Complete depigmentation of a small aperture corneal inlay implanted for compensation of presbyopia

Despigmentação completa de um implante corneano de pequena abertura para correção da presbiopia

Mauro Campos1, Sandra Beer1, Eliane Mayumi Nakano1, Cristina Muccioli1, Rubens Belfort Jr.1, Wallace Chamon1,2

ABSTRACT
We describe a case of late-onset remarkable depigmentation of a small aperture corneal inlay implanted for presbyopia compensation. The patient was a participant in a clinical trial designed to evaluate the safety and efficacy of the AcuFocus™ ACU-10R160, which is a 10 µm-thick polyimide film tinted with an organic dye. Inlay implantation occurred under mechanical microkeratome Lasik flaps set for a depth of 120 µm. The patient returned to the clinic 11 years after surgery and reported loss of near-vision acuity. Clinical examination showed the complete absence of pigments in the device and the total loss of the initial effect on near vision, despite normal distance vision. Manifest refraction remained stable during the follow-up period. Scheimpflug images characterized the loss of the small aperture effect on incoming light. Confocal analysis revealed small hyper-reflective round images on the endothelium and no signs of inflammation.

Keywords: Corneal transplantation; Corneal stroma; Presbyopia/surgery; Polyvinyl; Visual acuity; Case report

RESUMO
Descrevemos um caso de importante despigmentação de início tardio de implante corneano de pequena abertura implantada para compensação de presbiopia. O paciente foi um dos participantes de ensaio clínico destinado a avaliar a segurança e eficácia do AcuFocus™ ACU-10R160, uma peça de polimida de 10 microns de espessura, tingida com um corante orgânico. A implantação ocorreu sob um flap de Lasik criado por microcirurgia mecânica ajustado para profundidade de 120 µm. O caso aqui descrito foi avaliado 11 anos após a cirurgia, relatando diminuição total de acuidade de visão para perto. O exame clínico mostrou ausência total de pigmentos no dispositivo e perda total do efeito inicial na visão de perto, apesar da visão normal para distância. A refracção permaneceu estável durante o período de seguimento. As imagens de Scheimpflug caracterizaram a perda do efeito da abertura pequena na luz entranca. A análise de microscopia confocal revelou pequenas imagens hiper-reflexivas redondas sobre o endotélio, sem sinais de inflamação.

Descritores: Transplante de córnea; Substância própria; Presbiopia/cirurgia; Polivinil; Acuidade visual; Relatos de casos

INTRODUCTION
Presbyopia develops with aging and currently affects millions of people around the world(1). Near-vision impairment can significantly affect daily activities, and its surgical correction remains a challenge(2). Small-aperture corneal inlays increase the depth of focus and have the potential advantage of modifying the refractive status of the eye while preserving corneal tissue and allowing possible reversibility(3-8). During the last 4 decades, inventors have filed a series of patents based on small apertures optical devices to enhance vision. These inventions include masked contact lenses and intracoronal lenses(9). A system and method for increasing the depth of focus of the human eye was assigned to AcuFocus Inc. (Irvine, USA) and, recently, the Food and Drug Administration (FDA) approved the use of the Kamra™ Inlay for compensation of presbyopia(10).

The case reported herein involves a patient who underwent implantation of a small aperture corneal inlay and returned for evaluation 11 years later presenting marked depigmentation of the device and loss of the achieved near vision improvement. According to her medical records, the patient had undergone monocular implantation of a small aperture corneal inlay 11 years earlier, under an approved Institutional Review Board protocol. Five patients included in the protocol had normal eye examination results, except for presbyopia. Full preoperative evaluation was performed. The non-dominant eye was selected for surgery, which consisted of creation of a corneal flap by using a mechanical microkeratome for a depth of 120 µm. After flap lifting, the device was placed in the center of the visualized pupil, and the flap was replaced. The routine postoperative medical regimen included a combination of topical antibiotic and a steroid for 14 days. All surgeries were performed in 2004.

The implanted device was an AcuFocus™ ACU-10K160, a 10 µm-thick opaque polyimide inlay with an overall outer diameter of 3.8 mm and an inner diameter of 1.6 mm. The polyimide material was a liquid formulation designed for thin-film casting, supplied by Dupont®. The radius of curvature of the inlay was 7.5 mm. An organic dye (Sudan Black B) was incorporated in the inlay to provide opacity. The inlay had visible light transmission of 6.0% to 7.5%. This device had laser-drilled 25 µm diameter holes (1,600 pores) designed to facilitate nutrient and particle flow to the cornea. The outer and inner edges were free of these porosity holes(10).

Although initially all the patients showed improvement in uncorrected near visual acuity (UNVA), four eyes underwent inlay removal

CASE REPORT
A 67-year-old female returned to our university-based refractive surgery clinic for evaluation with a complaint of progressive near-vision disturbance in her left eye following surgery for near-vision improvement. According to her medical records, the patient had undergone monocular implantation of a small aperture corneal inlay 11 years earlier, under an approved Institutional Review Board protocol. Five patients included in the protocol had normal eye examination results, except for presbyopia. Full preoperative evaluation was performed. The non-dominant eye was selected for surgery, which consisted of creation of a corneal flap by using a mechanical microkeratome for a depth of 120 µm. After flap lifting, the device was placed in the center of the visualized pupil, and the flap was replaced. The routine postoperative medical regimen included a combination of topical antibiotic and a steroid for 14 days. All surgeries were performed in 2004.

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1 Department of Ophthalmology and Visual Sciences, Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil.
2 Department of Ophthalmology & Visual Sciences, College of Medicine, University of Illinois at Chicago (UIC), Chicago, IL, USA.

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Corresponding author: Mauro Campos. Rua Monsenhor Alves, 166 - São Paulo, SP - 05412-030 - Brazil - E-mail: mcampos@pobox.com
The patient reported herein was the only with an eye having the implant in place. She had been followed up for 3 years but did not return until recently. Data obtained under the original clinical protocol regarding her first year of follow-up visits are included in Table 1. The patient showed improvement in UNVA after implantation, with no other remarkable clinical findings.

At the most recent evaluation, provocative questioning revealed that she had experienced glare and halos besides decreased UNVA. She had been followed up for 3 years but did not return until recently. Data obtained under the original clinical protocol regarding her first year of follow-up visits are included in Table 1. The patient showed improvement in UNVA after implantation, with no other remarkable clinical findings.

Table 1. Summary of clinical findings

<table>
<thead>
<tr>
<th></th>
<th>Preop</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>11 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncorrected distance VA</td>
<td>20/16</td>
<td>20/16</td>
<td>20/16</td>
<td>20/20</td>
<td>20/16</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>Uncorrected near VA</td>
<td>20/63</td>
<td>20/32</td>
<td>20/40</td>
<td>20/25</td>
<td>20/25</td>
<td>20/40</td>
<td>20/60</td>
</tr>
<tr>
<td>Corrected distance VA</td>
<td>20/16</td>
<td>20/16</td>
<td>20/16</td>
<td>20/20</td>
<td>20/20</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>Distance-corrected near VA</td>
<td>20/63</td>
<td>20/32</td>
<td>20/40</td>
<td>20/20</td>
<td>20/20</td>
<td>20/20</td>
<td>20/60</td>
</tr>
<tr>
<td>Near-corrected near VA</td>
<td>20/32</td>
<td>20/12</td>
<td>20/16</td>
<td>20/20</td>
<td>20/16</td>
<td>20/16</td>
<td>20/20</td>
</tr>
<tr>
<td>Manifest refraction</td>
<td>+0.25</td>
<td>0.00</td>
<td>0.00</td>
<td>+0.25</td>
<td>0.00</td>
<td>-0.50-0.50@110°</td>
<td>-0.25-0.50@165°</td>
</tr>
<tr>
<td>K1</td>
<td>45.10</td>
<td>44.23</td>
<td>43.80</td>
<td>45.30</td>
<td>44.94</td>
<td>44.06</td>
<td>40.70</td>
</tr>
<tr>
<td>K2</td>
<td>45.50</td>
<td>44.46</td>
<td>44.80</td>
<td>45.73</td>
<td>45.18</td>
<td>44.88</td>
<td>43.40</td>
</tr>
<tr>
<td>Steep axis</td>
<td>063°</td>
<td>072°</td>
<td>088°</td>
<td>068°</td>
<td>068°</td>
<td>099°</td>
<td>089°</td>
</tr>
</tbody>
</table>

VA= visual acuity.
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our series and had to explant four because of persistent epithelial defects and topographic irregularities within the first 2 years after implantation. The other two studies did not report epithelial healing problems or relevant topographic changes. Careful observation of the topographic maps obtained from our patient reveals increased corneal irregularity. Although a considerable amount of keratometric flattening was detected, refraction and uncorrected vision remained unchanged. The current standard of care with an implantation depth of ≥200 µm of a 6 µm-thick inlay will most likely not produce surface changes.

The most significant finding in the present reported case is depigmentation of the inlay, which occurred between 3 and 11 years of follow-up. Unfortunately, because the patient did not return to our institution between years 3 and 11 postoperatively, we were unable to estimate the pattern or the onset of depigmentation. The material used in this case, polyimide, is similar to Kapton® HN polyimide film, which has been approved by the FDA for IOL haptics (10). The material approved by the FDA in the current AcuFocus inlay model, PVDF, has proved to be biocompatible (4-7). In our case, polyimide was considered to be biocompatible by means of the slit-lamp and confocal appearance. Depigmentation was the only detected structural change. The drilled pores were difficult to detect and appeared to be clogged with collagen deposits. None of the long-term studies cited here addressed the issue of depigmentation. To our knowledge, this is the first report of this occurrence in an inlay designed to have a pinhole effect.

Carbon black nanoparticles, the dye currently used for pigmentation in the FDA-approved Kamra device, is widely used for pigmentation. In 2013, the European Scientific Committee on Consumer Safety, evaluated the use of carbon black and found no evidence of photo toxicity (11). Carbon black particles in other tissues, such as the alveolar region of lungs, can produce oxidation and have been considered to be risk factors for lung cancer in rats (12).

One concern raised in our case is that there may be hazards related to the migration of smaller particles used for pigmentation. Determining if the primary mechanism of clearance is by macrophage phagocytosis or simple drainage through conventional aqueous humor routes may be helpful because they can present as aggregates or agglomerates with particle sizes varying from 100 to 800 nm. Considering the size on our confocal images, the structures seen at the endothelial level are very likely to represent Sudan black particle agglomerates.

We had partial access to technical details of the manufacturing process of the inlay used here. The correct size of the dye particle,
Figure 4. Scheimpflug sagittal view of the implanted eye clearly shows the effect on the light intensity passing through the cornea at one (A) and 11 years (B). Mis-read pachymetric results (C) were not as prevalent (more reliable) at 11 years (D).

Figure 5. Confocal evaluation obtained during the follow-up. (A) 1 month after implantation showing the pores of the inlay; (B-D) show recent images; the arrow in (SB) shows remaining pigment, and the double arrows point to clogged holes; (SC) the curved dense image shows the border limits of the inlay; and (SD) shows presumed inlay-originated pigments on the endothelium level.
amount used to tint a single inlay, form (liquid or powder), and the potential hazards of systemic migration of the particle from a single inlay, could not be evaluated by us. When addressing the differences between the inlay presented here and the current FDA approved implant, the authors were informed that during the product development, the manufacturer detected a presumed UV sensitivity of the polyimide material and instability of the material and dye composite, but this information was not made publicly available[10].

REFERENCES