Glistenings in Modern IOL Materials
A Summary of the Peer-Reviewed Literature
Glistenings in IOL Materials

Abstract
Glistenings, or microvacuoles, have been observed with most modern IOL materials. Glistenings are tiny inclusions of water present within the matrix of the IOL material that may be seen after implantation. While glistenings can be identified by the eye care professional at the slit lamp, they are cosmetic in nature, and are not generally observed by the patient. A large body of peer-reviewed literature demonstrates that glistenings do not adversely affect visual function, as measured using best-corrected visual acuity, contrast sensitivity, glare testing or wavefront measurements in human eyes. Glistenings also appear to have no measurable effect on lens optics when measured in a laboratory setting.

Glistenings - Definition
Glistenings, or microvacuoles, are reflections of light that occur from migrations of water within the matrix of hydrated IOL material.\(^1,2\) Glistenings typically are 1 to 20 μm in size\(^3,4,13,32\) and present from 1 to 6 months postoperatively.\(^3,5,7,9,32\) Some studies suggest they are stable over time,\(^3,7,8,32\) while others suggest they may be progressive.\(^5,9-11,32\)

Glistenings in Different Intraocular Lens Materials
Glistenings have been observed in most modern IOL materials including polymethylmethacrylate (PMMA),\(^12-14,32\) silicone,\(^9,13,15-17,32\) hydrophilic acrylic\(^9,18,19,32\) and hydrophobic acrylic.\(^1-11,13,17,18,20-28,32\)

Glistenings are visible due to differences in refractive indices between the IOL material and water within the IOL material. The larger the difference between these 2 refractive indices, the more apparent the microvacuoles. IOL material refractive indices are as follows:

- PMMA (1.49)
- silicone (1.43-1.46)
- hydrophilic acrylic (1.47)
- hydrophobic acrylic (1.47 to 1.55)

Water has a lower refractive index [1.33] than any IOL material, which means that glistenings will be most apparent in those IOL materials with the highest refractive index. If the index of refraction were equal, for instance, glistenings would be unnoticeable, since the deviation of any light at the interface is a function of the angle of incidence and the difference between the refractive indices of the materials on either side of the interface.

The observance of microvacuoles changes as the angle of the slit beam changes. Microvacuoles are usually best observed with a thin slit beam at a 45° angle. They are usually more difficult to observe with retro illumination.

Formation of Glistenings
Microvacuoles result from water absorption and subsequent condensation (phase separation) within the matrix of the IOL material.\(^1,2,32\) Their formation appears to be influenced by temperature,\(^1,3,4,29\) inflammation\(^21\) and aqueous composition.\(^30-32\)

Microvacuoles are not visible when an IOL is in a dry state. When an IOL is implanted, a certain amount of water is absorbed. About 1 to 6 months postoperatively, phase separation may occur within the matrix of the IOL material, allowing minute water particles to condense and form microvacuoles.\(^32\)

All IOL materials have a limited uptake of water, thus, the self-limiting factor in glistening formation is the achievement of a state of equilibrium in water content within the IOL. For example, hydrophilic acrylic IOLs reach a state of equilibrium at 18% to 33% water content, and hydrophobic acrylic IOLs at 0.3% to 1.5%.\(^32\)

A change in temperature is the most commonly-used method of generating glistenings in vitro.\(^4,9,29,33\) The glistenings formed in this manner are generally similar to those that form in vivo; however, the density of in vitro glistenings can sometimes exceed those that would be expected in a clinical setting.\(^34\) While not directly comparable, glistenings created in vitro will have optical properties and effects consistent with those in-vivo, when they are formed at clinically-relevant densities.
Methodology
The US National Library of Medicine has an on-line medical publication search engine (pubmed.com) and database. This on-line database was searched using a wide range of terms designed to capture all potential articles related to glistenings.

The search term below was used to identify all potential articles:
(glistening* IOL) or (refractile IOL) or (vacuole* iol) or (discolor* iol) or (deposit* IOL) or (glistening* intraocular lens) or (refractile intraocular lens) or (vacuole* intraocular lens) or (discolor* intraocular lens) or (deposit* intraocular lens)

The intent was to ensure that misclassified articles (those that referenced internal deposits, for instance) would not be missed. The expectation was that a high number of unrelated articles would be returned, in order to capture these few potentially misclassified articles. A total of 472 articles were identified.

Each abstract was reviewed and the article was classified as related or unrelated to glistenings. Where there was any doubt, the article was classified as related to glistenings. A more detailed review of the text of each article potentially related to glistenings was then conducted, and the article retained or discarded as the detailed review indicated. In this manner 428 articles were eliminated and 44 articles were retained. Of the retained articles, one was an editorial with no new information, one described a general technique for measuring glistenings, one concerned lens opacification but mentioned glistenings as a related phenomenon and one was a single case report in a French journal and was not translated. The final 40 articles are referenced in this paper.

Impact on Optical Quality, Measured In Vitro
Of 18 in vitro studies of glistenings, the majority were concerned with their formation and characteristics. Only 2 studies measured optical quality as well.

Oshika et al measured spectral transmittance, forward scatter, the modulation transfer function and resolving power at various contrasts with and without a glare source. Several degrees of glistenings in the optic were experimentally created by immersing lenses in water at 37°C for 48 hours and then at 25°C for 24 hours. Glistenings were graded by inspection according to a visual scale provided in the article, with Grade 1 being minimal density. Grade 4+ glistening density was characterized as “extremely intense and... beyond the range of clinical settings”. They found “the optical quality of the acrylic foldable intraocular lens is not significantly affected by the level of glistenings usually seen in the clinical setting” (See Figure 1) In a separate study, Miura et al created glistenings by immersing IOLs in in normal saline solution at 50°C for 2 hours and then at 35°C for 3 days. They examined possible polarization effects from glistenings and found no significant effect.

Impact on Vision
Seventeen studies, each with a minimum enrollment of 20 eyes, report on glistenings and their association with vision loss. A total of 1,843 eyes are included.

Three of the studies in question include patient evaluations 8 years or more after implantation, and account for 278 eyes (15% of the total). Monestam et al examined 103 eyes of 103 patients and graded the intensity of glistenings according to the photographic classification of Dhaliwal et al. They found that most patients had “severe glistenings”, but that “no detectable impact on BCVA, LCVA 10% and 2.5% was found”. Hayashi et al studied 35 eyes more than 10 years after implantation, grading glistenings according to the method of Miyata et al. They found “At more than 10 years postoperatively, visual function, including contrast sensitivity, and ocular HOAs were comparable among eyes that received acrylic, silicone, and PMMA IOLs. Glistenings with the acrylic IOLs were not significantly correlated with visual function and optical aberrations.” The only significant differences found between lenses were higher light scatter and better corrected visual acuity in the acrylic group. Wilkins et. al. examined patients an average of 8 years postoperatively with a PMMA lens and found a similar result; they saw significant glistenings but “did not document any clinical impact.”
Table 1 shows a summary of the 17 studies in question and the differences that were noted with regard to glistenings and visual performance. The bulk of the evidence points to the fact that glistenings, even when severe, have an insignificant impact on visual acuity and other measures of visual function such as contrast sensitivity. In less frequent severe cases, glistenings did not have a significant impact on high and low contrast visual acuity and other common measures of visual function such as contrast sensitivity.

In addition, three case studies suggested an effect on visual function. In one case where glistenings were suspected as the cause of reduced visual acuity, a repeat YAG capsulotomy was performed that restored visual acuity. In the second case, the effects from glistenings could not be separated from the lens tilt and the progressive hyperopia that the patient experienced after undergoing a YAG capsulotomy. In the third case, the retina was compromised, so the visual impact of the glistenings could not be measured: the presentation of glistening formation in this case was also atypical.

**IN SUMMARY:**
- Glistenings are an observable phenomenon, using a slit lamp with an off-axis beam, in a wide array of intraocular lens materials, more evident in those materials with a high index of refraction.
- Glistenings have been extensively investigated both in vitro (artificially created) and in vivo.
- In vitro testing has shown no effect of clinically-relevant levels of glistenings on image quality or the modulation transfer function of intraocular lenses.
- In vivo clinical testing has included almost 2,000 eyes (some control eyes) reported in 17 different clinical studies.
  - Long term studies, which included a significant percentage of eyes with severe glistenings, have shown no effect on best corrected visual acuity, low contrast visual acuity or higher order aberrations of the eye.
  - There has been no reported effect of glistenings on contrast sensitivity.
  - 16 of 17 studies representing 99.9% of all eyes studied show no significant difference in best corrected visual acuity.

<table>
<thead>
<tr>
<th>Ref</th>
<th>Title</th>
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<th>BCVA</th>
<th>Difference reported due to glistenings in:</th>
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<tr>
<td></td>
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<td></td>
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<td>Contrast Sensitivity</td>
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<td>9</td>
<td>Glistenings in foldable intraocular lenses</td>
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<td>7</td>
<td>Glistenings in a large series of hydrophobic acrylic intraocular lenses</td>
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<td>18</td>
<td>Image analysis of implanted rigid and foldable intraocular lenses in human eyes using Scheimpflug photography</td>
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<td>21</td>
<td>Clinical factors related to the frequency and intensity of glistenings in AcrySof® intraocular lenses</td>
<td>129</td>
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<td>10</td>
<td>Long-term results of wagon wheel packed acrylic intraocular lenses (AcrySof®)</td>
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<td>20</td>
<td>Incidence of glistenings with the latest generation of yellow-tinted hydrophobic acrylic intraocular lenses</td>
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<td>Impact on visual function from light scattering and glistenings in intraocular lenses, a long-term study</td>
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<td>Long-term effect of surface light scattering and glistenings of intraocular lenses on visual function</td>
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<td>Glistenings on intraocular lenses in healthy eyes: effects and associations</td>
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<td>27</td>
<td>Effects on visual function of glistenings and folding marks in AcrySof® intraocular lenses</td>
<td>91</td>
<td>No</td>
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<td>14</td>
<td>Glistenings with long-term follow-up of the Surgidev**** B20/20 polymethylmethacrylate intraocular lens</td>
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<td>5</td>
<td>Clinical evaluation of the transparency of hydrophobic acrylic intraocular lens optics</td>
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<td>30</td>
<td>Surfactant induced glistenings: surface active ingredients in ophthalmic solutions may enhance water entry into the voids of implanted acrylic intraocular lenses</td>
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<td>26</td>
<td>Visual significance of glistenings seen in the AcrySof® intraocular lens</td>
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<td>11</td>
<td>Glistenings in the single-piece, hydrophobic, acrylic intraocular lenses</td>
<td>53</td>
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<td>24</td>
<td>Glistenings in the AcrySof® intraocular lens: pilot study</td>
<td>42</td>
<td>Yes***</td>
<td>No, with or without glare</td>
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<td>16</td>
<td>Glistenings in the Artiflex**** phakic intraocular lens</td>
<td>20</td>
<td>No</td>
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</table>

* non-standard contrast acuity test, different only at highest spatial frequency
** eye with partial iridotomy in AcrySof® IOL group
*** Snellen acuities averaged (yields incorrect results, equivalent logMAR shows no significant difference)
**** Trademarks are property of their respective owners
References


CONCLUSION: The presence of numerous microvacuoles in the SI40NB means there may be GP. The light clouding in the AQ110NV that was resolved with drying is thought to be due to particles in the material which cause discoloration.


CONCLUSION: Glistenings appeared some Artiflex* pIOLs to varying degrees, although they were not visually significant in any case. A larger study of this IOL is needed to determine whether severe cases of glistenings affect visual function and assess their cause and evolution over time. Trademarks are property of their respective owners.


CONCLUSION: The findings show that a sharp-edged optic design is, to date, the most effective method of reducing the rate of PCO. Despite a subclinical foreign-body reaction in the AcrySof® group, both lenses had a high degree of capsular and uveal biocompatibility.


CONCLUSION: Thus, we found in foldable IOLs ‘glistenings’, which did not have any influence on functional results and we could distinguish them from lens damage. We propose to use Scheimpflug tests regularly for the examination of implanted new types of IOLs.


CONCLUSION: The MA IOLs exhibited a low level of adhering cells but a high level of glistening formation, the HEMA IOL exhibited the reverse tendency, and the MA/HEMA IOL exhibited a low level of both, thus indicating that hybrid MA/HEMA IOLs are less susceptible than HEMA IOLs to cell adhesion and less susceptible than MA IOLs to glisten formation.


CONCLUSION: Glistenings were common in eyes with the blue light-filtering hydrophobic acrylic IOL and increased over time.


CONCLUSION: The frequency and intensity of glistenings in AcrySoF® IOLs increased with time after surgery and were higher when postoperative inflammation was present. Glistenings developed more frequently in cases of phacotrabeculectomy but not after combined phacoemulsification and deep sclerectomy. Glistenings did not result in decreased Snellen BCVA.


CONCLUSION (EDITORIAL COMMENT): Even significant glistenings and high-level light scattering from the IOLs have not been shown to have a detectable impact on CDVA or low contrast visual acuity.


CONCLUSION: Soft acrylic IOL unfold slowly, resulting in controlled insertion, but it is possible to crack the lens and some lenses develop glistenings due to water accumulation. There are significant socioeconomic implications to the large differences in posterior capsule opacification rates between the various biomaterials and the lens styles.


CONCLUSION: Glistenings occurred frequently in AcrySoF® IOLs, with most cases mild. A larger study of this lens is needed to determine whether severe presentations affect visual function and to understand how glistenings change over time.


CONCLUSION: Both the CeeOn* Edge and AcrySoF® groups had a low incidence of PCO after an 18-month follow-up. The CeeOn* Edge group had significantly less PCO than the AcrySoF® IOL group. These results confirm that IOLs with square truncated edges create a barrier effect at the optic edge, reducing the overall incidence of PCO.

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References


CONCLUSION: Patients who received AcrySof® IOLs that came in the AcryPak® had some degree of glistenings. There was also a significant decrease in contrast sensitivity compared with that of fellow eyes with silicone IOLs. The glistenings are likely caused by water vacuoles that form within the lens after hydration within the eyes. Further studies are necessary to assess the exact cause of these glistenings.


CONCLUSION: Although glistenings and folding marks were observed after the implantation of AcrySof® IOLs, they did not significantly affect visual function.


CONCLUSION: One year after implantation of foldable, highly refractive silicone and hydrophobic acrylic IOLs using a self-sealing tunnel incision and phacoemulsification, no significant functional or morphological differences between the two IOL types were observed.


CONCLUSION: The glistenings in AcrySof® IOLs were temperature dependent and confined to IOLs packaged in AcryPak® System folders and maintained at constant (body) temperatures. These findings are believed to be consistent with fluid formation within the acrylic optic, somehow related to the AcryPak® packaging system.


CONCLUSION: The Diclod test group had a greater number of glistenings than the Rinderon test group. Both drugs have similar anti-inflammatory properties and Diclod, unlike Rinderon, also contains the surfactant polysorbate. We proposed that the presence of surfactant, or other ingredient, in commercially available eyedrops may enhance the development of glistenings.


CONCLUSION: The number of vacuoles increases with incubation time in aqueous humor containing serum. The addition of serum increased the proportion of lipids and proteins in the solution, which also occurs with a breakdown in the blood-aqueous barrier. The results of the present study point to a physiological factor that may lead to vacuole formation in IOLs and may aid clinicians in identifying risk factors involved in the formation of vacuoles.


CONCLUSION: Although the impact of glistenings on postoperative visual function and the evolution of glistenings in the late postoperative period remain controversial, IOL explantation has rarely been reported.


CONCLUSION: AcrySof® lenses soaked in warm water for a short time may change characteristics, and therefore, close monitoring of the temperature and time of soaking is necessary to prevent glistening formation.


CONCLUSION: The optical quality of the acrylic foldable intraocular lens is not significantly affected by the level of glistenings usually seen in the clinical setting.


CONCLUSION: The birefringence of the 824C IOL could be a source of error during polarization measurements of the fundus or with instruments that transmit polarized light through the IOL.


CONCLUSION: Although IOL exchange surgery was considered, a second Nd:YAG laser intervention successfully removed the proliferated lens materials and restored the visual acuity. The glistenings were not the cause of the reduced vision.


CONCLUSION: The glistenings in the explanted AcrySof® IOL were likely caused by temperature changes and not mechanical stress from folding.
CONCLUSION: Analyses of the explanted IOL and the control IOL under differential scanning calorimetry, as well as by attenuated total reflection Fourier transform infrared spectroscopy, revealed slight differences between the IOLs.

CONCLUSION: Most patients in this case series operated 10 years previously had severe glistenings and a high level of light scattering from their intraocular lenses. No detectable impact on BCVA, LCVA 10% and 2.5% was found.

CONCLUSION: At more than 10 years postoperatively, visual function, including contrast sensitivity, and ocular HOAs were comparable among eyes that received acrylic, silicone, and PMMA IOLs. Surface scattering and glistenings with the acrylic IOLs were not significantly correlated with visual function and optical aberrations.