29]).

2.3. Image quality metrics

For on-axis imaging, $W_{20}$ and $W_{40}$ equations are sufficient to describe analytically the shape of the geometrical optics retinal spot (as first approximation). Diffraction effects were not considered because the consideration of diffraction integrals would prevent an algebraic expression. The root-mean square error (RMS) of the wavefront [31] is usually used to describe the geometrical optical quality. We obtained an analytical expression of the equation for the RMS of the eye model using the $W_{20}$ and $W_{40}$ equations (equation 34.14 in Smith et al. [31]). We point out that since we are using the Taylor terms of the wavefront to compute the RMS, the interaction between the defocus and the spherical aberration is explicitly included, which does not occur if the balanced Zernike polynomials terms were used [32]. In order to use an optometric unit (Diopters), we used the concept of equivalent defocus (Me), proposed by Thibos [26], i.e the amount of defocus (in diopters) required to produce the same amount of wavefront
variance. We converted RMS into Me using equation 3 in Thibos et al. [26]. Me depends on the wavelength.

For a single wavelength, Me defines a monochromatic optical quality metric. We explored geometrical optical quality metrics considering polychromatic effects. Color human vision is trichromatic because it is based on the recording of luminous signal from three types of cone photoreceptors, each one with different spectral sensitivity: short-(S) cones (420.7 nm sensitivity peak), middle-(M) cones (530.3 nm sensitivity peak) and long-(L) cones (558.9 nm sensitivity peak) [33]. We defined a polychromatic weighted equivalent defocus Mew:

$$M_{ew} = Me(420.7) + 0.5 * (Me(530.3) + Me(558.9))$$

(4)

This metric was just an example, selected following a heuristic procedure after a posteriori evaluation of the results in order to obtain lower values of Me values for 420.7 nm.

2.4. Optimization procedures

Possible IOL designs were explored by representing the IOL optical performance (equivalent defocus) in bi-dimensional plots as a function of two IOL design parameters, for example anterior and posterior surface radii of curvature (Ra and Rp) or anterior radius of curvature and anterior asphericity (Ra and Qa). These graphics showed specific regions where the combination of the design parameters produce acceptable equivalent defocus. Analytical optimization algorithms were used to search for the optimal combination of radii and asphericities. A merit function was built defining a target (e.g. Me) as function of design parameters (radii or asphericities).

We compared two types of optimization algorithms. The first type (gradient-based) estimates the first derivatives of the merit function with respect to the different design parameters, and subsequently uses this information as an input for the search algorithm. The second type does not use gradient information and is based on direct search algorithms. A priori the gradient-based algorithm is expected to be more efficient and accurate [34] because it includes additional information.

There are many different gradient-based optimization algorithms. However the relation of Me with respect to the radius of curvature or asphericities is highly non-linear. This implies that it is convenient to select a quadratic model optimization scheme [34] where not only the first but also the second derivatives are computed. We selected a quasi-Newton algorithm, that uses an iterative procedure to establish the direction of search [34]. Among the non gradient-based algorithms we selected a Nelder-Mead simplex direct search algorithm. We used built-in functions available in the Optimization toolbox of Matlab to implement these algorithms.

2.5. Tolerance analysis

Among the several IOL manufacturing techniques, molding is the most widely used [35]. Manufacturing techniques present some accuracy limits and henceforth some deviations between the design specifications and the actual parameters may be expected. If these differences do not affect considerably the final optical performance of the IOL, it can be said that the IOL design is sufficiently robust. Tolerance limits, i.e. the maximum allowed difference between the values of a designed and its associated manufactured parameter not to decrease the optical performance below a specific target, are therefore essential in the manufacturing process.

We used the derived equations relating the equivalent defocus with the IOL design parameters to compute the tolerance limits of our IOL design parameters: radii of curvature, asphericities, thickness and refractive index. We set a value of 0.25 D for the equivalent defocus as the upper threshold target in the tolerance limits computations. This is just an arbitrary threshold based
Table 2. Parameters of a case example customized pseudoaphakic eye model (patient AA with an 22 D Tecnis Z9000 IOL). R denotes the apical radius. Q denotes the asphericity (or deformation factor) defined by the conic explicit formula: 
\[ Y^2 = 2Rz - (1 + Q)z^2, \]
where \( n(\lambda)_a, n(\lambda)_c, \) and \( n(\lambda)_v \) denote the refractive index dispersion formulae for the aqueous, vitreous, corneal and silicon media. I1: Air-Tear. I2: Tear-Epithelium. I3: Epithelium-Stroma. I4: Stroma-Aqueous. I5: Aqueous-IOL. I6: IOL-Vitreous

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<th>Interface</th>
<th>I1</th>
<th>I2</th>
<th>I3</th>
<th>I4</th>
<th>I5</th>
<th>I6</th>
</tr>
</thead>
<tbody>
<tr>
<td>R (mm)</td>
<td>7.79</td>
<td>7.79</td>
<td>7.56</td>
<td>6.4[18]</td>
<td>11.043</td>
<td>-11.043</td>
</tr>
<tr>
<td>Q</td>
<td>-0.49</td>
<td>-0.49</td>
<td>-1.9</td>
<td>-0.38[18]</td>
<td>-1.036</td>
<td>0</td>
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</tbody>
</table>

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<tr>
<th>Medium</th>
<th>Tear</th>
<th>Epithelium</th>
<th>Stroma</th>
<th>Aqueous</th>
<th>IOL</th>
<th>Vitreous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central thickness (mm)</td>
<td>0.004[18]</td>
<td>0.0537[18]</td>
<td>0.473[18]</td>
<td>4.29</td>
<td>1.164</td>
<td>17</td>
</tr>
<tr>
<td>Refractive index</td>
<td>( n(\lambda)_a )</td>
<td>( n(\lambda)_c )</td>
<td>( n(\lambda)_c )</td>
<td>( n(\lambda)_a )</td>
<td>( n(\lambda)_s )</td>
<td>( n(\lambda)_v )</td>
</tr>
</tbody>
</table>

on a a simple generic value for depth of field of the human eye [31]. Other threshold could be used.

3. Results

3.1. Custom pseudoaphakic models for IOL design

Table 1 presented a generic pseudoaphakic eye model where several parameters are customized for different individuals. As a case example we configured a custom pseudoaphakic eye model using biometric data measured in a specific patient (Eye 17) from a previous study [5]. The individual data for this pseudoaphakic eye are presented in Table 2.

The anterior chamber depth (ACD), distance from posterior cornea surface vertex to anterior IOL surface vertex, and eye axial length were measured with slit-lamp imaging and partial coherence interferometry (IOL Master, Zeiss, Jena, Germany) respectively. The anterior corneal surface (air-tear film interface [18]) topography was measured using a videokeratographer (Atlas Humphrey Instruments, Zeiss, San Leandro, Calif.) and subsequently fitted to a conic surface using customize software [37]. The radii of curvature and asphericities of tear-epithelium and epithelium-stroma interfaces were calculated from the shape of the interface air-tear film following a procedure explained elsewhere [18]. A 22 D Tecnis Z9000 IOL was implanted after cataract surgery in Eye 17. The design parameters of the 22 D Tecnis Z9000 IOL were obtained from published literature [7]. This IOL was made of a HRI silicone [7], with dispersion formula taken from Zemax (Zemax, Optima Research, 2006 Tucson) glass catalog.

3.2. Optimization algorithms

The two optimization algorithms proposed (Quasi-Newton and Nelder-Mead) were tested in a case example. The pseudoaphakic eye model of Table 2 was used, setting four design parameters to be optimized: the two radii of curvature and the asphericities and setting fixed values for the IOL thickness and the index of refraction. We compared the final design achieved in both optimizations and the efficiency of the algorithm.

The efficiency was tested by means of the number of iterations taken to achieve the design and the number of function evaluations. The lower these values the more efficient the algorithm. Table 3 shows the results of the optimization algorithms. Both algorithms reached an
Table 3. Design specifications and efficiency of the optimization algorithm. Ra and Rp denote the anterior and posterior radii of curvature of the IOL. Qa and Qp denote the anterior and posterior asphericities of the IOL. Me denotes the equivalent defocus for the IOL design in the pseudoaphakic for the eye model of Table 2. N iterations denotes for the number of iterations needed by the optimization searching algorithm and N functions the number of functions evaluated.

<table>
<thead>
<tr>
<th>Optimization algorithm</th>
<th>Ra (mm)</th>
<th>Qa</th>
<th>Rp (mm)</th>
<th>Qp</th>
<th>Me (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quasi-Newton</td>
<td>8.97</td>
<td>-2.82</td>
<td>-10.48</td>
<td>-2.25</td>
<td>$4 \times 10^{-7}$</td>
</tr>
<tr>
<td>Nelder-Mead</td>
<td>5.92</td>
<td>-0.82</td>
<td>-32</td>
<td>0.91</td>
<td>$2.4 \times 10^{-4}$</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Optimization algorithm</th>
<th>N iterations</th>
<th>N functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quasi-Newton</td>
<td>30</td>
<td>226</td>
</tr>
<tr>
<td>Nelder-Mead</td>
<td>480</td>
<td>800</td>
</tr>
</tbody>
</table>

An optimized design as denoted by a very small final equivalent defocus (Me), although the Quasi-Newton algorithm achieved a smaller value than the Nelder-Mead algorithm. The number of iterations and function evaluations is much lower in the Quasi-Newton algorithm, implying that the gradient-based algorithm is more efficient than the simplex direct search algorithm. It is also important to point out that the IOL design parameters found were quite different, although they both provided an equivalent defocus non-significantly different from zero.

3.3. Bi-dimensional exploration of IOL designs

In order to acquire a global visualization of different IOL designs options we represented the results in the form of bi-dimensional graphics. The graphics were contour plots where the equivalent defocus (Me) was plotted as function of two design parameters. Contour lines are plotted every 0.25 D. The colorbar pattern represents equivalent defocus in Diopters. The custom pseudophakic eye model of Table 2 was used, setting two design parameters as variables. Pupil radius was set to 2 mm. Figure 1 shows radii of curvature (Ra: anterior radius of curvature and Rp: posterior radius of curvature) combinations for bi-convex and meniscus designs. The scale of Ra and Rp were different to allow better visualization. The graph shows two different regions, corresponding to combinations of radii of curvature, with Me smaller than 0.25 D.

It can be observed that, in case of being limited by a constraint in one of the radii of curvature, it is still possible to find a good IOL design by modifying the other radius. Figure 2 shows combinations of radii of curvature (R) and asphericities (Q) for anterior surface and posterior surface designs. In contrast to Fig. 1 the region where Me is below 0.25 D is very limited to a particular area. This implies that IOL designs which use one radius and one asphericity rather than two radii offer a more reduced space of acceptable solutions.

3.4. Step procedure analysis

In Table 3 we present an optimization procedure where all the geometry parameters of the IOL were allowed to be varied. However, in practical situations some of the parameters of the IOL geometry are affected by some constraints. In addition a goal in IOL design is to search for “economic” designs, i.e. IOL designs where optimal performance can be obtained using the minimum number of parameters. A good on-axis design can be obtained with less than four parameters.

In order to evaluate the most efficient IOL optimization procedure we performed a scheme of cascade optimization steps, using different targets and different design parameters in each
Fig. 1. Contour plots of the equivalent defocus (Me) as function of the two radii of curvature of: (a) Biconvex IOL design (b) Meniscus IOL design. The colorbar represents Me in Diopters. Contour lines are plotted every 0.25 D. The scale of the x-axis and y-axis are different to allow better visualization. Results are for the custom pseudoaphakic eye model of Table 2. Pupil radius is set to 2 mm.

Fig. 2. Contour plots of the equivalent defocus (Me) of a biconvex IOL design as function of: (a) The anterior radius of curvature and asphericity (b) The posterior radius of curvature and asphericity. The colorbar represents Me in Diopters. Contour lines are plotted every 0.25 D. The scale of the x-axis and y-axis are different to allow better visualization. Results are for the custom pseudoaphakic eye model of Table 2. Pupil radius is set to 2 mm.
Fig. 3. Scheme of cascade optimization steps, using different targets and different design parameters in each step. Radii of curvatures (Ra and Rp) and asphericities (Qa and Qp) were used as design parameters. IOL thickness was set as fixed parameter (custom value of Table 2). The merit function, with the target and design parameters used, is shown in the circular shaped rectangular boxes, whereas the designs obtained in each step appear in rectangular boxes and are labelled with IOL followed by a number code. See text for details.

Table 4. Design specifications and optical performance of the IOL designs obtained by different procedures. Ra and Rp denote the anterior and posterior radii of curvature of the IOL. Qa and Qp denote the anterior and posterior asphericities of the IOL. W20, W40 and Me denote the equivalent defocus (D) due to the defocus term, spherical aberration and the combination of both for several IOL designs.

<table>
<thead>
<tr>
<th>IOL</th>
<th>Ra (mm)</th>
<th>Qa</th>
<th>Rp (mm)</th>
<th>Qp</th>
<th>Me (D 555 nm)</th>
<th>W20 (D)</th>
<th>W40 (D)</th>
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<tr>
<td>IOL A1</td>
<td>9.05</td>
<td>0</td>
<td>-11.04</td>
<td>0</td>
<td>0.12</td>
<td>-0.48</td>
<td>0.49</td>
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<tr>
<td>IOL A2</td>
<td>8.63</td>
<td>0</td>
<td>-11.04</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>IOL B1</td>
<td>9.05</td>
<td>-0.27</td>
<td>-11.04</td>
<td>0</td>
<td>0.12</td>
<td>-0.47</td>
<td>0.46</td>
</tr>
<tr>
<td>IOL B2</td>
<td>9.05</td>
<td>0</td>
<td>-11.04</td>
<td>-0.59</td>
<td>0.12</td>
<td>-0.47</td>
<td>0.46</td>
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<tr>
<td>IOL B3</td>
<td>8.63</td>
<td>-3.38</td>
<td>-11.04</td>
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<td>0.0030</td>
<td>-0.0029</td>
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<td>IOL B4</td>
<td>8.63</td>
<td>-3.37</td>
<td>-11.04</td>
<td>0</td>
<td>0.003</td>
<td>0.003</td>
<td>0</td>
</tr>
<tr>
<td>IOL B5</td>
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<td>0</td>
<td>-11.04</td>
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<td>0.0007</td>
<td>0.003</td>
<td>-0.003</td>
</tr>
<tr>
<td>IOL B6</td>
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<td>0</td>
<td>-11.04</td>
<td>-8.69</td>
<td>0.003</td>
<td>0.003</td>
<td>0</td>
</tr>
<tr>
<td>IOL C1</td>
<td>8.63</td>
<td>-3.37</td>
<td>-11.04</td>
<td>0</td>
<td>$0.1 \times 10^{-6}$</td>
<td>$-0.5 \times 10^{-6}$</td>
<td>$0.5 \times 10^{-6}$</td>
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<tr>
<td>IOL P1</td>
<td>8.71</td>
<td>-3.45</td>
<td>-11.04</td>
<td>0</td>
<td>0.09</td>
<td>-0.09</td>
<td>$-4 \times 10^{-4}$</td>
</tr>
</tbody>
</table>

step. Radii of curvature and asphericities were used as design parameters. IOL thickness was set as fixed parameter (custom value of Table 2) because its value is in practice usually selected following mechanical constraints. The scheme is shown in Fig. 3.

The merit function, with the target and design parameters used, is shown in the circular shaped rectangular boxes, whereas the designs obtained in each step are labelled with IOL followed by a number code. The specific calculated designs and the values obtained for W20, W40 and Me appear in Table 4.

In a first cascade of optimization procedures we set one single design parameter: IOL anterior radius. We configured two merit functions with two different targets: one using the defocus term (W20) and the other the equivalent defocus (Me). We obtained designs IOL A1 & A2. Subsequently, using these output designs, we performed a second cascade of optimization procedures using the anterior or the posterior IOL asphericity as additional design parameters and
the spherical aberration term \(W40\) or the equivalent defocus \(Me\) as targets in the merit function. Finally we performed an optimization procedure configuring a merit function with two design parameters: anterior radius and asphericity of anterior IOL surface of and the equivalent defocus as target, obtaining design IOL-C1.

Designs obtained optimizing one single parameter (IOL A1&A2) did not achieved good optimal performance \(Me < 0.25\) D. Following a two-step optimization procedure the best designs (IOL B3-B4-B5&B6) where obtained optimizing \(W20\) and subsequently \(Me\). In these cases, higher asphericities (-14.91) where needed in designs with posterior aspherical surfaces (IOL B5&6) than in designs with anterior aspherical surfaces (-5 in IOL B3&B4). The best design (IOL C1) was obtained optimizing the radius of curvature and asphericity of the IOL surface by minimizing \(Me\).

3.5. Case example optimization

Table 2 presented a custom pseudoaphakic eye model with a IOL of known design parameters (22 D Tecnis Z9000). We computed equivalent defocus for this custom model eye with the particular IOL implanted, and plotted the results in the optical performance bi-dimensional graphics of Fig. 1 and 2 (green star) as a comparison with the results obtained from the optimized designs (blue stars). The equivalent defocus of this model is 1.2 D, being significantly shifted from areas of optimal performance (below 0.25 D).

3.6. Optimization for polychromatic light

So far the optimization procedures optimized the equivalent defocus for the photopic spectral peak wavelength (555 nm). In the IOL-C1 design, \(Me\) was optimized for 555 nm and reached a minimum value of 0.3e-6 D. For this design, \(Me\) corresponding to the wavelength of maximum absorbance of the different cones classes were 0.1 D (530.3 nm), 0.01 D (558.9 nm) and 0.71 D (420.7 nm). We performed an optimization procedure using the polychromatic target \(Mew\) (see methods section) using the radius of curvature and asphericity of the IOL anterior surface as design parameters. We obtained the design IOL P1 (Table 4) which is slightly different from the monochromatic design IOL C1 because it slightly balances the values of \(Me\) for the different spectral peaks: 0.09 D (555 nm), 0.002 D (530.3 nm), 0.1 D (558.9 nm) and 0.61 D (420.7 nm).

3.7. Pupil size in IOL design

Pupil size affects significantly the spherical aberration and the interaction of defocus with spherical aberration. Pupil size for similar luminance levels declines with age, although there is a large scattering in the data [28]. Pupil size changes with lighting level and with accommodation [37] in normal eyes, although pupil dynamics in pseudoaphakic eyes has not been studied in detail.

We analyzed the effects of pupil size changes using the equations 1-4. Figure 4 shows changes in the spherical aberration and the equivalent defocus with pupil size using pseudoaphakic eye model of Table 2. Interestingly, the equivalent defocus dependency with pupil radius followed a parabolic behaviour in a range of pupil radii from 2 to 5 mm, with a well localized minimum. This result indicates that a specific IOL design in a specific pseudoaphakic eye is optimized for a specific pupil radius, or alternatively, that an IOL design can be optimized for a specific pupil radius, that can be selected according to the patient characteristics. In the case example of Table 2 the optimal design was achieved for a pupil size of 4.7 mm (\(Me=0.58\) D).
3.8. Effect of ocular biometry uncertainty

So far we assumed that the exact values of the biometric parameters of the eye model were known. However, the experimental measurement or the estimation of these parameters suffers from errors that propagate to the estimation of the refractive properties of the eye model. Olsen reported that the main errors are due to the measurement of axial length, the estimation of the post-surgery corneal surface shape and the estimation of pseudoaphakic anterior chamber depth (ACD) [38].

The post-operative ACD (defined as the distance from posterior cornea surface vertex to anterior IOL surface vertex) can only be estimated because it depends on some postoperative changes, particularly capsular bag shrinkage [9]. The estimation uses the measurement of the pre-operative ACD (distance from the posterior corneal vertex to anterior iris plane) plus some heuristic estimation of the IOL location with respect to the anterior iris plane [8]. Olsen [39] calculated a standard deviation error of 0.52 mm (17.9% of the mean) in the estimation of ACD in population of 6698 eyes. Using these estimated errors we calculated the changes in W20, W40 and Me versus different estimations of ACD for the pseudoaphakic model of Table 2 (Fig. 5). Errors in ACD affected very slightly W40 but had a significant impact on W20 and hence Me. A 17.9% standard deviation in the estimation of ACD resulted in a standard deviation of 0.92 D in the estimation of the equivalent defocus. This large value reveals that the uncertainty in the estimation of the post-surgery ACD is a critical limitation for any type of IOL design strategy.

The posterior chamber depth is obtained measuring the axial length of the whole eye and using the estimated post-surgery ACD. Axial length is conventionally measured by ultrasound or optical interferometry, where the sound velocity or refractive index inside ocular medium must be known. Because the error associated to the axial length measurement (accuracy of the
Fig. 5. Defocus term (W20), spherical aberration (W40) and the equivalent defocus in Diopters as function of the anterior chamber depth (mm) using the pseudoaphakic eye model of Table 2.

Table 5. Tolerance limits of the pseudoaphakic eye model of Table 2 for the design parameters: anterior and posterior radii and asphericities, thickness and refractive index.

<table>
<thead>
<tr>
<th>Anterior radius</th>
<th>Posterior radius</th>
<th>Anterior asphericity</th>
<th>Posterior asphericity</th>
<th>Thickness</th>
<th>Refractive Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>±0.23 mm</td>
<td>±0.33 mm</td>
<td>±1.66</td>
<td>±4.28</td>
<td>±0.12</td>
<td>±0.0017</td>
</tr>
</tbody>
</table>

ultrasound or optical technique) is very small compared to the error in the estimation of post ACD, the posterior chamber depth error affects to the equivalent defocus similarly to the error in the estimation of the ACD.

3.9. Tolerance analysis

We computed the tolerance limits of the pseudoaphakic eye model of Table 2 for all the possible design parameters of an IOL: anterior and posterior radii and asphericities, thickness and refractive index. Results are shown in Table 5. Tolerance limits for the posterior radius of curvature and asphericity were higher than that of the anterior IOL surface.

4. Discussion

4.1. State of the art in IOL design and limitations of the technique

We have presented a complete analytical framework to analyze the refractive optical quality of on-axis IOL designs and propose optimal designs.

Besides earlier (70’s) IOL design techniques based on caustic surface computations [40] [41], most of IOL design techniques appeared in the 80’s can be classified in two groups: ray-
Table 6. Comparison of optical performance of the custom design and the Tecnis IOL design in the more realistic pseudoaphakic eye model of Table 2. The different metrics were computed through a ray tracing analysis using Zemax (Zemax, Optima Research, 2006 Tucson). Mes: Me contribution of symmetric terms. Mea: Me contribution of asymmetric terms.

<table>
<thead>
<tr>
<th></th>
<th>W20 (D)</th>
<th>W40 (D)</th>
<th>Mes (D)</th>
<th>Mea (D)</th>
<th>Me total (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecnis IOL</td>
<td>-3.02</td>
<td>0.99</td>
<td>2.05</td>
<td>0.86</td>
<td>2.22</td>
</tr>
<tr>
<td>Custom IOL (IOL-C1)</td>
<td>0.04</td>
<td>0.49</td>
<td>0.59</td>
<td>0.75</td>
<td>0.95</td>
</tr>
</tbody>
</table>

tracing or primary aberration (Seidel) methods. Ray tracing analysis [16, 20, 22] provide exact computations of the rays trajectories through an eye model, hence an exact computation of ray aberrations. On the other hand, paraxial optics and primary aberrations theory are convenient because they provide equations relating the optical performance with the different parameters of the pseudoaphakic eye, hence providing an efficient and controlled way of searching for different possible designs.

Our methodology introduces some important improvements with respect to previous methods based on primary aberration theory. We considered a more realistic pseudoaphakic eye model (multilayer cornea and thick IOL) and the effect in the spherical aberration of a shift in the location of the retina plane with respect to the paraxial plane. In the analytical framework we have proposed, for the first time, to use analytical optimization and tolerance analysis algorithms.

The technique is in principle limited to primary aberrations. However, in practice it is possible to use primary aberrations theory for a preliminary design and subsequently perform a ray tracing simulation for refinement of designs [2, 19]. Smith et al. [11] studied the contributions of aberrations of higher order than primary to the spherical aberration. He found that for pupil radius of 2 mm the contribution was 5% or less. We tested that both our analytical procedure and a ray tracing technique provided similar outcomes of optimal performance for the same pseudoaphakic eye model (presented in Table 2). We compared the optimized equivalent defocus (Me) from the analytical procedure with that obtained by ray tracing using Zemax (Zemax, Optima Research, 2006 Tucson) on the pseudoaphakic eye model of Table 2 with the optimized design IOL-C1. We obtained a difference of 0.12 D, which is below our threshold.

While our pseudoaphakic eye model considers presents several sophistications with respect to conventional pseudoaphakic eye model used in IOL design (i.e. a multilayer corneal model and the explicit consideration of the thick nature of IOLs) there are still some limitations with respect to more realistic models that consider the actual corneal topography, tilt and decentrations of the IOL and the misalignment of the line of sight with respect to the optical axis of the eye [24].

To evaluate the effect of this simplification, we included the post-operative corneal topography [5] and the actual IOL tilt and decentration [25] measured for the particular the pseudoaphakic eye model of Table 2. We compared the final optical performance of two designs (the Tecnis Z-900 and our optimized custom IOL-C1 designs) in this more realistic model by calculating several optical outputs through a ray tracing analysis. Results are shown in Table 6.

The total amount of Me increased significantly with respect to the rotationally symmetric eye model, mainly because of the presence of high order corneal aberrations but also because of the slight contribution of the shift of the line of sight, and possibly IOL misalignments [24]. We found a difference of around 1 D in the final performance considering the custom design with respect to the Tecnis IOL design. The compensation of the equivalent defocus due to the symmetrical terms (defocus and spherical aberration) is well preserved in the custom design,
and there is a higher correction of asymmetric aberration terms in the custom design with respect to the Tecnis design.

Finally both ordinary ray tracing and the analytical procedure do not consider diffraction effects and cone directionality [42]. These additional effects may produce shifts of the subjective best refraction with respect to the best focus obtained by minimizing the RMS wavefront error [43, 44]. The exact location of the plane of best visual focus is still an open question. However strategies can be found to incorporate these effects into a geometrical scheme. For example, it has been proposed to weight the efficiency of rays according to their pupil entrance to account for cone directionality and diffraction [20]. In a similar way we could introduce a different weight to the defocus (W20) versus the spherical aberration term (W40) to consider these effects.

4.2. Implications of the results

The analytical procedure that we have presented allows to achieve an optimal design, customized to biometric parameters of individual eyes. On the other hand, since it provides simultaneously the optical performance of IOLs with multiple combination of design parameters, we are able to extract conclusions of relevance to IOL design. By comparison of IOL design strategies where either the two radii of curvature are modified or one radius of curvature and one asphericity are let to vary, we found that the latter has more limited space of solutions than the former. We also found that if the designer is limited by a constraint in one of the radii of curvature it is sometimes possible to find a good on-axis design (Me below 0.25 D) without the need of aspherizing the surface.

The analytical procedure allowed to compare different cascade optimization procedures (Table 4 and Fig. 3 which allow to draw conclusions on the best IOL design strategy. First, the optimization procedure that allows the best results is that one based on a merit function using two design parameters (anterior radius and asphericity and Me as target. If the procedure is performed in two steps, with a single design parameter merit function in each step, the best procedure is to use W20 as the target in the first step and Me in the second step. Second, using a single design parameter (the anterior surface radius), a much better design is obtained selecting a target based on the equivalent defocus (Me) rather than the defocus term (W20). One single parameter is not sufficient to achieve optimal designs (Me < 0.25D). Third, using a second design parameter (asphericity), similar optimal optical performances (Me < 0.25D) are obtained whether the asphericity is set in the anterior or in the posterior IOL surface. However, a higher value of asphericity is needed for the posterior surface to achieve the same performance.

These observations, along with the tolerance analysis presented in Table 5, provide quantitative information on strategic issues when designing an IOL, such as which surface should be aspherized. The tolerance limit of the posterior surface asphericity is much higher than that of the anterior surface. This difference is due to the fact that the effective aperture of the anterior IOL surface is larger than that of the posterior surface, hence aspherizing the anterior surface changes more drastically spherical aberration (and also coma) than aspherizing the posterior surface. The asphericity value also affects the thickness of the IOL. The peripheral IOL edge thickness is usually set to secure a haptic to the lens body and to ensure the mechanical stability of the IOL. Therefore, the IOL central thickness depends on the IOL surfaces. More hyperbolic IOL surfaces (more negative asphericity values) for the same optical diameter produce lower central thickness.

All together, there is a trade-off between aspherizing the anterior or the posterior IOL surface. On one hand, from theory of aberrations [30], it can be inferred that it is easier to find an aplanatic design (simultaneous correction of spherical and coma aberrations) aspherizing the anterior surface (closer to pupil size). On the other hand, aspherizing the posterior surface is less...
sensitive to manufacturing errors (higher tolerance limit) and allows thinner IOLs. This would explain the existence of different strategies of IOL manufacturers in the location of the aspheric profile; the Tecnis IOL (Advanced Medical Optics, Inc.) and KS-3 Ai IOL (Staar Surgical) have the aspheric profile in the anterior IOL surface, whereas the Acrysof IQ (Alcon Surgical) has the profile in the posterior surface and SofPort IOL (Bausch&Lomb) in both surfaces [45]. Finally, we have presented optimization procedures for the photopic peak (555 nm).

The monochromatic designs showed good performances for M&L-cones spectral peaks, but not very good for the S-cones peak. However using a merit function with a polychromatic weight target can provide more balanced polychromatic designs. We have not tried to propose a final polychromatic metric. Defining the optimal visual polychromatic metric target is a complex task where interactions between monochromatic and chromatic aberrations [46] and neural aspects need to be taken into account. A final refinement of the IOL design should consider using visually relevant metrics.

4.3. Future work

All the analysis has been done for on-axis and monofocal designs. However, primary aberration expressions for the off-axis aberrations (astigmatism, coma and curvature of field) can be obtained in a similar manner to the one used for the spherical aberration. From the off-axis equations, more sophisticated merit functions can be configured including off-axis image quality. In addition, the effect of the different axial object location (vergence) can also be included in the equations, and therefore be used for multifocal designs.

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