https://doi.org/10.5114/oku/199991 (Original Paper)

Received: 07.05.2024 Accepted: 15.09.2024

Calcification of Hydrophilic Acrylic Intraocular Lenses with a Hydrophobic Surface Following Uneventful Descemet's Stripping Automated Endothelial Keratoplasty

Urszula Kołodziejska[1], Monika Udziela[2], Ewaryst Mendyk[3], Michał Rawski[3], Krzysztof Skrzypiec[3], Anna Gumieniczek[4], Jacek P. Szaflik[2,5]

1 LASER Eye Microsurgery Centre of Warsaw, Poland
2 SPKSO Ophthalmic University Hospital of Warsaw, Poland
3 Analytical Laboratory, Faculty of Chemistry, Maria Curie-Sklodowska University of Lublin, Poland
4 Department of Medicinal Chemistry, Medical University of Lublin, Poland
5 Department of Ophthalmology, Faculty of Medicine, Medical University of Warsaw, Poland

Abstract:

Purpose: This is a retrospective, observational case series of 43 patients who underwent Descemet's striping automated endothelial keratoplasty with implants of hydrophilic acrylic intraocular lenses with hydrophobic surface (Lentis LS-302-Y or Lentis L-302-1).

Methods: Patients diagnosed with intraocular lens opacification after Descemet's striping automated endothelial keratoplasty were identified from clinic records, with minimal 18-month postoperative follow-up guaranteed in 36 eyes. Analysis included demographic data, indication for Descemet's striping automated endothelial keratoplasty, ocular comorbidities, intraocular lens specification, complications, postoperative course, incidence of lens exchange due to intraocular lens opacification, and corrected distance visual acuity (Snellen) before surgery and before and after intraocular lens opacification. Two explanted intraocular lenses were subjected to detailed light microscopy, optical profilometry, and scanning electron microscopy with energy dispersive X-ray spectroscopy (SEM/ EDS).

Results: Opacification occurred in 81% of Lentis LS-302-Y (25/31) and in 92% of Lentis L-302-1 (11/12) intraocular lenses. The morphology of surface irregularity indicates that formation begins inside the intraocular lens material, with deformation of the polymer surface is secondary to the growth of crystal granules in the anterior subsurface area. SEM/ EDS analysis revealed significant peaks for calcium and phosphate. The presence of silicon in the examined areas of an opacified intraocular lens is worth noting. The high incidence of this complication with this particular type of intraocular lens after Descemet's striping automated endothelial keratoplasty suggests that material-related factors may play an important role in the development of calcification.

Conclusion: Because of the increased risk of opacification after Descemet's striping automated endothelial keratoplasty, hydrophilic and hydrophilic-hydrophobic acrylic intraocular lenses should be avoided in patients with endothelial cell disorders.

Key words: Descemet's stripping automated endothelial keratoplasty (DSAEK), intraocular lens (IOL), intraocular lens explantation, opacification.

Intraocular lens (IOL) opacification is a very rare complication in terms of absolute numbers. This phenomenon is well described in the literature for different types of IOLs [1]. Calcification is one of the types of opacification typical for IOLs made of hydrophilic material [2]. It was described after complicated cataract extraction or combined procedures but also after uneventful cataract extraction with IOL implantation. Neuhann et al. [3] classified IOL calcification as primary when there are errors in the IOL manufacturing or as secondary where environmental factors cause deposition of calcium on the IOL. It appears to be a multifactorial problem. Renal failure [4], diabetes [5, 6], uveitis [7], asteroid hyalosis [7, 8], and excessive postoperative ocular inflammation [7] have been reported as patient-related factors which increased the risk of IOL calcification. Another group comprises surgical factors such as use of ophthalmic viscosurgical devices [9, 10], tamponade agents such as silicon oil [11], intracameral use of tissue plasminogen activator (tPA) [12] and intracameral injections of intraocular gas (air, SF6, 20% C3F8) [13].

Since the first publication in 2011 [14], several authors have reported their experience with this vision-threatening late complication after posterior lamellar keratoplasty. Descemet's stripping automated endothelial keratoplasty (DSAEK) has been described as a procedure associated with increased risk of hydrophilic IOL opacification. The mechanism whereby DSAEK causes this complication remains unestablished. Many authors suggest that prolonged or repeated exposure of the IOL surface to intracameral air, elevated IOP or conditions connected with breakdown of the blood-aqueous barrier may play a role [13, 15]. Also a diagnosis of Fuchs dystrophy, which is one of the main indications for DSAEK, is suspected to play a role in development of this phenomenon because of metabolic changes in the anterior chamber [15, 16]. However, the exact cause or mechanism responsible for this phenomenon of secondary IOL calcification remains speculative thus far.

In this study we report 36 cases of IOL calcification after uneventful DSAEK. All affected lenses were hydrophilic acrylic with a hydrophobic surface. Laboratory analysis of 2 explanted and 1 new IOL were performed with optical profilometry and scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDX) analysis. To the best of our knowledge, this is the first study describing such a large number of cases of IOL calcification after DSAEK.

Methods

This study was a retrospective, noncomparative, observational case series of 43 patients who underwent DSAEK between January 2012 and December 2013 when hydrophilic acrylic IOLs with the hydrophobic surface Lentis LS-302-Y or Lentis L-302-1 were routinely implanted. We reviewed clinical records from patients attending the corneal service (corneal outpatients clinic) at the Public Ophthalmic Teaching Hospital in Warsaw. Patients who had been diagnosed with IOL opacification after DSAEK were identified from clinic records (Tab. I). The minimal follow-up of 18 months postoperatively was guaranteed in 36 eyes. Seven eyes with shorter time of observation were excluded from the study. Analysis of clinical aspects was performed including: demographic data, indication for DSAEK, ocular comorbidities, IOL specification, corrected distance visual acuity (CDVA) (Snellen) before surgery, before and after the appearance of IOL opacification, complications, postoperative course, and incidence of lens exchange due to the IOL opacification.

DSAEK – 125	
DSAEK – 46 Redo DSAEK – 2	**DSAEK+PHACO+PCIOL– 79** *Lentis LS-302-Y* – 31 (hydrophilic acrylic with a hydrophobic surface) Opacified – 25 (81%) *Alcon SA60AT* – 24 (hydrophobic acrylic) Opacified – 0 (0%) *Lentis L-302-1* – 12 (hydrophilic acrylic with a hydrophobic surface) Opacified – 11 (92%) *Alcon SN60WF* – 6 (hydrophobic acrylic) Opacified – 0 (0%) *Croma NS-60YG* – 4 (hydrophobic acrylic) Opacified – 0 (0%) *Alcon MZ60BP* – 1 (PMMA) Opacified – 0 (0%) *Alcon MA60AC* – 1 (hydrophobic acrylic) Opacified – 0 (0%)

Tab. I. DSAEK procedures in 2012–2013 with implanted IOL's specification.

Two explanted IOLs (cases 1 and 2) and one new IOL (all Lentis LS-302-Y) were sent to the laboratory for detailed light microscopy (using Nikon microscopes Eclipse MA 200M and Eclipse 80i), optical profilometry (using the Bruker-Veeco profilometer Contour GTK-1) and scanning electron microscopy with energy dispersive X-ray spectroscopy using an SEM/EDS microscope (FEI DualBeam Quanta 3DFEG with silicon drift detector).

First, the lenses were photographed using optical microscopes and subjected to analysis by profilometry. The working principle of a profilometer is the light interference phenomenon used as "imaging of interference fringes". In a profilometer, half the beam from a test material which is passed through the focal plane of a microscope is objective, and the other half of the beam is reflected from the reference mirror. When the split beams are recombined, constructive and destructive interference occurs in the combined beam while the length of the light beams varies. In this way, the light and dark bands known as interference fringes are created. In effect, profilometry allows one to measure metrological parameters of the surface precisely and to generate a 3D image of the surface texture.

After that, saline was cleaned from IOLs using an ultrasonic bath, then they were subjected to scanning electron microscopic analysis (SEM/ EDS). This method allows one to determine the composition of elements and their local distribution, using the spectral mapping of the examined micro areas. In the present experiment, micrographs of the surfaces and elemental microanalysis were taken using the low vacuum mode without spraying (sputtering) the examined samples. IOLs were examined after their immobilization on aluminum slabs covered with a conductive carbon double-stick tape.

All these tests were performed in the Analytical Laboratory of the Faculty of Chemistry of Maria Curie-Sklodowska University of Lublin and in the Chair and Department of Medicinal Chemistry of the Medical University of Lublin.

Results

A total of 36 patients underwent uneventful Descemet's strapping automated endothelial keratoplasty with simultaneous cataract phacoemulsification and posterior chamber intraocular lens (PCIOL) implantation: in 25 cases Lentis LS-302-Y, in 11 cases Lentis L-302-1; both hydrophilic acrylic with a hydrophobic surface manufactured by Oculentis GmbH, Berlin, Germany. All patients underwent surgery between June 2012 and September 2013. The operations were performed by the same surgeon (J.P.S.). The DSAEK technique was similar to that previously described [17]. After cataract phacoemulsification and PCIOL implantation, intracameral carbachol (Miostat) was injected for miosis. All donor lenticules were prepared from corneas stored in in EUSOL C solution. After placing it into the recipient anterior chamber the posterior lamellar disc was unfolded and pushed up against the recipient cornea with an air bubble. In 13 cases phacoemulsification was performed with the support of a femtosecond laser. There was around 70% air fill and it took more than 3 days to absorb in 19 eyes and more than 4 days in 17 eyes (an air bubble was present in the anterior chamber on the day of hospital discharge). Three eyes (8.3%) required additional intracameral air injection ("rebubbling") during first 2 days after surgery because of donor lenticule detachment.

Corneal decompensation secondary to Fuch's endothelial dystrophy (FED) and cataract were indications for the surgery in 35 eyes. In 1 eye corneal decompensation was secondary to posterior polymorphous dystrophy. The mean age at the date of surgery was 72.1 years (range 36–90 years), and sex distribution was 3: 1 F: M, which corresponded to the epidemiology of Fuchs dystrophy. The most frequent concomitant medical problems were arterial hypertension and glaucoma. None of the patients was known to suffer from any calcium metabolic disorder.

In all cases, central IOL opacification consisted of fine granular areas confined to the pupillary zone of the superficial, anterior IOL surface (Fig. 1), diagnosed on average after 14.9 months (range 7–30 months). This time interval decreased as we became more aware of the complication. Clinical examinations revealed that after its initial development, over time, there was almost no change in the intensity of opacification. The influence of opacification on CDVA varied widely between patients, from almost no influence to serious deterioration. The mean Snellen CDVA was 0.64 (range: 0.2–0.8) after DSAEK (before opacification occurrence) and 0.48 (range: 0.1–0.8) after opacification of the IOL was diagnosed. In 18 cases impairment of vision was significant and IOL exchange was necessary. Replacement by a three-piece hydrophobic lens (Acrysof MA60AT, Alcon) implanted in the sulcus was performed. In this group the mean preoperative CDVA was 0.39 (range: 0.1–0.8) and 0.55 (range: 0.3–0.8) postoperatively. The average time from diagnosis of IOL opacification to the surgery was 21.8 months (range 13–40 months). Five more are still awaiting surgery.

Gross laboratory analyses of all 18 IOLs revealed a round area of white discoloration present in the central part of the optic.

Light photomicrographs of explanted IOL's surface in reflected light are presented in Figure 2.

Texture imaging and evaluation of surface roughness were performed with an optical profilometer Contour GTK-1 (Bruker-Veeco). Respective 3D maps are presented in Figure 3. The measurement indicates that the anterior surface of affected IOLs (cases 1 and 2) is much (>70 times) rougher than the posterior and than the surface of the new one. Surface roughness (Ra) respectively: Ra = 0.34 μm and Ra = 0.88 μm vs. Ra = 0.0049 μm and Ra = 0.0045 μm. The morphology and character of surface irregularity indicate that formation of lumps starts inside the IOL's material. The deformation of the polymer surface is secondary to growth of crystal granules in the anterior subsurface area. This observation was confirmed with the microscopic analysis (Fig. 4). The thickness of the external hydrophobic membrane was 5 μm and the maximal depth of crystallites was 40 μm. Intensive growth of clusters in the central part of the affected area finally ruptured the external hydrophobic membrane (Fig. 4C, D). The highest concentration of calcic deposits was just under the hydrophobic membrane and gradually decreased with depth. Reduction of average diameter and quantity of crystals with depth was also observed (Fig. 4B, D).

Scanning electron micrographs of the new and affected IOLs are presented in Figures 5, 6 and 7. Tables show the weight and atomic percentage of elements displayed in the spectrum. Carbon (C) and oxygen (O) are normal components of the polymer lens. Significant peaks for calcium (Ca) and phosphate (P) confirm the calcified nature of deposits. The presence of silicon in the examined areas of opacified IOL (case 1) is worth noting (Fig. 6).

Discussion

IOL opacification is one of the late complications of cataract surgery. Progressive visual deterioration in some cases is the most common indication for IOL explantation. Calcic nature was found to be the major cause of hydrophilic acrylic IOL opacification. Gartaganis et al. [18] emphasized the important role of the polymeric material itself. The presence of hydroxyl groups on the polyacrylic material seems to be essential for the process of calcification. These groups, mostly ionized at physiological pH, facilitate nucleation and further growth of calcium phosphate crystallites. The majority of publications about IOL calcifications concern hydrophilic acrylic IOLs. This complication was described for IOLs from different manufacturers and different polymer sour-

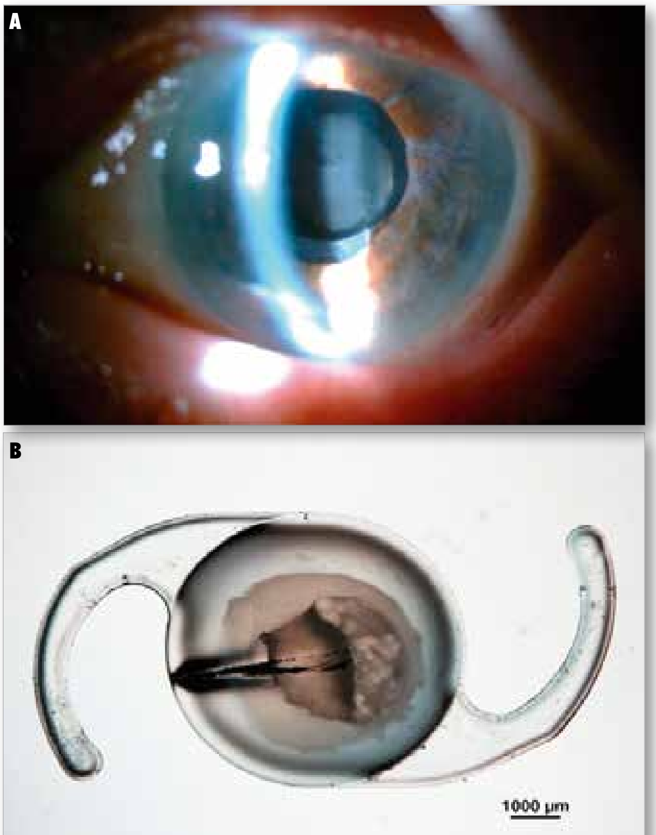


Fig. 1. Anterior segment photo showing clear graft and anterior opacification of IOL in pupillary zone (case 1). (A) Light microphotograph of explanted IOL (case 2) – overall round central/ paracentral area of opacification of optic with clear haptics (B).

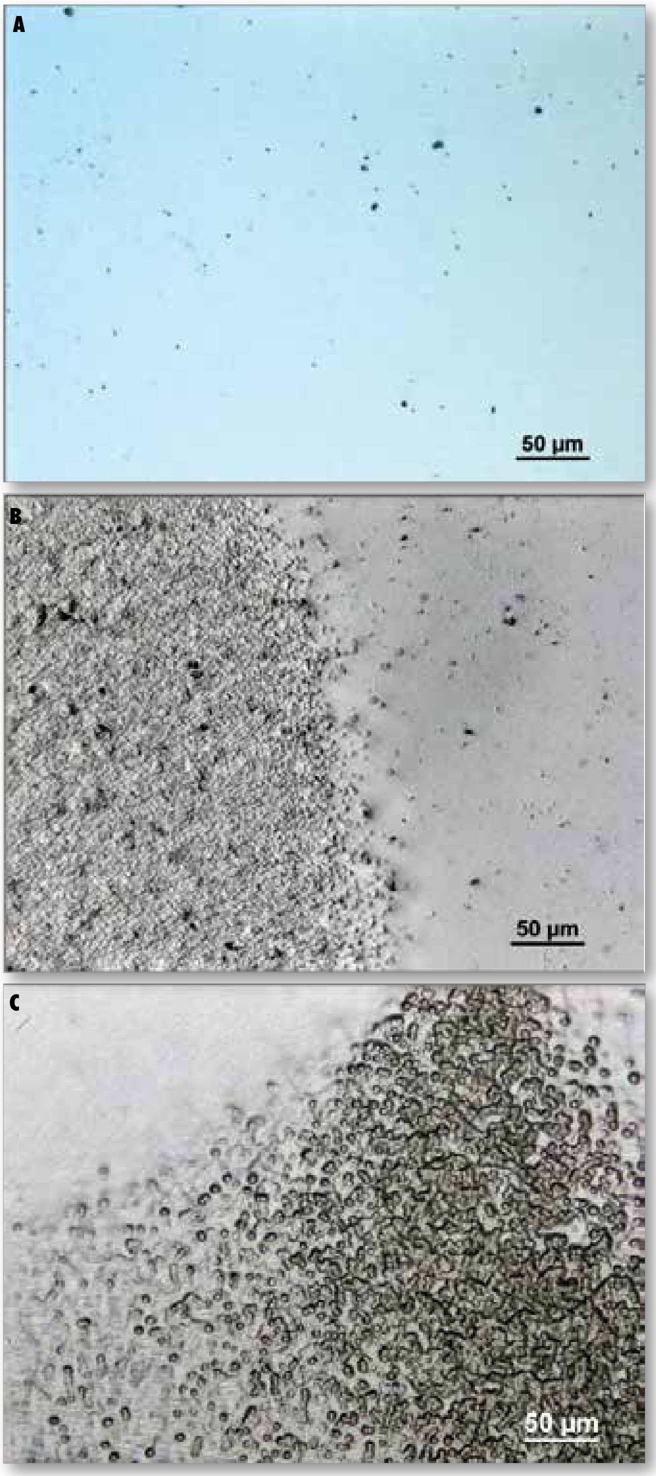
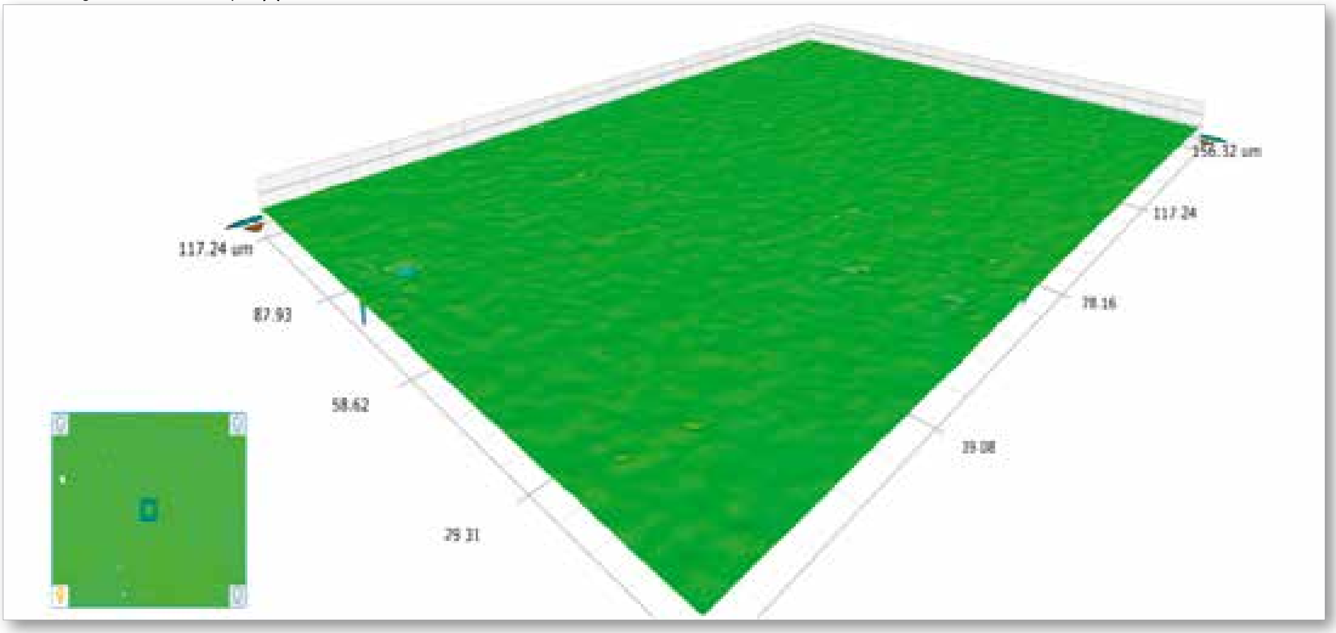


Fig. 2. Light photomicrographs of new (A), and affected lens: case 1 (B) and case 2 (C). A margin of opacified area and granular structure of IOL surface are well distinguished.

ces (Tab. II). This observation confirms the predilection to the specific group of polymers (hydrophilic one) then to the defined model of IOL.

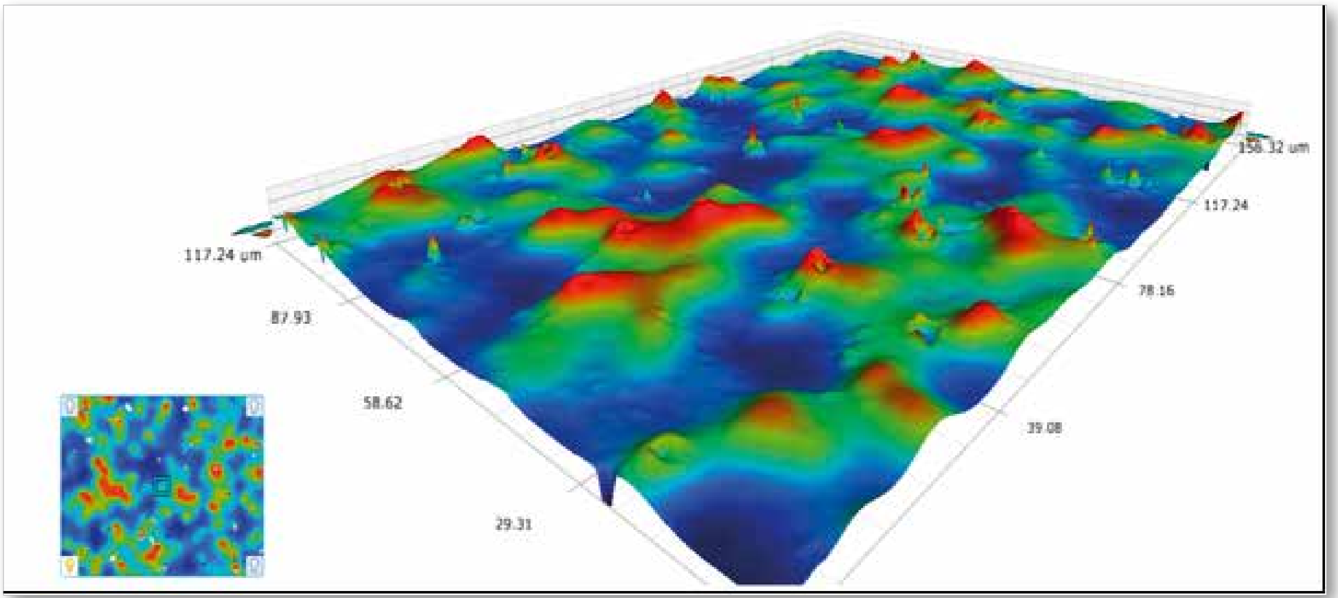
Some modifications in IOL construction were implemented in the new design of hydrophilic acrylic IOLs. The combination of a hydrophilic acrylic body with a hydrophobic surface has been proposed to improve capsular biocompatibility and avoid primary calcification. The present study demonstrated that hydrophobic surface did not prevent initiation of calcification. Calcification turned out to be a potential complication of this model of IOL as well. Lentis L-302-1 and Lentis LS-302-Y are made of Hydro-Smart copolymer. It consists of acrylates, with a hydrophobic surface with UV absorber. Lentis LS-302-Y additionally has a violet light filter. Pathological materials were found in the subsurface hydrophilic compartment. Secondary irregularities of the hydrophobic surface were detected with optical profilometry. This observation indicates the dual nature of this complication: chemical and mechanical. SEM and SEM/ EDS analyses confirmed the calcic nature of deposits. Calcific clusters were observed in the case of uninterrupted hydrophobic membrane (case 1) and could be a reason for its secondary rupture (case 2, Fig. 4D). Gartaganis et al. presented a similar observation [19]. Analysis of 6 hydrophilic IOLs with hydrophobic surface (Lentis LS-502-1) explanted due to significant impairment of vision was described. Four eyes underwent uneventful phacoemulsification, and 2 eyes underwent pars plana vitrectomy and silicone oil instillation combined with

Surface roughness Ra = 0.0049 μm (A)



Surface roughness Ra = 0.0045 μm (C)

Surface roughness Ra = 0.34 μm (B)



Surface roughness Ra = 0.88 μm (D)

Fig. 3. 3D maps of IOLs' surfaces. Anterior surface of new (A) and opacified IOLs – case 1 (B). The measurement indicates that the surface of the new (fresh) IOL is very smooth. Rear (C) and front (D) surface of the opaque IOLs – case 2. The measurement indicates that the surfaces are significantly rougher than the surface of the new one. The morphology and character of surface irregularity indicate that formation of lumps starts inside the IOL's material. The deformation of the polymer surface is secondary to growth of crystal granules in the subsurface area.

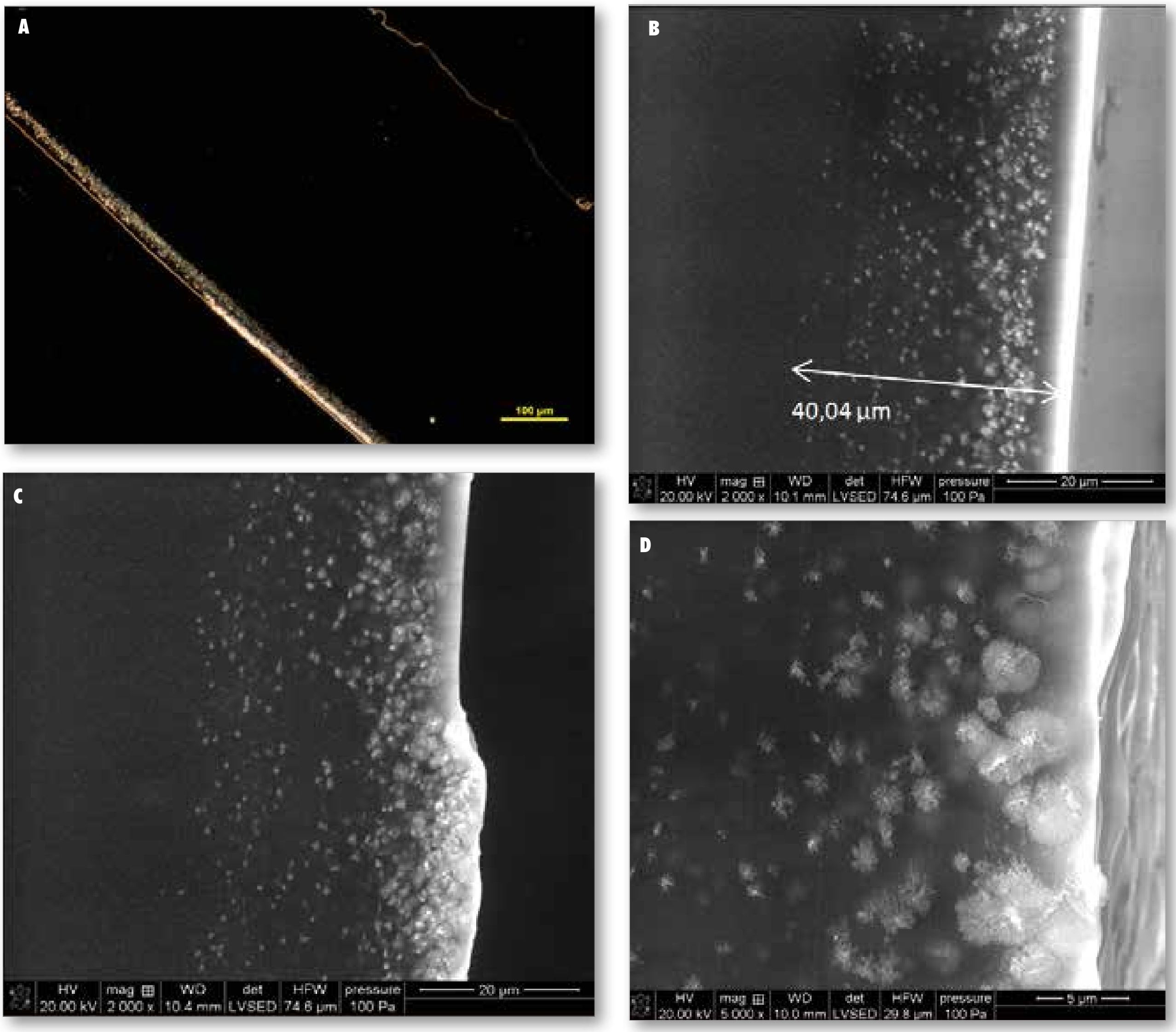
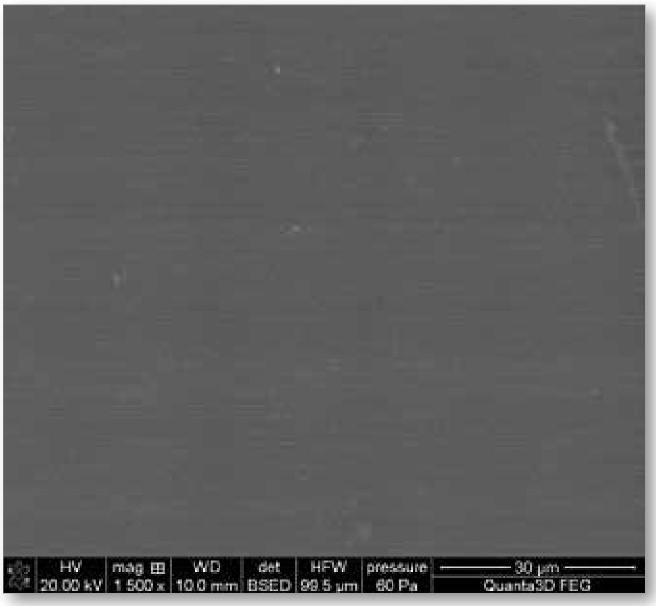
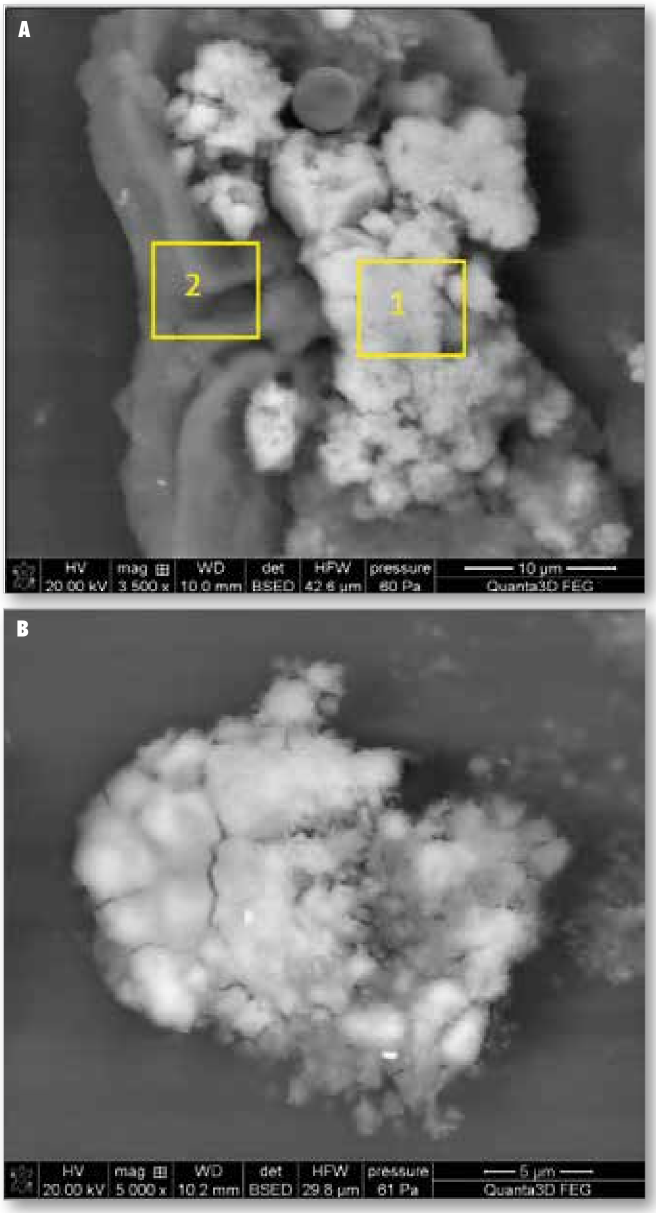


Fig. 4. Cross-section of the opacified IOL (case 2). Light photomicrograph (A), SEM micrographs (B, C, D). Deposits are seen along the anterior surface of the IOL in hydrophilic subsurface area. Deformation of surface is secondary to subsurface localization of crystallites (C, D).



Element	Wt %	At %
C	57.97	64.80
O	41.27	37.74
Al	0.94	0.47
Total	100	100

Fig. 5. The new intraocular lens. SEM micrograph and SEM/ EDS microanalysis (scanning electron microscopy/energy-dispersive X-ray spectroscopy). The composition in the table refers to the entire area of the image.



Element	Wt %	At %
C	36.18	47.62
O	43.37	42.86
Na	0.32	0.22
Mg	0.22	0.15
Al	1.16	0.62
Si	6.26	3.52
S	0.34	0.17
K	0.23	0.09
Ca	12.03	4.74
Total	100	100

Element	Area 1		Area 2	
	Wt %	At%	Wt %	At %
C	31.45	42.91	56.58	64.94
O	46.44	47.47	37.81	32.58
Na	0.53	0.38	1.07	0.64
Mg	0.20	0.14	0.07	0.04
Al	0.1	0.10	0.29	0.15
Si	0.86	0.50	1.07	0.52
P	0.45	0.11	0.09	0.04
S	1.15	0.23	0.14	0.06
Cl	0.27	0.13	0.70	0.27
Ca	19.42	7.94	2.17	0.75
Total	100	100	100	100

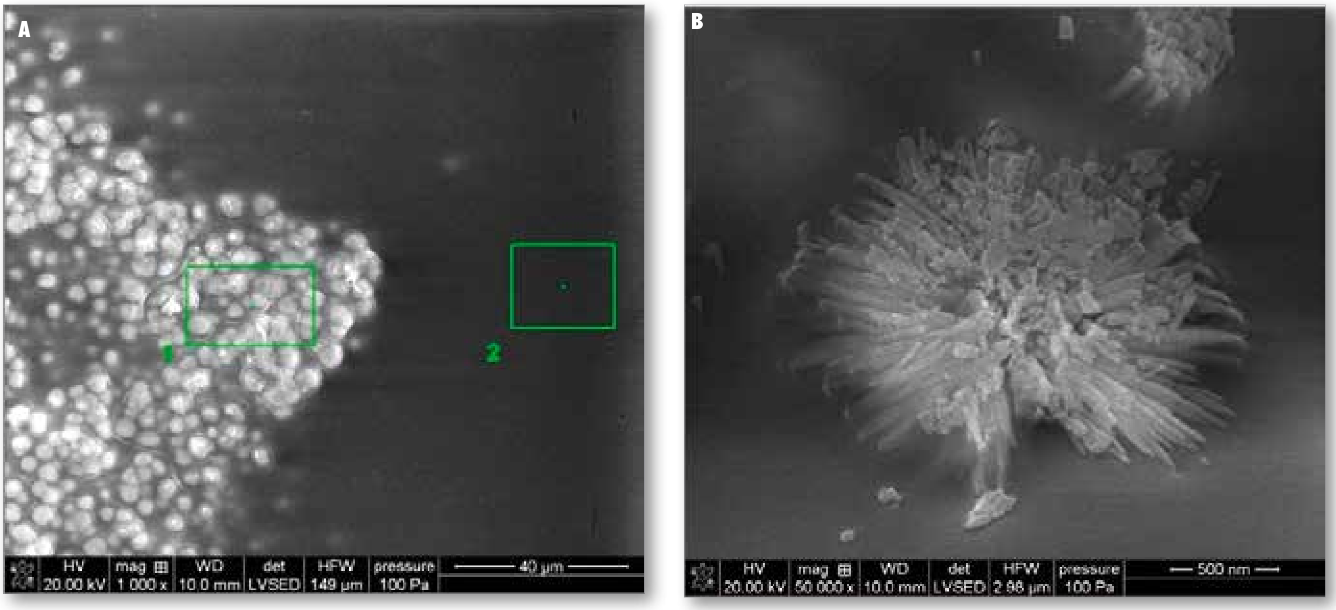
Fig. 6. Deposits in the damaged IOL (case 1). SEM micrograph and SEM/ EDS elemental microanalysis (A). The yellow frames show the areas which underwent SEM/ EDS microanalysis. The quantity of calcium and phosphorus may indicate the presence of carbonate hydroxyapatite and silicon-substituted carbonate hydroxyapatite deposits, especially within area 1. In contrast, the grain with loose and spongy (cloud-like) morphology in the material of the affected IOL (B) probably consists of silicates and carbonates.

phacoemulsification and implantation of IOL. The authors noted that no calcium phosphate deposits were identified on the IOL surface. The formation of calcic deposits took place exclusively in the interior of the IOLs. In one case, emerging calcium phosphate clusters finally ruptured the intact polymeric surface.

Calcification of hydrophilic acrylic intraocular lenses seems to be a multifactorial phenomenon and the exact mechanism remains unknown. The main risk factors suggested in the literature are repeated or/and prolonged contact of the IOL surface with air and breakdown of the blood-aqueous barrier (BAB) [21, 25].

Dhital et al. described 3 cases of hydrophilic IOL calcification. All occurred in complicated traumatized eyes with a history of intraocular gas use [13]. In 1 eye decentration of IOL was observed. The authors pointed that the opacification was centered on the pupil rather than the IOL. This observation suggests the protective role of the iris. Iris tissue is thought to limit the contact between the IOL surface and the causative factor in the anterior chamber. Presence of a small area of opacification on the peripheral part of the IOL which corresponds to an atrophic area of the iris supports this theory. Ahad et al. also noted a correlation between the size of opacification and size of the pupil during the surgery. In strongly mydriatic eyes the diameter of the opacified area was larger [15]. There are no analogical observations for the lens capsule. Central localization of deposits tends to show a predilection to the pupil area rather than the anterior capsulorhexis area. Calcifications were observed in the area of the capsulorhexis but also under the anterior capsule [26]. In our study all patients underwent carbachol injection for miosis before air insufflation. In all cases opacification occurred in the central, pupillary area. The diameters of the affected area were larger than the diameter of the pupil without a pharmacological influence. Detection of the calcified area margin was usually possible after mydriasis.

DSAEK is a procedure connected with an air injection into the anterior chamber. Khan and Muhtaseb [14] in 2011 were the first to describe hydrophilic IOL opacification after DSAEK. They observed opacification of the anterior surface of the IOL in a central disc-like pattern in an eye after uneventful DSAEK and a single attempt of air injection into the anterior chamber after 8 days because of partial



Element	Area 1		Area 2		Area 1 – Area 2	
	Wt %	At %	Wt %	At %	Wt %	At %
C	39.11	52.48	60.58	67.89		
O	36.26	36.52	37.03	31.15		
Na	0.75	0.53	0.29	0.17	3.11	4.89
P	7.43	3.86	0.81	0.35	29.30	34.19
Ca	16.45	6.61	1.29	0.43	67.59	60.93
Total	**100**	**100**	**100**	**100**	**100**	**100**

Fig. 7. SEM micrographs of deposits in the damaged IOL (case 2). The table show the results of microanalysis within the frames, as well as the atomic composition calculated by the difference between normalized EDS spectra from areas 1 and 2. (A) The net result confirms the presence of calcium in the form of hydroxyapatite rather than tricalcium phosphate, $Ca_3(PO_4)$. Morphology of mineral deposit in large magnification (50 000x) of SEM microscope (B).

detachment of donor tissue. Further publications also point to the connection between the presence of air in the anterior chamber and increased risk of IOL opacification after DSAEK [23, 24]. As one of main risk factors of this complication they suggest the necessity of additional intracameral air injection in cases of donor lenticule detachment and dislocation. Dhital et al. hypothesized that presence of intraocular gas in the anterior chamber could induce changes in the surface of the central part of the hydrophilic IOL and additional mineral supersaturation in direct proximity of the IOL surface. Increased permeability of material and increased concentration of substratum in the closed chamber between the IOL and lens capsule could initiate crystal formation [13]. The observation of the influence of the presence of an air bubble in the anterior chamber and increased risk of IOL calcification was partially confirmed in our study. All patients with IOL opacification underwent intracameral air injection as a routine part of the DSAEK procedure. But rebubbling was indicated in 3 of 36 (9%), which is lower rate than seen in the literature (Tab. II).

Also worth noting is the very high incidence of this complication in a group of hydrophilic-hydrophobic IOL in our study. Opacification occurred in 81% of Lentis LS-302-Y (25/31) and in 92% of Lentis L-302-1 (11/12). We did not find similar observations in the literature for simple phacoemulsification with IOL implantation. Bompastor-Ramos et al. described 20 cases of calcification of hydrophilic-hydrophobic acrylic IOL (Lentis LS-52-1) after simple phacoemulsification [27]. The opacification rate in this study was 5.1%. The very high incidence of this complication in this particular type of IOL after DSAEK suggests that material related factors seem to play an important role in the development of calcification or rather the correlation between material and specificity of any stage of the procedure.

Early high incidence of calcification with some models of IOLs was observed in the 1990s. It was termed primary calcification because of initial problems with the lens material [3]. Also several processing steps during manufacturing as well as packing may facilitate opacification of lens material after surgery. Increased incidence of opacification of Bausch and Lomb Hydroview was found to be connected with the presence of a silicone gasket in the packing system [28]. Bompastor-Ramos et al. [27] described 20 cases of calcification of Lentis LS-502-1 (hydrophilic-hydrophobic) after planned phacoemulsification and implantation of IOL in the capsular bag. Based on information from the manufacturer, the increased risk for postoperative opacification of IOLs was because they were sealed in a glass gasket. After that observation all HydroSmart Lentis IOLs with serial numbers starting with 20000 produced before the year 2012 were requested to be returned. In our group 9 IOLs (25%) had the serial number starting with 20000 (20000623527–20000454314). But the serial number of the remaining 27 opacified IOLs (75%) ranged between 91275253009 and 91253958021. There were no differences between these two groups of IOLs in the appearance of IOL opacification in slit lamp examination and in gross evaluation in cases

Authors	IOL model	No. of IOLs	Rebubbling rate
Dhital et al. (13)	C-flex 570C (Rayner) – *hydrophilic* Akreos (Bausch & Lomb) – *hydrophilic*	1 2	Not DSAEK; all eyes with injection of intraocular gas
Khan et al. (14)	Centerflex 570H (Rayner) – *hydrophilic*	1	100% (1/1)
Vardeguer et al. (20)	Akreos-Adapt (Bausch & Lomb) – *hydrophilic*	1	100% (1/1)
Werner et al. (21)	Akreos-Adapt (Bausch & Lomb) – *hydrophilic* Akreos-Adapt AO (Bausch & Lomb) – *hydrophilic* Softec (Lenstec) – *hydrophilic* MI60 (Bausch & Lomb) – *hydrophilic* MemoryLens (Ciba Vision) – *hydrophilic* Lentis-L312 (Oculentis) – *hydrophilic* Konstrukcja statywu (nieznany producent)	1 1 1 1 1 1 1	71% (5/7)
Morgan-Warren et al. (22)	Softec I (Lenstec) – *hydrophilic* 570C (Rayner) – *hydrophilic*	5 1	83% (5/7)
Neuhann et al. (23)	MemoryLens (Ciba Vision) – *hydrophilic* EasyCare600 (Technomed) – *hydrophilic* 47C (Acrimed, obecnie Oculentis) – *hydrophilic* Akryl CF (HumanOptics) – *hydrophilic* Model 1-częściowy (nieznany producent) – *hydrophilic*	1 6 1 1 1	70% (7/10)
Ahad et al. (15)	Akreos-Adapt (Bausch & Lomb) – *hydrophilic* C lub S Flex (Rayner) – *hydrophilic* AcrySof (Alcon) – *hydrophobic*	12 2 1	62,5% (10/15)
Nieuwendaal et al. (24)	Stabibag (Zeiss) – *hydrophilic* 620H (Rayner) – *hydrophilic* Akreos 160 (Bausch & Lomb) – *hydrophilic*	3 3 2	37,5% (3/8)

Tab. II. Types of opacified IOLs and rebubbling rate in the literature.

of explanation. Whitish, well-circumscribed, central opacification was observed in all cases. This pattern of opacification was described only in 1 case from the Bompastor-Ramos group – a patient after phacoemulsification with IOL implantation and further vitrectomy with sulfur hexafluoride (SF6) injection. Three days after surgery, perfluorocarbon liquid and SF6 were observed in the anterior chamber with an intact posterior capsule. Apart from this 1 case, evaluation of all the explanted IOLs showed a yellowish diffuse opacification of the optic and haptics with no clear areas. The SEM revealed the presence of deposits on the anterior and posterior surface of the optic and haptics and within the IOL material. In our study, haptics, the posterior surface of IOLs and the peripheral part of the anterior surface remained clear. Also, the mean interval between the surgery and the diagnosis of opacification of the IOL was different. In our observation it was 14.9 months (range 7–30) compared with 29.15 months (range 6–45) in the Bompastor-Ramos group. All this suggests different or more combined etiology of the calcification of hydrophilic-hydrophobic IOLs in our study.

The calcic nature of the deposits present within the area of granular opacification of the IOL was confirmed by scanning electron microscopy coupled with energy dispersive X-ray spectroscopy (SEM/ EDS). Similar results are present in the literature for hydrophilic IOLs when histochemical staining or EDS was used to confirm the presence of calcium [13, 29]. What differentiated our results is additional presence of the element silicon in all analyzed areas of one of the affected IOLs. The potential role of the element silicon in the mechanism of hydrophilic IOL calcification was evaluated by Gun and associates in 2004 [30]. They describe the role of silicon compounds interacting with long-chain saturated fatty acids present in the aqueous humor in the process of calcification of IOLs (Hydroview). Werner et al. in 2006 [31] also detected the presence of the element silicon in relation to calcified deposits with the other three types of hydrophilic acrylic IOLs that have been associated with calcification. In our study the element silicon was detected in all tested areas of one calcified lens but was absent in the second and in the new one. This suggests possible contamination after removal from the original package. During the surgery, ophthalmic viscosurgical devices (OVDs) are routinely used and have contact with the IOL material. Ohrstrom and associates found in 2004 that small amounts of silicone oil are a common contaminant of these solutions [32]. In our study Eyefill devices from Croma-Pharma were used in all cases. Unfortunately, a sample of this OVD from the same batches that were associated with calcification could not be obtained to be tested.

Because of the late character of this complication, the potential influence of postoperative topical treatment should be taken into consideration. All subjects after DSAEK were using topical steroids continuously. The postoperative drop regimen was standardized in our clinic. Levofloxacin 4 times a day for the first 2 weeks and loteprednol etabonate 4 times a day were prescribed for the first 12 months and subsequently loteprednol etabonate, which were tapered down to once daily for 36 months postoperatively. In 4 cases with increased risk of rejection or recurrent uveitis 0.1% preservative-free dexamethasone was recommended. The observed disorder was non-reversible even after modification of the therapy. No progression was observed after ceasing steroid drops. In 1 eye rejection occurred 2 months after modification of treatment. Patryn et al. reported that intensification of anti-inflammatory topical treatment was also ineffective. Increasing the frequency of 0.1% dexamethasone to 6 times per day revealed no change in the IOL opacification density or in visual acuity, which remained unaltered [33]. In both situations it is not possible to determine whether this limitation of progression of IOL calcification was directly related to treatment modification or was connected with natural evolution of the process, which is more likely.

The influence of topical treatment on the pathogenesis of the process of opacification was also considered by Ahad et al. [15]. They compared the incidence of IOL calcification between two groups with different postsurgical drop regimens. A nonsignificant difference was seen between the use of dexamethasone and levofloxacin drops and IOL opacification, compared with dexamethasone, neomycin and polymyxin B drops (Maxitrol). In our study 0.5% levofloxacin was routinely recommended after DSAEK surgery (4 times per day for the first 2 weeks) in all patients so the analysis of their role in pathogenesis was impossible. There is information in the literature about the incidence of hydrophilic IOL calcification in eyes treated with different antimicrobial drugs: 0.3% tobramycin 6 times per day [24, 33], 0.5% chloramphenicol 4 times daily [22], ofloxacin 5 times a day. There is no evident predilection for one drug.

It is still not clear whether the localized calcification is a result of direct contact between the IOL surface and the exogenous substance or gas (air, gas, tPA, silicone oil), or metabolic reaction on the exogenous factor and secondary change in aqueous humor contents, or exacerbated inflammation after combined surgical procedures. All these are connected with breaking of the blood and aqueous humor barrier but also with prolonged topical steroid administration, so their role in the pathomechanism of calcification is difficult to exclude and should be taken into consideration.

There is information in the literature about ineffectiveness of removing the opacification with the aid of a YAG laser and surgically with a blade [24, 33, 34]. In the case of serious visual acuity deterioration, IOL exchange, to date, is the only effective therapy. This type of surgery is suggested to be a vigilance procedure. Dagres et al. described complications (e.g. zonular dehiscence, posterior capsular rupture, corneal decompensation) in 48% eyes after IOL exchange [35]. In our study, IOL explantation was necessary in 18 cases. Replacement by a three-piece hydrophobic lens (Acrysof MA60AT, Alcon) implanted in the sulcus was performed. Two eyes (18.2%) required additional air insufflation because of postsurgical donor lenticule detachment. No corneal/ graft decompensations were observed.

In our practice, the early stage of IOL calcification could be similar to posterior capsule opacification in the biomicroscopic aspect. YAG laser capsulotomy could increase the risk of complications in cases requiring IOL exchange in future. Because of that in pseudophakic eyes after DSAEK ophthalmologists should pay more attention to determining the nature of IOL haziness.

Conclusions

Because of increased risk of opacification after Descemet's stripping automated endothelial keratoplasty, hydrophilic and hydrophilic-hydrophobic acrylic intraocular lenses should be avoided in patients with endothelial cell disorders.

The decision about laser capsulotomy should be taken with caution in eyes with hydrophilic IOLs. The early stage of implant calcification could be misdiagnosed as posterior capsule opacification. IOL explantation or exchange to this day is the only possible treatment. The procedure is more predictable when the posterior capsule remains undisturbed.

Disclosure
Conflict of interests: none declared
Funding: no external funding
Ethics approval: Not applicable.

References:

1. Werner L: *Causes of intraocular lens opacification or discoloration*. J Cataract Refract Surg. 2007; 33: 713–726.
2. Werner L: *Calcification of hydrophilic acrylic intraocular lenses*. Am J Ophthalmol. 2008; 146930: 341–343.
3. Neuhann IM, Kleinmann G, Apple DJ: *A new classification of calcification of intraocular lenses*. Ophthalmology. 2008; 115: 73–79.
4. Yu AKF, Kwan KYW, Chan DHY, et al.: *Clinical features of 46 eyes with calcified hydrogel intraocular lenses*. J Cataract Refract Surg. 2001; 27: 1596–1606.
5. Pandey SK, Werner L, Apple DJ, et al.: *Hydrophilic acrylic intraocular lens optic and haptics opacification a diabetic patient; bilateral case report and clinicopathologic correlation*. Ophthalmology. 2002; 109: 2042–2051.
6. Lee DH, Seo Y, Joo CK: *Progressive opacification of hydrophilic acrylic intraocular lenses in diabetic patients*. J Cataract Refract Surg. 2002; 28: 1271–1275.
7. Purbrick RM, Stavrakas P, Porooshani H, et al.: *Calcification of a Rayner Centerflex 570H hydrophilic acrylic intraocular lens following vitrectomy for retinal detachment: a clinicopathologic report*. Eur J Ophthalmol. 2010; 20 (6 November–December): 1082–1085.
8. Stringham J, Werner L, Monson B, et al.: *Calcification of Different Designs of Silicone Intraocular Lenses in Eyes with Asteroid Hyalosis*. Ophthalmology. 2010; 117: 1486–1492.
9. Jensen MK, Crandall AS, Mamalis N, et al.: *Crystalization on intraocular lens surface associated with the use of Healon GV*. Arch Ophthalmol. 1994; 112: 1037–1042.
10. Sher JH, Gooi P, Dubinski W, et al.: *Comparison of the incidence of opacification of hydroview hydrogel intraocular lenses with the ophthalmic viscosurgical device used during surgery*. J Cataract Refract Surg. 2008; 34: 459–464.
11. Yu AKF, Ng ASY: *Complications and clinical outcomes of intraocular lens exchange in patients with calcified hydrogel lenses*. J Cataract Refract Surg. 2002; 28: 1217–1222.
12. Fung SS, Sykakis E, Islam NM, et al.: *Intraocular Lens Opacification following Intracamerai Injection of Recombinant Tissue Plasminogen Activator to Treat Inflammatory Membranes after Cataract Surgery*. J Ophthalmol. 2015; 2015: 975075.
13. Dhital A, Spalton DJ, Goyal S, et al.: *Calcification in hedrophilic intraocular lenses associated with injection of intraocular gas*. Am J Ophthalmol. 2012; 153: 1154–1160.
14. Khan MI, Muhtaseb M: *Opacification of the intraocular lens implant following uneventful Descemet's stripping endothelial keratoplasty*. Cont Lens Anterior Eye. 2011; 34: 92–93.
15. Ahad A, Darcy K, Cook SC, et al.: *Intraocular lens opacification after Descemet stripping automated endothelial keratoplasty*. Cornea. 2014; 33: 1307–1311.
16. Tuberville AW, Wood TO, McLaughlin BJ: *Cytochrome oxidase activity of Fuchs' endothelial dystrophy*. Curr Eye Res. 1986 Dec; 5(12): 939–947.
17. Hesham N, Schultze RL: *Impact of Donor Characteristics on 2-Year Descemet Stripping Automated Endothelial Keratoplasty Outcomes in Patients With Fuchs Endothelial Dystrophy*. Cornea. 2015; 34: 6–10.
18. 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(3): 395–403.
19. Gartaganis SP, Prahs P, Lazari ED, et al.: *Calcification of Hydrophilic Acrylic Intraocular Lenses With a Hydrophobic Surface: Laboratory Analysis of 6 Cases*. Am J Ophthalmol. 2016; 168: 68–77.
20. Verdaguer P, Gris O, Casaroli-Marano RP, et al.: *Intraocular Lens Opacification after Endothelial Keratoplasty as Analyzed by Environmental Scanning Electron Microscopy*. Cornea. 2015; 34: 972–975.
21. Werner L, Wilbanks G, Nieuwendaal CP, et al.: *Localized opacification of hydrophilic acrylic intraocular lenses after procedures using intracameral injection of air or gas*. J Cataract Refract Surg. 2015; 41(1): 199–207.
22. Morgan-Warren PJ, Andretta W, Patel AK: *Opacification of hydrophilic intraocular lenses after Descemet stripping automated endothelial keratoplasty*. Clinical Ophthalmology. 2015; 9: 277–283.
23. Neuhann IM, Neuhann TN, Rohrbach JM: *Intraocular Lens Calcification After Keratoplasty*. Cornea. 2013; 32: e6–e10.
24. Nieuwendaal CP, van der Meulen IJE, Patryn EK, et al.: *Opacification of the Intraocular Lens After Descemet Stripping Endothelial Keratoplasty*. Cornea. 2015; 34(11): 1375–1377.
25. Schmidinger G, Pemp B, Werner L: *Opacification of an intraocular lens: calcification of hydrophilic intraocular lenses after gas tamponade of the anterior chamber*. Ophthalmologe. 2013; 110(11): 1066–1068.
26. Habib NE, Freegard TJ, Gock G, et al.: *Late surface opacification of Hydroview intraocular lenses*. Eye (Lond) 2002; 16(1): 69–74.

27. Bompastor-Ramos P, Pavoa J, Lobo C, et al.: *Late postoperative opacification of a hydrophilic-hydrophobic acrylic intraocular lens*. J Catarct Refract Surg. 2016; 42: 1324–1331.

28. Green FG, Werner L, Apple DJ, et al.: *An issue resolved. The Hydroview intraocular lens: development, early reports of calcification and subsequent actions*. White paper Bausch and Lomb; 29 July, 2003.

29. Fellman MA, Werner L, Liu ET, et al.: *Calcification of a hydrophilic acrylic intraocular lens after Descemet-stripping endothelial keratoplasty: Case report and laboratory analyses*. J Cataract Refract Surg. 2013; 39: 799–803.

30. Guan X, Tang R, Nancollas GH: *The potential calcification of actacalcium phosphate on intraocular lens surfaces*. J Biomed Mater Res. 2004; 71A: 488–496.

31. Werner L, Hunter B, Stevens S, et al.: *Role of Silicon Contamination on Calcification of Hydrophilic Acrylic Intraocular Lenses*. Am J Ophthalmol. 2006; 141: 35–43.

32. Ohrstrom A, Svensson B, Tagenfeldt S, et al.: *Silicone oil content in ophthalmic viscosurgicsl devices*. J Catarct Refract Surg. 2004; 30: 1278–1280.

33. Patryn E, van der Meulen IJE, Lapid-Gortzak R, et al.: *Intraocular Lens Opacifications in Descemet Stripping Endothelial Keratoplasty Patients*. Cornea. 2012; 31: 1189–1192.

34. Tandogan T, Khoramnia R, Choi CY, et al.: *Optical and material analysis of opacified hydrophilic intraocular lenses after explantation: laboratory study*. BMC Ophthalmology. 2015; 15: 170–177.

35. Dagres E1, Khan MA, Kyle GM, et al.: *Perioperative complications of intraocular lens exchange in patients with opacified Aqua-Sense lenses*. J Cataract Refract Surg. 2004 Dec; 30(12): 2569–2573

Reprint requests to:

Urszula Kołodziejska, MD (e-mail: ula.kolodziejska@gmail.com)
LASER Eye Microsurgery Centre of Warsaw, Poland
Dolańskiego 2 Str., 00-215 Warsaw, Poland

 ISSN 1505-2753