

Opacification of AcriFlex 50CSE hydrophilic acrylic intraocular lenses

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PURPOSE: To determine the prevalence of and risk factors for AcriFlex 50CSE hydrophilic acrylic intraocular lens (IOL) opacification approximately 3 years after implantation.

SETTING: Selayang Hospital, Selangor, Malaysia.

DESIGN: Cross-sectional study.

METHODS: Patients who had AcriFlex 50CSE IOL implantation in 2005 and 2006 were identified from operating logbooks and recalled via telephone and letters. Opaque IOLs were explanted and sent for scanning electron microscopy (SEM) and energy-dispersive x-ray spectroscopy (EDS).

RESULTS: The review showed that 18 patients had died and 67 had declined examination or could not be contacted, leaving 239 eyes for evaluation. The age of the patients ranged from 25 to 85 years. Of the patients, 83 (34.7%) were Malay, 127 (53.1%) Chinese, and 29 (12.1%) East Indian. The male:female ratio was 1:1. Fourteen eyes of 13 patients (5.4%) had IOL opacification; 1 had bilateral opacification. Five eyes had fine deposits, and 9 eyes had dense opaque deposits. Seven opaque IOLs required explantation. There was no correlation between age ($P=.645$), sex ($P=.319$), or race ($P=.860$) and IOL opacification. Pearson chi-square analysis showed a strong association between diabetes mellitus and IOL opacification ($P=.019$). Nine (69.2%) of the 13 patients with opacification had diabetes. Scanning electron microscopy and EDS showed calcium and phosphate deposits on the optic surface and intralenticularly near the anterior surface of the optic.

CONCLUSIONS: Results indicate that diabetes mellitus is a risk factor for AcriFlex hydrophilic acrylic IOL opacification. In some cases, opacification affected vision, necessitating explantation. The pathophysiology of this complication is unknown.

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Phacoemulsification cataract surgery with implantation of foldable intraocular lenses (IOLs) is now the preferred method of ophthalmologists. In general, the introduction of foldable IOLs improved visual outcomes over those with rigid IOLs. Surgically induced corneal astigmatism, a complication of large-incision surgery, is now uncommon, and visual rehabilitation is rapid. Foldable IOLs are made of several materials, including silicone, hydrophobic acrylic, and hydrophilic acrylic. Silicone IOLs react with the silicone oil used in vitreoretinal surgery,^{1,2} and hydrophobic acrylic IOLs can scratch and develop glistenings.^{3,4} Hydrophilic acrylic IOLs, on the other hand, present the problem of opacification.

There are several reports in the literature of opacification and calcium deposits on different hydrophilic

IOL models.^{5–12} Although hydrophilic IOLs are widely used in Malaysia, primarily because they cost less than hydrophobic IOLs, until 2006 there were no reports of hydrophilic IOL opacification in the country. In October of that year, a patient presented at Selayang Hospital reporting decreased vision in an eye with an AcriFlex 50CSE IOL; examination showed clouding or opacification of the IOL. Two more patients presented with a decrease in vision associated with IOL opacification in August 2007 and December 2007. This triggered a recall process in which all patients who had implantation of the AcriFlex 50CSE IOL at the hospital were asked to return for an ocular examination to determine whether they had symptomatic or asymptomatic IOL opacification.

The AcriFlex 50CSE (Acimed GmbH) is a single-piece 3-haptic hydrophilic acrylic IOL made of poly (hydroxyethyl methacrylate) copolymer. It received Conformité Européenne 1275 certification. The biconvex optic diameter is 6.0 mm and the overall diameter, 10.5 mm. This article presents the results of the recall approximately 3 years after IOL implantation and of a study performed to determine the prevalence of and risk factors for opacification.

PATIENTS AND METHODS

In this cross-sectional review, patients who had implantation of an AcriFlex 50CSE IOL at Selayang Hospital from May 2004 to July 2007 were identified from surgery logbooks. In the recall process, patients were contacted by telephone; if there was no response, letters were sent to the patient's last known address. The hospital's Clinical Research Centre coordinated the study with advice from the Legal Department, Ministry of Health of Malaysia.

When patients returned for their eye evaluation, a data sheet developed for the recall was completed. Patients had a systemic assessment, in particular with regard to diabetes mellitus because the IOL insert had cautioned against the use of this IOL in patients with diabetes. Other data collected included the time between IOL implantation and first recognition of the IOL opacification, if applicable; the time between IOL implantation and IOL explantation, if applicable; and the duration of the follow-up after IOL explantation, if applicable.

The Clinical Research Centre then compiled the data to determine the prevalence of and risk factors for IOL opacification. The results were submitted to the Ministry of Health. The IOL was considered to be opacified when it appeared to be hazy and not fully transparent on slitlamp examination and when 2 consultant ophthalmologists agreed that the IOL was opacified. The IOL opacification was not graded because at present, there is no standardized methodology for doing so.

Patients with IOL opacification and who were symptomatic were given the option of IOL exchange; the benefits and risks of the surgery were fully explained. New IOLs were implanted at no cost to the patient. The IOL was explanted

through an approximate 3.5 mm clear corneal incision. Sodium hyaluronate 1.4% (Healon GV) was injected to release all adhesions between the IOL and lens capsule. The IOLs were sublaxed into the anterior chamber, bisected or trisected with scissors, and removed. A multipiece hydrophobic acrylic Tecnis IOL (Abbott Medical Optics, Inc.) was then implanted in the sulcus. Posterior capsule rupture was treated with triamcinolone-assisted anterior vitrectomy.

The explanted IOLs were sent for scanning electron microscopy (SEM) and energy-dispersive x-ray spectroscopy (EDS). Asymptomatic patients were kept under close observation. Patients without IOL opacification were given follow-up appointments in case opacification occurred at a later time. The recall process took 6 months to complete (from April to September 2008).

RESULTS

Of the 324 patients who had implantation of the AcriFlex 50CSE hydrophilic acrylic IOL, 52 (16.0%) had bilateral implantation, bringing the total number of eyes with the IOL to 376. Eighteen patients died by the time of recall. Of the remaining 306 patients, 67 could not be contacted or declined to attend clinic. The recall process resulted in 239 (78.1%) of 306 patients attending clinic appointments for detailed eye examinations. The mean age of the 124 men (51.9%) and 115 women (48.1%) was 64.8 years (range 25 to 85 years). Of the patients, 83 were Malay (34.7%), 127 Chinese (53.1%), and 29 East Indian (12.1%).

Intraocular lens opacification was noted in 14 eyes of 13 patients (5.4%); 3 cases were in patients with bilateral IOLs. Of the eyes with an opacified IOL, 5 had fine deposits and 9 had a dense opaque opacification. The mean interval between the cataract surgery and IOL opacification was 28.7 months (range 15 to 39 months). There was no correlation between age ($P = .645$), sex ($P = .319$), or ethnicity ($P = .860$) and IOL opacification.

Nine (69.2%) of the 13 patients with IOL opacification and 83 (36.7%) of 226 patients with a clear IOL had diabetes. Pearson chi-square analysis identified diabetes as a significant risk factor for IOL opacification ($P = .019$).

Scanning electron microscopy showed hyperluminous areas on the surface of the IOL (Figures 1 and 2). Under higher magnification, the areas consisted of crystal-like deposits, suggestive of calcium (Figure 3). Energy dispersive x-ray spectroscopy confirmed calcium and phosphate deposits on the surfaces of the optic and haptics of the IOLs (Figure 4).

Traces of calcium deposits were also detected intralenticularly near the anterior surface of the optic. These traces were away from the cut surface of the IOL and less likely to be the result of transference of calcium crystals from the surface of the optic. Traces of silicone and aluminium were also detected on 1 vertical haptic surface.

Seven IOLs were considered to be opaque enough to cause visual disturbance and were thus explanted.

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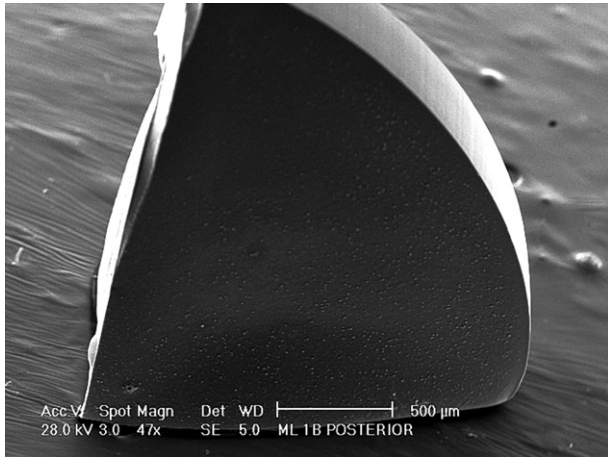


Figure 1. Scanning electron microscopy shows hyperluminous white speckles on the IOL surface.

One patient on the list had not received surgery at the time of this study for health reasons. Three patients had good visual outcomes (CDVA 6/12 or better) after IOL exchange. One had corneal decompensation after IOL explantation and was referred for corneal transplantation. Two patients with diabetes had a post-explantation CDVA of 6/18 and 6/36, respectively; both had increased foveal avascular zones on fundus fluorescein angiography.

DISCUSSION

Opacification of IOLs has medicolegal implications. After the first couple of cases of opacification were noted in late 2006 and 2007, a discussion was held with officers of the Ministry of Health of Malaysia, including the legal advisor. It was decided to recall all patients with the AcriFlex IOL. The process of recall

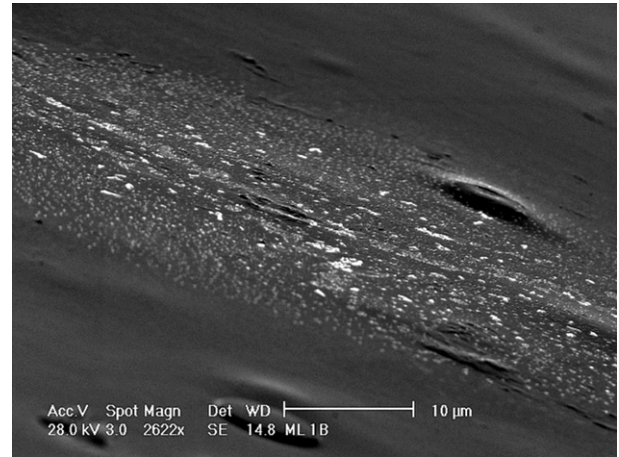


Figure 2. Hyperluminous white speckles under higher magnification.

was considered successful, with 78.1% of still-living patients having a full eye examination. The success of this process is due to 2 factors. The first is that Selayang Hospital has an electronic medical record system in which patient and clinical data are kept and can be easily retrieved. The second is the presence of the Clinical Research Centre within the hospital; the cataract surgery registry manager there was asked to trace patients, to telephone them to book appointments, to send letters if the telephone call was not answered, and to maintain a database of all patients with an AcriFlex IOL. This was the first large recall of patients with the IOL. The prevalence of IOL opacification in this cohort approximately 3 years after IOL implantation was 5.4%.

Patients who were recalled were kept under indefinite follow-up. When necessary, the opaque IOL was explanted and another IOL model implanted at no

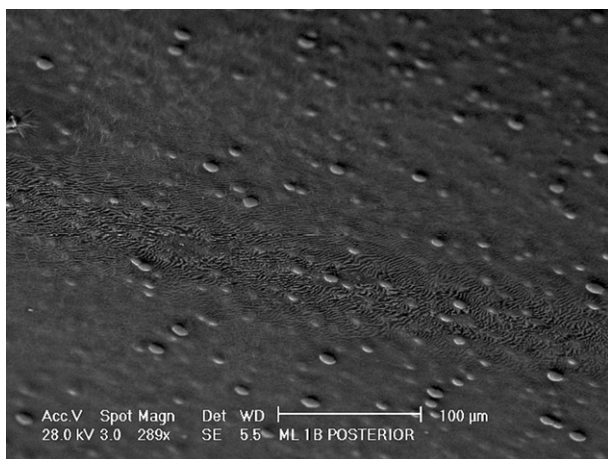


Figure 3. Under higher magnification, the areas consist of crystal-like deposits.

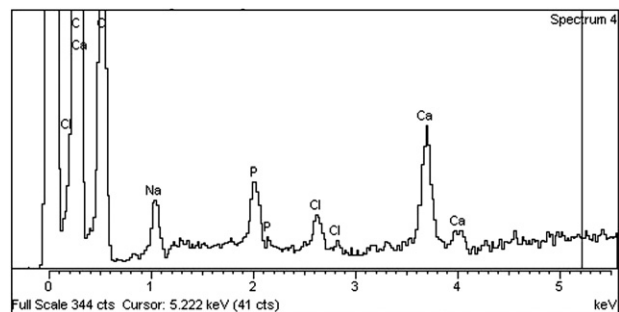


Figure 4. Energy dispersive x-ray spectroscopy confirmed calcium and phosphate deposits on the surfaces of the IOL optic and haptics.

cost to the patient. The patients were offered IOL explantation only if they were symptomatic and they understood the risks of the procedure. A directive was also sent to all ophthalmologists in the Malaysia asking them to stop using the AcriFlex IOL.

Histopathologic analysis by SEM and EDS found that the opacification was primarily calcium and phosphate deposits on both the surfaces of the IOL and intralenticularly, near the anterior surface of the optics. Intraocular lens opacification has been reported with many hydrophilic acrylic IOLs, including the Hydroview H60M (Bausch & Lomb), Aqua-Sense (Ophthalmic Innovations International, Inc.), MemoryLens (Ciba Vision), and SC60B-OUV and SC600-2 (Medical Developmental Research).^{13,14} Studies by Bausch & Lomb indicate that the surface calcifications are linked to the migration of silicone from the packaging onto the IOL surface. Studies by Ophthalmic Innovations International, Inc. of the Aqua-Sense IOL found that surface calcification was linked to silicone on the lens surface; the silicone migrated from the silicone sleeve used to hold the IOL in the vial.¹⁵ Calcification of the MemoryLens IOL was attributed to a change in the polishing process.⁸ Medical Developmental Research withdrew the SC60B-OUV and SC600-2 IOLs because of reported opacification but was unable to establish the cause, although some researchers believe it was the result of premature aging of the ultraviolet-blocking agent.¹⁶ The reported interval between implantation and opacification of hydrophilic acrylic IOLs ranges from 5 months to 5 years.^{7,8,9,17}

We were unable to convince the manufacturer of the AcriFlex 50CSE IOL to perform studies of the reason for the opacification. The process may be linked to migration of silicone from the packaging, as was the case with Hydroview and Aqua-Sense IOLs. Previous studies¹² found silicone and silicone compounds on all calcified hydrophilic acrylic IOLs, including the SC60B-OUV, SC600-2, and MemoryLens. In our study, traces of silicone were detected by EDS. Further studies are required to determine the source of silicone contamination of AcriFlex IOLs.

Analyses of explanted hydrophilic acrylic IOLs found various patterns of opacification caused by the deposition of calcium and phosphate. These included surface deposition, as in Hydroview H60M and MemoryLens IOLs. The deposition of calcium and phosphate was within the substance of the optic as well as on the surface of the SC60B-OUV and Aqua-Sense IOLs.¹² Scanning electron microscopy showed that opacification of the AcriFlex IOL was also within the substance and on the surface of the optic.

Our literature review found a possible association between glaucoma and hydrophilic acrylic IOL opacification and between diabetes and opacification of

these IOLs. In a cross-sectional study of hydrophilic acrylic IOL (Hydroview H60M) implantation after cataract surgery by Balasubramaniam et al.,⁹ 193 of 1330 eyes had evidence of IOL opacification. Of these, 56 (4.2%) had visually significant opacification and required IOL exchange. In addition, 21.5% of eyes in patients with diabetes had IOL opacification compared with 14.3% of eyes in patients without diabetes ($P=.06$), and 20.5% of glaucomatous eyes had IOL opacification compared with 14.0% of nonglaucomatous eyes ($P=.033$). The authors, however, cautioned that there might have been a bias toward more data forms that had more detailed completion (therefore recording comorbidities) in eyes with IOL opacification.

Macky et al.¹¹ report 2 cases of opacification of hydrophilic IOLs (SC60B-OUV) 3 months after implantation; both were in patients with diabetes. Pandey et al.¹⁸ also reported a case of bilateral optic and haptic opacification of a hydrophilic IOL (SC60B-OUV). Although there have been many case reports of hydrophilic IOL opacification in diabetic patients, to our knowledge there is no evidence to prove an association between this systemic disease and IOL opacification.

In our recall of patients, there was a correlation between diabetes mellitus and IOL opacification ($P=.019$). The data were insufficient to allow us to determine whether there was an association with glaucoma. Some kind of metabolic imbalance, altered fluid dynamics of aqueous, or breakdown of blood-aqueous barrier (BAB) in diabetic patients, combined with other factors, may be responsible for the opacification. Kim et al.¹⁹ performed a cross-sectional study comparing the levels of calcium and phosphorus in the aqueous humor and serum of nondiabetic patients and diabetic patients to determine a reason for the increased incidence of late opacification of hydrophilic acrylic IOLs in diabetes. They found that the level of calcium and phosphorus in the aqueous humor and serum of diabetic patients was significantly increased, especially in those with proliferative diabetic retinopathy. They concluded that these increases may be related to hydrophilic acrylic IOL opacification. Nakano et al.¹⁰ changed the levels of calcium and phosphate concentrations and found that a hydrophilic acrylic IOL (Hydroview H60M) had significantly higher amounts of calcified deposits than IOLs of other materials ($P<.01$), indicating that the hydrophilic acrylic IOL easily accumulated calcified deposits in the body when the concentrations of calcium, phosphate, and albumin in the aqueous humor fluctuated as a result of BAB breakdown.

As result of our recall, the following actions were implemented: (1) The importer of AcriFlex 50CSE voluntarily ceased marketing the IOL. (2) An

adverse-event reporting system was implemented in the Malaysian National Eye Database to allow early reporting of problems with IOLs. This reporting system is similar to the medical device alert in the United Kingdom. (3) The Health Technology Section of the Ministry of Health, Malaysia, performed a literature review of IOL opacification and recommended that caution be exercised when using hydrophilic acrylic IOLs, especially in the presence of conditions such as diabetes.²⁰ It must be cautioned, however, that the study did not conclude that all hydrophilic acrylic materials are associated with opacification. (4) All patients with the AcriFlex IOLs were kept under review because some of them may develop opacification in the future. The current plan is to maintain this follow-up for a minimum of 5 years because opacification has been documented up to this point.¹⁷ (5) As part of the informed consent, all patients having IOL implantation will be warned of potential IOL complications, such as opacification, over the long term.

The main limitation of this study is that several ophthalmologists performed the eye evaluations. The presence of opacification is relatively subjective and varies in degree. Very mild opacification can be missed, especially if the patient still retains good vision, and the opacification may worsen with time. It is also unfortunate that the manufacturer of the AcriFlex 50CSE IOL did not extend much assistance to help determine the reasons behind the opacification.

In conclusion, this is the first sample recall of patients with the AcriFlex 50CSE IOL. The prevalence of patients with IOL opacification was 5.4%. The IOL opacification was caused by deposition of calcium and phosphate on the IOL surface and intralenticularly near the anterior surface of the optics. Although the pathophysiology of this complication is unknown, we found a strong association with diabetes mellitus.

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