Delayed postoperative opacification of three hydrophobic acrylic intraocular lens: A scanning electron microscopic and energy dispersive spectroscopic study

Harsha Bhattacherjee, Suklengmung Buragohain, Henal Javeri, Dipankar Das, Kasturi Bhattacherjee

Purpose: The aim of this study was to report scanning electron microscopic (SEM) and energy dispersive spectroscopic (EDS) findings of three specimens of opaque hydrophobic acrylic intraocular lens (IOL) explanted in delayed postoperative period for visual indications. Methods: Clinical data and photographs from each subject were obtained. Explanted IOLs were examined under gross and light microscopy followed by SEM coupled with EDS. Results: All three subjects underwent IOL implantation following senile cataract extraction at an average age of 64.3 ± 0.3 years, and the IOLs were in situ for a duration of 11.3 ± 4.04 years. The IOL explantation and exchange were done due to late postoperative opacification of the IOL and significant visual deterioration. The milky iridescent opacity affected the full thickness of IOL optics in the first two specimens and in the third only two surfaces were involved. SEM detected surface cracks in the first specimen, typical conglutinated surface, pores and accumulation of crystals with surface deposit of nano-particles on the second specimen and uneven surface erosion in the third specimen. SEM detected mainly sodium (Na) and chloride (Cl) spikes. All patients recovered normal vision following IOL exchange. Conclusion: SEM features of the IOL optics and absence of calcium and phosphate spikes in EDS and other findings were consistent and suggestive of hydrolytic biodegradation of hydrophobic acrylic IOL polymer in ocular media and was responsible for delayed postoperative opacification of the hydrophobic IOLs and visual loss.

Key words: Biodegradation, delayed postoperative opacification, hydrophobic IOL

Cataract surgery and IOL implantation is one of the most frequent, safe, cost-effective and universally performed surgical procedures and its demand is ever increasing.[1] The estimated incidence of IOL exchange is 2 per 1000 surgeries[1‑4] Nowadays, the leading cause of IOL explantation is opacification or discoloration of IOL,[5‑9] whereas two decades ago the major indication of IOL exchange was dislocation, incorrect IOL power and inflammation.[6‑9] The changing trend behind IOL explantation is mainly due to continuous evolution of surgical techniques, advances in pharmacotherapeutics and introduction of newer IOL materials and design.[7] Opacification of IOL was first reported in the ’90s[11] but the diagnosis of IOL opacification remains a challenge and misdiagnosis as posterior capsule opacification prompts the surgeon to perform unnecessary surgical procedures.[9,11] JOL exchange also bears a potential risk of subnormal visual recovery.[4] Any IOL biomaterial may develop opacity but such a complication is mostly reported with hydrophilic or hydrophobic surface coated hydrophilic IOLs.[7,11‑14] Primary calcification is mainly responsible for late postoperative visually significant opacification of hydrophobic IOL and is inherent to its biomaterial.[7,9] Scanning electron microscopy (SEM), energy dispersive spectroscopy (EDS) and special staining have confirmed the deposition of calcium and phosphate on the surface and in the substance of opaque lens.[12,14,15] Cross-sectional studies suggest this secondary complex phenomenon that is seen selectively in some patients, may result from the interaction between unknown biological variables of the patient and the IOL itself.[9,15‑19] The assessment of the IOL performance and factors causing its slow degradation[20] is thorough and at multiple points manufacturers have had to issue field safety notice and withdraw their much-acclaimed product from the market.[11,20]

Single piece hydrophobic IOL is the most popular implant nowadays. Late postoperative opacification of hydrophobic IOL has not yet been reported. Cochrane database search using search strategy ‘postoperative hydrophobic IOL opacification’, found only two cases of secondary IOL opacification following vitrectomy,[21,22] three cases of reversible IOL opacity due to ocular inflammation in the immediate postoperative period,[23] some cases of intralenticular cell growth in piggy bag IOL[23] and glistening formation.[27]

The present report is on SEM material characterization of three opaque explanted specimens of hydrophobic IOLs which had spontaneously turned opaque in vivo, causing loss of visual function and IOL exchange at the terminal age of life. Considering the rarity and seriousness of the complication, this report has been submitted to the Indian literature.

Sri Sankaradeva Nethralaya, Guwahati, Assam, India

Correspondence to: Dr. Suklengmung Buragohain, Department of Ophthalmology, Sri Sankaradeva Nethralaya, 96 Baisinha Road, Guwahati - 781 028, Assam, India. E-mail: suklen.bgo@gmail.com

Received: 25-Aug-2020
Revision: 30-Sep-2020
Accepted: 02-Nov-2020
Published: 30-Apr-2021

© 2021 Indian Journal of Ophthalmology | Published by Wolters Kluwer - Medknow
Methods
The study was approved by the institutional review board and protocol adhered to the declaration of Helsinki. Informed consent was obtained from the participants. Only three patients (3 eyes) who underwent explantation of hydrophobic IOLs due to a significant decrease of visual function after having developed late postoperative opacification of the IOLs optics were included in this study.

Medical records, history and clinical findings were registered in each case. All the IOLs were of the same model and had a common manufacturer. Preoperative slit-lamp photograph of the IOLs in situ were recorded using Kodak easy-share M200 micro camera. Immediately after explantation, photographs of the IOLs were documented using an operating microscope (visu OPMI 150, Zeiss, Germany), condensed fiber-optic light and the above mentioned Kodak camera. Care was taken to avoid any damage during manipulation of IOL optics with the grasping forceps. The IOLs were subsequently transferred to the Centre of Nano Technology of the Indian Institute of Technology (IIT), Guwahati, in sterile containers in a dry state. In the laboratory, IOLs were air-dried for three days at normal room temperature after bi-section. For contrast enhancement and accurate measurement of surface deposits, the samples were gold coated (sputtered), 30 minutes before microscopy. Specimens were stabilized with adhesive carbon tape and mounted on round aluminum stubs for imaging. The samples were prepared properly to avoid any beam or specimen drift and minimum beam energy had been used to avoid breaking of chemical bond, mass loss, reduction of crystallinity and creation of volatile material from the polymer during the SEM process. For characterization of the surface and quantitative analysis of the material, scanning electron microscope (Hitachi S 3000 N EXAX Genesis VP SEM) and energy dispersive spectroscope (SEM-EDS) was used. Field emission scanning electron microscope (FESEM) was used for observation of small structures in the biological cells and materials on the polymer. Serial microphotographic images of the IOLs were captured in various magnifications, ranging from 500× to 80000× till the appropriate images were captured. Similarly, electron microscopic photographs were obtained from a virgin hydrophobic single-piece acrylic IOL immediately after its removal from the wagon wheel pack as a control specimen for comparison. The IOLs in the fellow eye were optically clear and without any obvious abnormalities, however, the make and model of the IOL couldn’t be determined even after thorough reviewing of the old medical records of the patients.

Results
All three patients were male and underwent senile cataract surgery at the mean age of 64.3 ± 0.3 years. Planned ultrasonic phacoemulsification was performed and single-piece acrylic hydrophobic IOL was implanted using injector in each of them. Opacification of IOL and deterioration of vision was the common indication for IOL explantation and exchange. The mean age at the time of explantation was 75.7 ± 4.5 years and the average duration of the IOL in situ was 11.3 ± 4.04 years. Duration of visual symptoms which led to IOL explantation ranged between 3 to 5 years. At the time of explantation, visual acuity of the affected eyes of the patient ranged from 20/40 to 20/80 (Snellen’s chart) with complaints of glare. On slit-lamp examination, opacity in the IOL optics was evident in all cases [Figs. 1a, 2a and 3a]. In case 1 both the surfaces of the IOL were involved and in the remaining two, the entire lens substance was affected by the opacity. The IOLs were in the bag and stable. The pupils showed resistance to pharmacological dilation and pseudo-exfoliation was noted in case no. 2. The third case had raised intraocular pressure (IOP) and open angles on gonioscopy. Otherwise, all ocular fundi were normal and the eyes were quiet in all cases. Medical history of the patients was also unremarkable [Table 1].

Light and electron microscopic findings were as follows:

All explanted specimens were that of a single piece hydrophobic IOL. Sample 1 - Light microscopy detected opacification of the entire IOL optic, except for a circular peripheral ring which was overlapped by the anterior capsule while the IOL was in situ [Fig. 1b]. SEM microphotograph of the surface structure of the IOL in 200× and 500× magnification captured cracks, erosion and the roughened surface of the IOL [Fig. 1c and d]. The surface appeared scaly.

Sample 2 - Light microscopy demonstrated brownish-white discoloration of the IOL optics and it was more evident when the photograph was taken keeping the IOL in an oblique position with fiber optic condensed xenon light focused at right angle to the optics [Fig. 2b and c]. The opacity involved both the surfaces only. SEM photograph of the surface structure captured a conglutated structure and pores in the polymer of the IOL optics [Fig. 2d and e]. FESEM photograph detected isolated areas of clumps of aggregated crystals of different sizes, mostly in hexagonal configuration. A magnification of 80000× demonstrated nanoparticles of about 10 nanometers in size, on the surface of the crystal [Fig. 2f and g]. EDS elemental analysis of the crystal detected sodium (Na), chloride (Cl), Sulphur (S), Silicon (Si) and Tantalum (Ta) and absence of calcium and phosphate peaks [Fig. 2h].

Sample 3– light microscopy detected opacification of the entire IOL optics which was not uniform in distribution [Fig. 3b]. SEM photograph in different magnifications demonstrated non-homogeneous licking and erosion of the surface. The advancing edge of erosion was also evident [Fig. 3c and d].

Discussion
Intraocular lens material should ideally be biocompatible and stable because host reaction to it, is important for IOL performance and lifelong transparency.[26] IOL biomaterials of various water contents, chemical composition, refractive indices and tensile strength are under constant evaluation, intending to minimize host cell response, reduce the incision size and obtaining a better refractive outcome. Presently, there is a progressive increase in the demand for IOL implantation in younger age groups due to an increase in refractive lens exchange and treatment of pediatric cataract.[27,28] The IOLs will, therefore, remain in the ocular environment for a much longer time in the future, in which case, though rare, this particular complication, especially because of its undetermined nature will always bear the risk of visual loss and IOL exchange at any point in the patient’s life post-implantation.

Degradation of a polymer in a biological environment is universal and results either from hydrolysis or enzymatic attack (produced by microorganisms). In aqueous media, water gets absorbed and induces simple chemical hydrolysis of the hydrostatically unstable polymer bond. As a result, cleaving or hydrolytic chain scission occurs and the long polymer chain converts into water-soluble fragments with polymer dissolution and surface erosion. Both, absorption of water and erosion, together or alone can produce cracks and pores in the polymer. Locally produced acids catalyze the degradation process and the polymer inside the pores further dissolves. Rate of erosion is determined by the chemical stability of the polymer bond, the hydrophilic/hydrophobic balance, morphology,
molecular weight and molecular distribution of the polymer and solubility of the low molar mass degradation product. Ultraviolet absorbing compounds, low molecular weight additives, blend or co-monomer are covalently integrated into the polymeric backbone of IOL polymer. Electromagnetic wave, which presents in the visible light or ultraviolet light can degrade the bond and change the property of IOL polymer. The chemical and physical changes due to the biodegradation processes are reflected on the surface of the polymer and can be easily characterized by electron microscopy. The only
drawback is that the beam damage may destroy the polymer specimen.[29,32] Reduction in optical quality and image contrast has been documented in opacified IOLs. In polymer science, electron microscopic techniques are in conventional use to study the morphology, composition, physical properties and dynamic behavior of a polymer.[29] Hydrophobic foldable IOL is a copolymer of phenyl ethyl acrylate and phenyl ethyl methacrylate cross-linked with butyrate diacrylate.[33]

In our study surface erosion and cracks in specimen 1 are suggestive of hydrolytic degradation of IOL polymer in an aqueous medium. In specimen 2, typical “conglutated” structures and pores on the surface suggest low molar mass degradation and absorption of polymer in aqueous media and in specimen 3, non-homogenous licking and erosion of surface and deeper layers indicates water–enzyme-catalyzed hydrolysis in biological environment due to random chain scission of the polymer. The electron microscopy of the control specimen detected a flat and homogenous structure without any cracks and pores on the surface [Fig. 1e]. In all the cases IOL was in vivo for an average of 11.3 ± 4.04 years. Co-morbid eye disease present in case 2 and 3 were pseudoexfoliation and glaucoma, respectively. On EDS analysis one of the samples detected carbon, oxygen and silicon peaks which are the normal composition of IOL.[34] Absence of calcium and phosphate peaks in the specimen and any other known factors and observing the electron microscopic findings and on comparing with the control specimen, we believe late postoperative opacification of the IOL is due to its slow biodegradation in the ocular media. In the degraded polymer, incident light gets scattered within the material at every point of refractive index inhomogeneities. Thus the once transparent IOL polymer following degradation looks opaque without any deposition of material in it and produces haze in the transmitted image.[35] However selective nature of biodegradation could not be explained in our cases.

There were a few limitations of the study, one of them being the limited number of specimens and the wide variation in the duration of pseudophakia among them. We would have benefited from studying more specimens, however, obtaining

| Sample and Case no. | Age (years) | Gender | Age at Implantation (years) | Duration of Pseudophakia (years) | Slit lamp findings | IOL status | Indication of Explanation | SEM findings |
|---------------------|------------|--------|-----------------------------|---------------------------------|-------------------|-----------|--------------------------|-------------|
| 1                   | 80         | Male   | 65                          | 15                              | Quiet eye         | Diffuse, hazy IOL optics | Blurring of vision | Surface cracks. Evidence of hydrolytic degeneration in aqueous media |
| 2                   | 76         | Male   | 64                          | 12                              | Quiet eye         | Diffuse, hazy IOL optics | Blurring of vision | Crystalline structure and pore on the IOL surface |
| 3                   | 71         | Male   | 64                          | 7                               | Quiet eye         | Diffuse, hazy IOL optics | Gross visual impairment | Homogenously hazy IOL optics involving mainly both surfaces |

Figure 3: (a) – Clinical slit-lamp photograph. Note the cloudiness of the IOL. (b) – Light microscopy of the explanted single piece hydrophobic IOL (Sample 3). Note dense opacification of the IOL optics as seen by fiber optic guided condensed xenon light. (c and d) – SEM photograph of IOL surface topography in two different magnifications. Note homogenous licking and uneven erosion of the IOL surface and deeper layers. Erroding edges are evident (arrow).
a large number of samples with specifically primary type of biodegradation of IOLs, was difficult. Second, the presence of pseudoxfoliation in the second specimen could have had an influence in the biodegradation process and this needs to be studied in the future. Thirdly, further analysis of the nanoparticles and the cut-section of the specimens could not be done as after undergoing scanning electron microscopy (SEM), the specimens got burnt and charred and could not be utilized further.

**Conclusion**

To conclude, SEM features of the opaque IOL optics and absence of calcium and phosphate spikes in EDS and other findings were consistent and suggestive of hydrolytic biodegradation of hydrophobic acrylic IOL polymer in ocular media, responsible for delayed postoperative opacification of those IOLs and visual loss. No biomaterial used at present seems to be free from this process of biodegradation. This report demonstrates that other than secondary and tertiary opacification, primary opacification of the hydrophobic IOL is possible due to the inherent structure of the IOL polymer. Further research on this subject is essential and encouraged, safe prospective human application of IOLs, particularly with regards to the pediatric population, in whom a longer pseudophakic life is expected, making them more at risk for an IOL exchange, owing to the biodegradation of the IOL.

**Acknowledgements**

Mr. Apurba Dekha, MSLMT for laboratory assistance, Prof. Dipankar Bandypadhyay, Ph. D, Mr. Surjendu Maity, M. Sc. Center for Nano Technology (IIT Guwahati) for SEM and EDS imaging and Mr. Santanu Barman for secretarial assistance.

**Financial support and sponsorship**

Sri Kanchi Sankara Health and Educational Foundation for grant funding for the study.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Eric J. Raising cataract surgery rates: Demand and supply. Ophthalmology 2014;121:2-4.
2. Haymore J, Zaidman G, Werner L, Mamalis N, Hamilton S, Cook J, et al. Misdiagnosis of hydrophobic acrylic intraocular lens optic opacification. Ophthalmology 2007;114:1689-95.
3. Abdalla Elsayed MEA, Ahmad K, Al-Abdullah AA, Malik R, Khandaker R, Martinez-Osorio H, et al. Incidence of intraocular lens exchange after cataract surgery. Sci Rep 2019;9:12877.
4. Davies EC, Fineda R. Intraocular lens exchange surgery at a tertiary referral center: Indications, complications, and visual outcomes. J Cataract Refract Surg 2016;42:1362-7.
5. Gurabardhi M, Höberle H, Aurich H, Werner L, Pham D-T. Serial intraocular lens opacifications of different designs from the same manufacturer: Clinical and light microscopic results of 71 explant cases. J Cataract Refract Surg 2018;44:1326-32.
6. Yildirim TM, Affarth GU, Labuz G, Bopp S, Son H-S, Khoramnia R. Material analysis and optical quality assessment of opacified hydrophilic acrylic intraocular lenses after pars plana vitrectomy. Am J Ophthalmol 2018;193:10-9.
7. Neuhann T, Yildirim TM, Son H-S, Merz PR, Khoramnia R, Affarth GU. Reasons for explantation, demographics, and material analysis of 200 intraocular lens explants. J Cataract Refract Surg 2020;46:20-6.
8. van der Mooren M, Steinert R, Tyson F, Langeslag MJM, Piers PA. Explanted multifocal intraocular lenses. J Cataract Refract Surg 2015;41:873-7.
9. Werner L. Causes of intraocular lens opacification or discoloration. J Cataract Refract Surg 2007;33:713-26.
10. Affarth GU, Wilcox M, Sims JCR, McCabe C, Wesendahl TA, Apple DJ. Analysis of 100 explanted one-piece and three-piece silicone intraocular lenses. Ophthalmology 1995;102:1144-50.
11. Balasubramaniam C, Goodfellow J, Price N, Kirkpatrick N. Opacification of the hydroyv H60M intraocular lens: Total patient recall. J Cataract Refract Surg 2006;32:944-8.
12. Stringham J, Werner L, Monson B, Theodosios R, Mamalis N. Calcification of different designs of silicone intraocular lenses in eyes with asteroid hyalosis. Ophthalmology 2010;117:1486-92.
13. Yildirim TM, et al. Glistening formation and light scattering in six hydrophobic-acrylate intraocular lenses. Am J Ophthalmol 2018;196:112-20.
14. Neuhann T, Werner L, Izak A, Pandey S, Kleinmann G, Mamalis N, et al. Late postoperative opacification of a hydrophilic acrylic (hydrogel) intraocular lens: A clinicopathological analysis of 106 explants. Ophthalmology 2004;111:2001-11.
15. Balendiran V, MacLean K, Mamalis N, Tetz M, Werner L. Localized calcification of hydrophilic acrylic intraocular lenses after posterior segment procedures. J Cataract Refract Surg 2019;45:1801-7.
16. Guan X, Tang R, Nancollas GH. The potential calcification of octalcalcium phosphate on intraocular lens surfaces. J Biomed Mater Res A 2014;71:889-96.
17. Werner L, Wilbanks G, Nieuwenendaal CP, Dhital A, Waite A, Schmidinger G, et al. Localized opacification of hydrophilic acrylic intraocular lenses after procedures using intracameral injection of air or gas. J Cataract Refract Surg 2015;41:199-207.
18. Khurana RN, Werner L. Calcification of a hydrophilic acrylic intraocular lens after pars plana vitrectomy. Retin Cases Brief Rep 2018;12:204-6.
19. Costa JF, Bompastor-Ramos P, Marques M, Henriques J, Póvoa J, Lobo C, et al. Large-scale opacification of a hydrophilic/hydrophobic intraocular lens. Eur J Ophthalmol 2020;30:307-14.
20. Oculentis. Field safety notice from oculentis Gmbtt: Recall for Lentis L or LS or LV. 2017.
21. Prasad PS, Oliver SCN, Gonzales CR. Midlenticular optic opacification of a hydrophilic acrylic intraocular lens in association with retained perfluorocarbon liquid following vitreoretinal surgery. Ophthalmic Surg Lasers Imaging 2010;1:2. doi: 10.3928/15428877-20100215-18. Online ahead of print.
22. Ma S-T, Yang C-M, Hou Y-C. Postoperative intraocular lens opacification. Taiwan J Ophthalmal 2018;8:49-51.
23. Kim DJ, Chuck RS, Lee JK, Park CY. Reversible opacification of hydrophobic acrylic intraocular lens- two cases report. BMC Ophthalmol 2017;17:111.
24. Quigley C, Ashraf MO, Manning S. Reversible opacification of a hydrophobic acrylic intraocular lens. J Cataract Refract Surg 2020;46:319.
25. Gayton JL, Apple DJ, Peng Q, Visesook N, Sanders V, Werner L, et al. Interlenticular opacification: Clinicopathological correlation of a complication of posterior chamber piggyback intraocular lenses. J Cataract Refract Surg 2000;26:330-6.
26. Orphal P, Orzol E, Karel F. Biocompatibility of Intraocular Lenses. Turk J Ophthalmol 2017;47:221-5.
27. Kim T, Alió del Barrio J, Wilkins M, Cohen B, Ang M. Refractive surgery. Lancet 2019;393:2085-98.
28. Sreebandyoy S, Lawson RN, Fielder AR, Suttle CM. Global prevalence of childhood cataract: A systematic review. Eye (Lond) 2016;30:1160-9.
29. Rydz J, Sišková A, Andicsová Eckstein A. Scanning electron microscopy and atomic force microscopy: Topographic and dynamical surface studies of blends, composites, and hybrid functional materials for sustainable future. Adv Mater Sci Eng 2019;2019:1-16.
30. Pérez-Vives C. Biomaterial influence on intraocular lens performance: An overview. J Ophthalmol 2018;2018:2687385.
31. Werner L. Biocompatibility of intraocular lens materials. Curr Opin Ophthalmol 2008;19:41-9.
32. Rydz J. Forensic engineering of advanced polymeric materials. Part 1 – Degradation studies of polylactide blends with atactic Poly[R, S-3-hydroxybutyrate] in paraffin. Chem Biochem Eng Q 2015;29:247-59.
33. Tetz M, Jørgensen MR. New hydrophilic IOL materials and understanding the science behind them. Curr Eye Res 2015;40:869-81.
34. Werner L, Kollari CR, Mamalis N, Olson RJ. Surface calcification of a 3-piece silicone intraocular lens in a patient with asteroid hyalosis. Ophthalmology 2005;112:447-52.
35. Hall C. Electrical and optical properties. In: Hall C, editor. Polymer Materials: An Introduction for Technologists and Scientists. London: Macmillan Education UK; 1981. p. 92-112.