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A unique late-onset intraocular lens opacification 23 years after implantation: a clinical and laboratory case report

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***Abstract*:** We report an unusual, rare case of opacification of the hydrophilic acrylic intraocular lens (IOL) 23 years after the initial surgery with significant visual deterioration. Opacification of the hydrophilic acrylic IOL was primarily due to the formation of folds on the surface of the lens material, and less so due to calcium phosphate deposits. Calcification opacification can be attributed to recent events, as evidenced by deposits of dicalcium phosphate dihydrate ($CaHPO_4 2H_2O$) and octacalcium phosphate ($Ca_8H_2(PO_4)_6 5H_2O$), both of which are transient calcium phosphate phases, converting hydrolytically to the thermodynamically most stable hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). To our knowledge, this case of hydrophilic acrylic IOL opacification is the only one that has been described so late, 23 years after cataract surgery.

Keywords: calcification, hydrophilic IOL, IOL opacification

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Introduction

Phacoemulsification with intraocular lens (IOL) implantation in the capsular bag is the gold standard in cataract surgery, with excellent anatomic and functional outcomes and a significantly lower complication rate.[1] However, the potential of an IOL material to be transparent must be taken into consideration when evaluating the long-term biocompatibility of the material, particularly for the hydrophilic acrylic IOLs, which are at a higher risk of developing calcification of the lens material.[2–4] Here, we present the clinical and laboratory characteristics of an unusual case of hydrophilic IOL opacification 23 years after a successful phacoemulsification procedure due to traumatic cataracts.

Case report

A 55-year-old male was referred to one of us (HH) complaining of blurred vision in his left eye. He had undergone phacoemulsification with IOL implantation due to a traumatic cataract 23 years earlier, in July 1998. According to the history, the implanted IOL was a hydrophilic acrylic IOL, the model SC60B-OUV (Medical Developmental Research Inc., Clearwater, FL, USA), made from poly-2-hydroxyethyl methacrylate (pHEMA) polymer. The patient did not have any history of systemic illness. A slit lamp examination showed pseudophakia with an opacified IOL and otherwise unremarkable ocular findings. The opacification had a very well-demarcated and round edge in the central optic zone of the IOL, similar to a white cataract [Figure 1(a) and (b)]. According to the red reflex assessment of the dilated eye by retro-illumination on slit lamp examination, the edges of the optic and the haptics appear transparent [Figure 1(c)]. The anterior capsular opening was quite irregular and did not fit the border of the opacification. The patient underwent an exchange of the opacified IOL in September 2021 by the HH at the Department of Ophthalmology of the Regensburg University Hospital, Regensburg, Germany. He had an uneventful IOL explantation, followed by secondary implantation of a hydrophobic acrylic IOL. The explanted IOL was sent to the laboratory at the Department of Chemical Engineering, Laboratory of Inorganic

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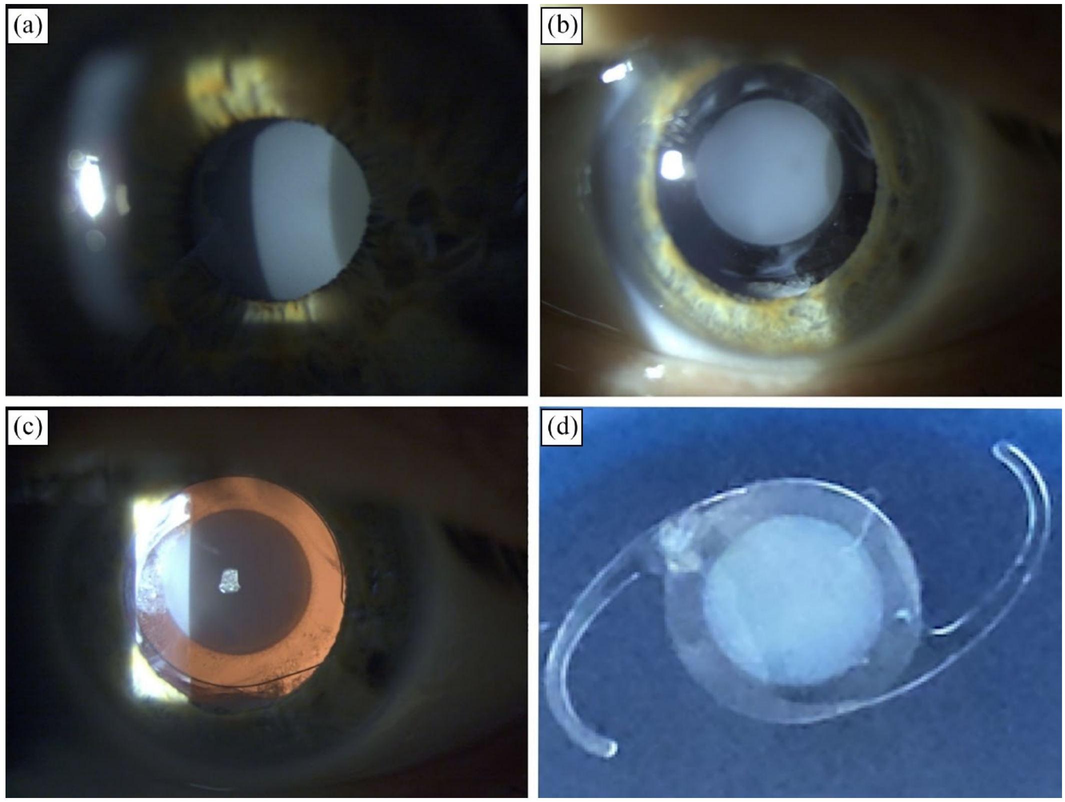

Figure 1. Slit lamp photographs of the patient implanted with the SC60B-OUV IOL 23 years after implantation. (a) Note the opacity present on the anterior surface of the optic of this lens. (b) A central grayish opacity involves the optic area of the IOL. Postoperative fibrosis of the anterior capsule is seen at the capsulorhexis margin, which is greater than the diameter of the opacity. (c) The red reflex assessment of the dilated eye with a slit lamp examination shows that the central opacity is similar to a white cataract. (d) A gross photograph of the explanted SC60B-OUV lens demonstrates a circular area of white opacification in the central optic and an opacified band of approximately 1.0 mm at 360°. (d) A gross photograph of the explanted SC60B-OUV lens demonstrates a circular area of white opacification in the central optic and a milder opacified band of approximately 1.0 mm at 360°. In addition, it has a haptic clear, while the other has various degrees of opacification.
IOL, acrylic intraocular lens.

and Analytical Chemistry, University of Patras, Greece, intact in dry state for further analysis. Gross macroscopic examination of the explanted IOL showed a dense well-circumscribed opacification confined to the central 4 mm of the optic with a milder opacification of the edges of the IOL and clear haptics [Figure 1(d)]. Images from calcified IOLs similar to our SC60B-OUV IOL have been described by several researchers.[5,6]

According to optical microscopy, deposits were only found on the anterior surface of the IOL that covered the opacified portion of the IOL in a scattered pattern. Scanning electron microscopy (SEM) and energy-dispersive X-ray spectrometric microanalysis of the explanted IOL showed that the deposits consisted of calcium and phosphorus [Figure 2(a) and (b)] forming platy crystals on the anterior surface of the opacified IOL. In Figure 2(c) and (d), these crystals showed clearly that they consisted of dicalcium phosphate dihydrate (DCPD) and octacalcium phosphate (OCP) crystallites. The morphology of DCPD and OCP, which are transient calcium phosphate phases hydrolyzed to the thermodynamically more stable hydroxyapatite (HAP), is shown in Figure 3. In addition to sporadic calcium phosphate deposits, SEM images from the surface of the explanted opacified IOL showed numerous folds on its anterior surface [Figure 2(a)]. IOL anterior surface folds were present throughout the optic diameter of the IOL but were more pronounced and dense in the area of the capsulorhexis. Despite that, the presence of calcium

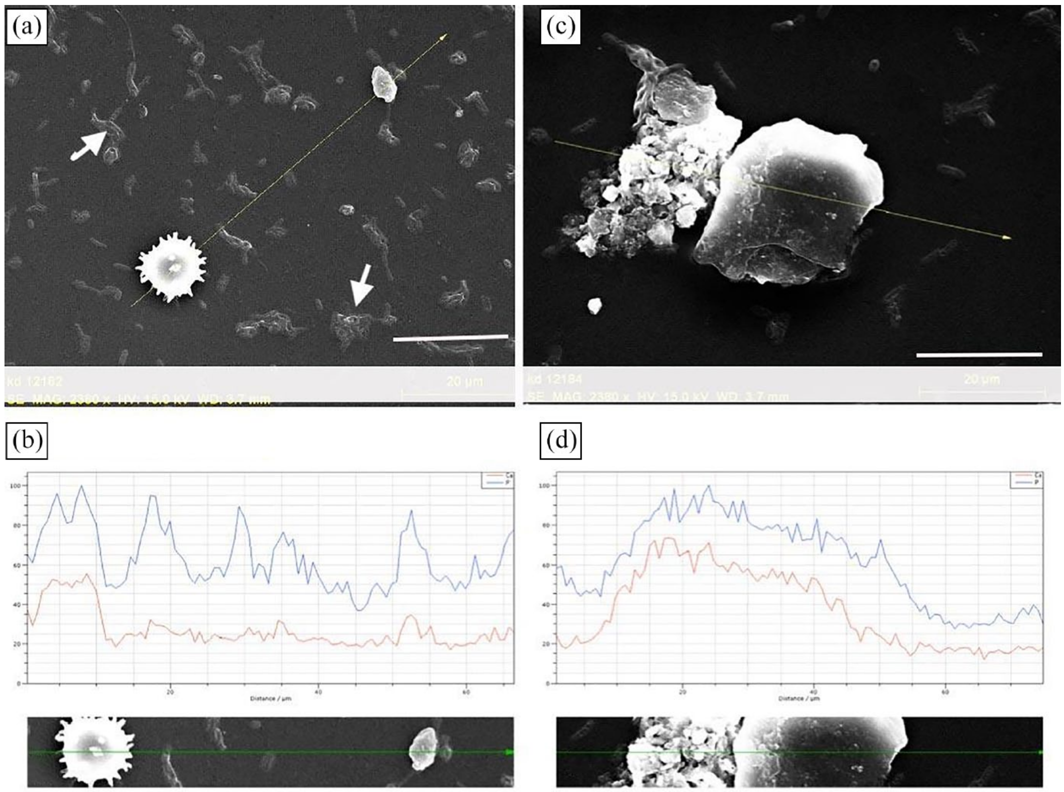

Figure 2. (a) SEM of the lens's central optic area (2380×) reveals folds on the anterior surface (white arrows) and two deposits that resemble calcium phosphate salts (scale bar: 5 µm). (b) Energy-dispersive spectroscopy microanalysis over the length of the arrow line (a) shows OCP deposits formed on the anterior surface of the IOL. (c) SEM of the anterior surface of the lens shows crystalline deposits (scale bar: 10 µm). (d) Energy-dispersive spectroscopy microanalysis of the calcific deposits shows DCPD, OCP, and HAP. Both OCP and HAP are from the hydrolysis of DCPD.

DCPD, dicalcium phosphate dihydrate; HAP, hydroxyapatite; IOL, acrylic intraocular lens; OCP, octacalcium phosphate; SEM, scanning electron microscopy.

phosphate deposits on the surface of the IOL was limited to the area of capsulorhexis (Figure 4).

Discussion

IOL opacification is a rare but serious complication that can occur after cataract surgery. It may be necessary to undergo IOL explantation and exchange as it can significantly impair visual acuity. There have been a number of clinical and laboratory reports regarding late postoperative opacification of IOLs. The majority of opacified IOLs, with confirmed calcification, were hydrophilic acrylic materials.[7] Several studies have shown a late opacification of hydrophilic acrylic IOLs attributable to calcium deposition.[3,5,6] Despite time variation in the time of appearance of opacification in these particular studies, calcification was mainly the cause of opacification rather than surface alterations or degradation of the polymeric matrix. The clinical appearance of the opacity in this case was a large, dense, round, regular-shaped central opacification and did not correspond to the capsulorhexis as it was larger and irregular. The lens, in this case, was the model SC60B-OUV lens (Medical Developmental Research Inc., Clearwater, FL, USA); the material used in the production of this IOL is a cross-linked copolymer of pHEMA and methyl methacrylate, with an integrated UV absorber. This IOL is a water-containing single-piece hydrophilic acrylic lens with a water content of 28%.[6] Even though IOL opacifications are very rare, this case was quite different in comparison with other cases reported by us. Specifically, the opacification of SC60B-OUV reported in earlier clinical and experimental investigations was attributed to intraoptical calcium phosphate deposits, distributed over a plane parallel to the external optic surface, and separated by a clear

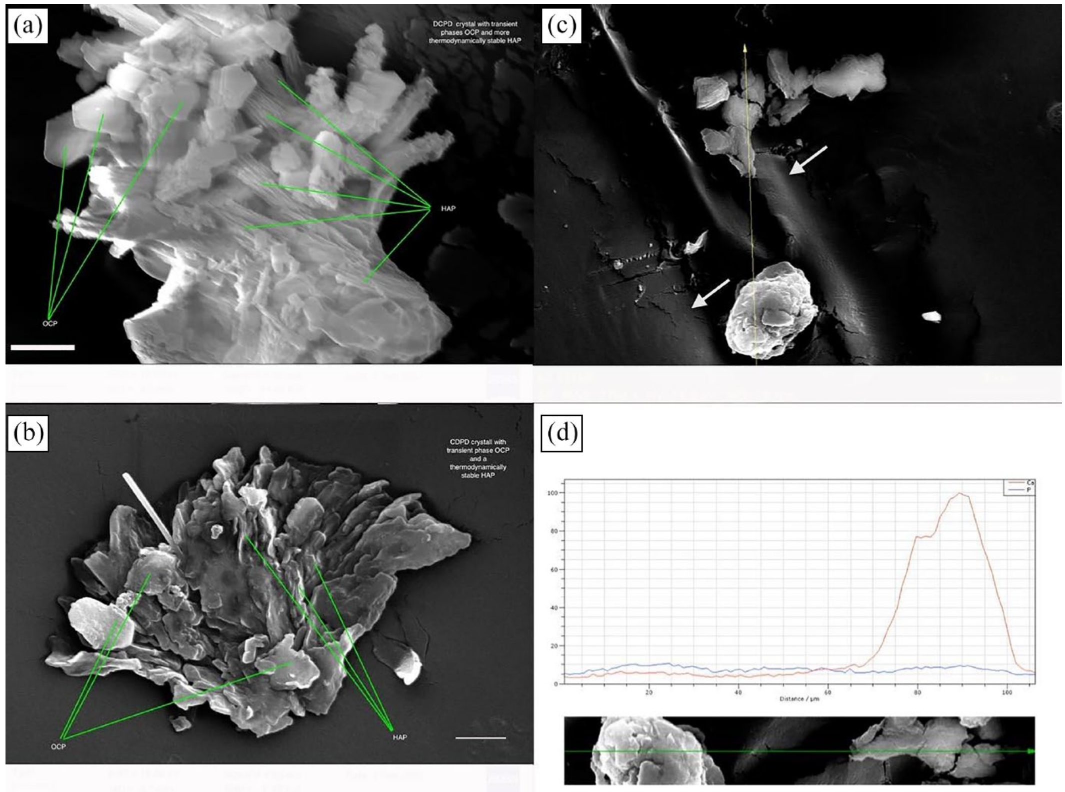

Figure 3. (a, b) SEM images show large crystallites of DCPD and OCP transient phase and thermodynamically stable HAP nanocrystallites [scale bar: 1 µm in both (a) and (b)]. (c) An SEM image shows folds (arrows) and a few calcific deposits. (d) Energy-dispersive line scan microanalysis of deposits confirmed the formation of HAP crystals.
DCPD, dicalcium phosphate dihydrate; HAP, hydroxyapatite; OCP, octacalcium phosphate; SEM, scanning electron microscopy.

zone just beneath the surface, similar to descriptions in the literature.[3,5,6,8] However, what is unusual in this case is that, according to SEM findings, opacification was mainly attributed to a pattern of folds, primarily distributed over the anterior optic surface bounded by the anterior capsulorhexis. Moosavi *et al.*[9] reported a degraded layer of the outer surface of the explanted IOL, giving it a sponge-like morphology. They suggested a slow degradation of the polymer matrix and swelling of incompletely polymerized material in the core of the optic. The same degenerative process may be suggested in our case, but the period of time for the appearance of the opacification and explantation appears to be very different in both studies. Nevertheless, the reason for this late timing of the appearance of opacification in our case is unknown. Morphological instabilities of soft materials incurred by non-uniform volumetric swelling/shrinkage or other external stimuli have been described in a comprehensive review.[10] On the other hand, in our case, the findings, in particular the presence of transitional calcium phosphate phases such as DCPD and OCP, may indicate an acidic environment of the aqueous humor. The calcification process, which was not the main factor for opacification at the stage of extraction of the IOL, was most probably initiated recently, a maximum 2 years earlier may be suggested, as indicated by the presence of unstable precursor crystalline calcium phosphate phases of HAP, which are relatively short-lived at physiological conditions of the aqueous humor. Nonetheless, a degradation of the outer surface of the explanted IOL may have started years ago. The opacity observed on the lens removed from the patient corresponds to the capsulorhexis diameter and extends beyond the visible opaque section of the explanted lens with a decreasing form of opacity toward the optic edges, as evidenced by the morphology of the opacification. In any case, it seems very likely that the lens opacification was driven by the interaction of the aqueous humor with the lens material. Since

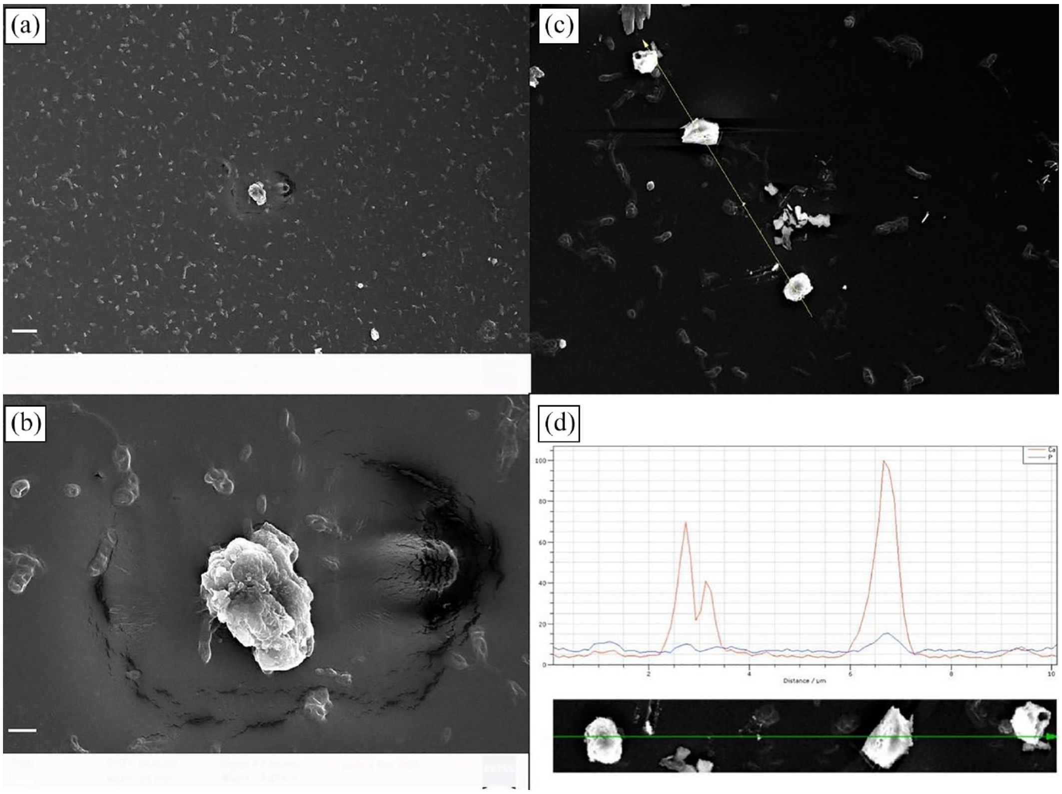

Figure 4. (a) SEM image from the anterior optic surface of the explanted opacified IOL showing numerous folds of the surface and sporadic calcific deposits (scale bar: 10 µm). (b) Higher magnification of the above image (scale bar: 2 µm). (c) SEM image and (d) energy-dispersive spectrometric microanalysis along the length of the arrow line (c) shows HAP formed with a scattered pattern on the anterior surface of the IOL.
HAP, hydroxyapatite; IOL, acrylic intraocular lens; SEM, scanning electron microscopy.

hydrophilic materials are more sensitive to pH changes in the aqueous humor, it may be suggested that a recent change in the aqueous humor's pH, as suggested by the presence of the precursor crystalline phases of DCPD and OCP, which are stabilized at acidic pH values ($pH \leq 6$), could activate the lens surface alteration mechanism and, at a second stage initiated, the opacification process. The potential for uveitis, medications, vascular, or systemic diseases that compromise the blood–aqueous barrier could lead to such pH alterations.[11] However, our patient had no signs of such risk factors. On the other hand, with regard to calcium deposits, they were observed on the anterior surface of the lens and not within the optic material of the IOL, as reported earlier in our clinical and experimental investigations.[3,5,6] From a mechanistic point of view, the transient calcium phosphate phases convert by hydrolysis to the thermodynamically more stable HAP. Recent results of our *in vitro* experiments[12] support the hypothesis that the increase in the pHEMA surface charge is due to the ionization of the hydroxyl groups of pHEMA, which provide the active sites needed for the initiation of nucleation and further growth of the HAP crystals on the surface of the hydrophilic acrylic IOLs. Upon HAP formation on the IOLs, the negative zeta potential increases, to values significantly higher than the zeta potential of each of pHEMA or HAP separately, suggesting synergistic enhancement of the magnitude of the surface potential. The apparent implication is the enhancement of the calcification with increasing HAP deposits on the IOLs and through the surface diffusion favors the development of calcium deposits in the interior of the hydrophilic IOL with time. As demonstrated in our case and other studies,[6] the opacification/calcification of hydrophilic acrylic IOLs can occur from months to 23 years after IOL implantation. The reason for the late denaturation of the anterior surface of the IOL material in the form of multiple folds and the late onset of calcification of the IOL remains unclear. Nevertheless, the association of multiple folds of the surface with superficial calcific deposits in this patient supports the possibility of a factor that stimulates such a pattern of opacification. Further research is needed to understand the nature of this factor and its potential role in early opacification diagnosis and treatment, a task complicated by the relative rarity of patients presenting with IOL opacification/calcification. The phenomenon is very uncommon, the opacification/calcification of the IOL is harmful, and the consequences of the therapeutic explantation of the IOL are unknown to a large extent. Our findings suggest that patients with acrylic hydrophilic IOLs may have the potential for opacification even years following cataract surgery.

In conclusion, the findings from this case suggest that the optical transparency of IOLs is of paramount importance to support long-term improvement in visual acuity after cataract or intraocular surgery. Adherence to follow-up is of particular importance for hydrophilic acrylic IOLs, especially for people who might suffer from diseases (e.g. diabetes, uveitis) or who are undergoing ocular surgery that compromises the blood–ocular barrier. To our knowledge, this is the first study to report the longest interval between cataract surgery with IOL implantation and IOL opacification, 23 years after cataract surgery.

Declarations

Ethics approval and consent to participate

This study was a retrospective case report and it did not contain human trials and therefore did not require ethical board approval.

Consent for publication

A written informed consent was obtained from the patient to publish medical data and figures described in this case report.

Presentations

Part of the manuscript was presented at the 56th Panhellenic Ophthalmological Congress on 8–10 June 2023, Ioannina, Greece.

Author contributions

Panos S. Gartaganis: Conceptualization; Formal analysis; Investigation; Methodology; Validation; Writing – original draft.

Panagiota D. Natsi: Data curation; Investigation; Methodology; Software.

Sotirios P. Gartaganis: Methodology; Project administration; Supervision; Validation; Writing – review & editing.

Petros G. Koutsoukos: Conceptualization; Data curation; Investigation; Methodology; Project administration; Supervision; Validation; Writing – review & editing.

Horst Helbig: Conceptualization; Data curation; Supervision; Validation; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author (PSG) on request.

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References

1. Rossi T, Romano MR, Iannetta D, *et al.* Cataract surgery practice patterns worldwide: a survey. *BMJ Open Ophthalmol* 2021; 6: e000464.
2. Werner L. Calcification of hydrophilic acrylic intraocular lenses. *Am J Ophthalmol* 2008; 146: 341–343.
3. Gartaganis SP, Kanellopoulou DG, Mela EK, *et al.* Opacification of hydrophilic acrylic intraocular lens attributable to calcification: investigation on mechanism. *Am J Ophthalmol* 2008; 146: 395–403.
4. Koutsoukos PG, Natsi PD, Gartaganis SP, *et al.* Biological mineralization of hydrophilic intraocular lenses. *Crystals* 2022; 12: 1418.
5. Werner L, Apple DJ, Kaskaloglu M, *et al.* Dense opacification of the optical component of a hydrophilic acrylic intraocular lens: a clinicopathological analysis of 9 explanted lenses. *J Cataract Refract Surg* 2001; 27: 1485–1492.
6. Izak AM, Werner L, Pandey SK, *et al.* Calcification of modern foldable hydrogel

intraocular lens designs. *Eye (Lond)* 2003; 17: 393–406.

7. Grzybowski A. Recent developments in cataract surgery. *Ann Transl Med* 2020; 8: 1540.

8. Drimtzias EG, Rokidi SG, Gartaganis SP, *et al*. Experimental investigation on mechanism of hydrophilic acrylic intraocular lens calcification. *Am J Ophthalmol* 2011; 152: 824–833.

9. Moosavi A, Fox P, Harrison M, *et al*. Opacification of SC60B-OUV lens implant following routine phacoemulsification surgery: case report and EM study. *Br J Ophthalmol* 2003; 87: 800–801.

10. Li B, Cao YP, Feng XQ, *et al*. Mechanics of morphological instabilities and surface wrinkling in soft materials: a review. *Soft Matter* 2012; 8: 5728–5745.

11. Occhiutto ML, Freitas FR, Maranhao RC, *et al*. Breakdown of the blood–ocular barrier as a strategy for the systemic use of nanosystems. *Pharmaceutics* 2012; 4: 252–275.

12. Gartaganis P, Ziomas G, Kourassi T, *et al*. Hydrophilic intraocular lens calcification and the role of surface charge. *Paper presented at The American Society of Cataract and Refractive Surgery Annual Meeting*, 5–8 May 2023, San Diego, USA.

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