Etiology of Negative Dysphotopsia

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Introduction

Cataract is the leading cause of visual impairment worldwide. Cataract surgery, the removal of clouded crystalline lens and subsequent implantation of an artificial intraocular lens (IOL), is the most commonly performed ocular surgical procedure. In 2015, approximately 3.6 million patients in the United States and more than 20 million worldwide underwent cataract surgery. With an increasing aging population, the number of patients undergoing this surgery is expected to increase each year.¹ Modern cataract surgery is generally considered a safe and effective procedure due to the advancement of surgical equipment, intraocular lens design, and surgical technique. However, in a minority of cases, undesired visual phenomena may still occur following an uneventful cataract surgery. These phenomena may take different forms, such as glare, halo, starburst, dark shadows, etc., and have been collectively named as "dysphotopsia." Most pseudophakic patients who notice these symptoms either tolerate them or neurologically adapt to them over time. However, visually significant dysphotopsiae persist in a small fraction of patients. Persistent dysphotopsiae are considered the leading cause of patient dissatisfaction and surgeon frustration after cataract surgery because of the complicated causes and management strategies.² Therefore, it is important for both surgeons and industry to have a better understanding of the etiology, prevalence and clinical manifestations to provide better treatment options and methods to minimize their occurrence including new IOL designs, better patient selection methods and pre/post-operative counseling.
Clinical Manifestation and Prevalence

The term dysphotopsia was first defined in 2000 by Tester et al.\textsuperscript{3} to describe any light-related, unwanted patterns, which superimpose over the true retinal image and lead to degradation of visual performance and/or visual quality. There are two types of pseudophakic dysphotopsia after uncomplicated cataract/monofocal IOL surgery, positive and negative dysphotopsia.\textsuperscript{4,5} In some rare cases, they can be present simultaneously. Patients after cataract surgery with multifocal (MF) IOL implantation may, in addition, present increased photic phenomena, such as halo and starburst for the reason related to the MFIOL optic design.\textsuperscript{6}

Positive Dysphotopsia (PD) was first discussed as a clinical finding by Masket et al.\textsuperscript{6} in 1993. It was described as undesirable central and peripheral light streaks emanating from oblique light with ovoid IOLs. These clinical findings were described much earlier than the name of dysphotopsia was coined by Tester et al. PD is characterized by any undesirable bright artifacts somewhere in a patient's visual field. PD can appear in a variety of forms, such as bright flashes, arcs, streaks, halos or starbursts. These artifacts usually appear at the center or in the mid-periphery of visual field under certain lighting conditions or for certain glare source orientations. The reported incidence of PD shortly after uneventful cataract surgery (i.e., within the first weeks) varies widely from as low as 0.2% to as high as 77.7%.\textsuperscript{7} Such photic phenomena often resolve over time, but in approximately up to 2.2% patients, the symptoms present from post-operative day 1 and persist months after surgery without improvement, and eventually may require treatment.\textsuperscript{8}

Negative Dysphotopsia (ND) is characterized by the perception of a dark shadow that is typically crescent-shaped (Figure 1) and is usually in the patient's temporal peripheral field. The perception is most often noted shortly after surgery (within the first days to weeks) in photopic conditions, and can be stimulated or exacerbated by a bright light source in the temporal field.\textsuperscript{9} It has also been shown that the shadow can change in shape and intensity as the direction of gaze changes.\textsuperscript{10} The phenomenon can be suppressed or eliminated by blocking the temporal light or pharmacologically dilating the pupil.\textsuperscript{9} Negative Dysphotopsia is the focus for the remainder of this white paper.

Figure 1: Illustration of Negative Dysphotopsia
ND has been reported after uncomplicated cataract surgery in eyes implanted with many types of posterior chamber IOLs placed in the capsular bag. Most often these IOLs are well centered in the capsular bag. No cases have been reported in eyes implanted with anterior chamber IOLs or posterior chamber IOLs positioned in the ciliary sulcus. Unlike positive dysphotopsia, ND has never been reported in phakic eyes or eyes that underwent other ocular procedures such as Radial Keratotomy, LASIK or penetrating keratoplasty. ND is much less common than positive dysphotopsia. As is the case with positive dysphotopsia, the published incidence of ND also varies. Higher incidence rates have been shown to be related to actively asking the patient about specific symptoms after surgery. Up to 15.2% of patients on the first post-operative day and 20% of patients one-week following cataract surgery report ND when they were specifically asked about shadows or dark crescents on the edge of their vision. Similar to positive dysphotopsia, most patients adapt with time and only up to 2-3% show persistent symptoms two to three years later. The number of patients that require IOL exchange as the result of ND is lower than the number of exchanged due to PD.

**Etiology for Negative Dysphotopsia**

In addition to Masket’s initial description of PD reported in 1993, negative dysphotopsia was described in 2000 by Davison. Since then, numerous associations have been made, and several theories intended to explain the etiology have been presented. However, gaps are still present between some of the laboratory predictions and clinical evidence. The exact cause remains elusive and is currently considered to be multifactorial. Predicting which patient will develop ND and determining appropriate treatments, therefore, remain very challenging. In this article, we review multiple theories related to 1) IOL material or design 2) surgical technique used 3) predisposing patient anatomy and neuro-adaptation ability. Efforts will be made to clarify those suppositions that have clear clinical evidence and to discuss those which are theoretical but to date, lack clinical evidence.

1. ND and IOL material and design

**Edge design and refractive index of material**

Supposition 1: ND is induced by square edged design and high refractive index of acrylic material (e.g. AcrySof® IOLs)

In Davison’s first report of ND, he proposed that a particular edge design, sharp square edge, and an acrylic IOL material with high refractive index may be causes of negative dysphotopsia. Such acrylic IOLs were first introduced into the market in the mid-1990s and quickly became widely adopted because of their lower rate of posterior capsule opacification (PCO) compared with other IOLs, including silicone IOLs. Several clinical reports published after Davison agreed with the proposed etiology. An initial laboratory ray tracing study by Holladay et al. also supported this association by showing that the shadow seen in ND is likely the result of light discontinuity created by refraction at the sharp edge of the IOL. The study proposed that in the rounded edge IOLs, the curved edge creates dispersed refracted rays, which reduce or completely eliminate the shadow seen with sharp edge IOLs. Holladay et al also proposed that the high refractive index of acrylic IOLs allows for a larger range of distances between the posterior iris and the anterior capsule as compared to IOLs with a lower index of refraction, such as silicone. He proposed that this can result in shadow formation. Therefore, it is thought that ND is more likely to occur in patients implanted with higher refractive index IOLs with a square edge. However, numerous clinical studies have noted exceptions to this hypothesis. Trattler, Narvaez, Masket and Fram reported the occurrence of ND in patients with low refractive index silicone IOLs, with either square or rounded edge design, implanted in the capsular bag. Vamosi et al described 5 cases of ND associated with varied in the bag hydrophobic and hydrophilic acrylic IOLs. Radmall et al compared two hydrophobic acrylic single piece IOLs, which differed mainly by refractive index (1.55 for AcrySof® SN60WF vs. 1.47 for Tecnis® ZCB00). The pseudophakic dysphotopsia scale (including both PD and ND) was 2.98 ± 4.8 and 3.57 ± 5.04 for SN60WF and ZCB00 respectively (the higher the score, the higher the incidence/severity). It was concluded that increasing the refractive index does not increase the incidence and severity of pseudophakic dysphotopsia or decrease overall visual satisfaction. Burke et al reported five ND cases, in which the IOLs were placed in the capsular bag, were successfully treated with IOL exchange and replacement.
with a 3-piece IOLs (AcrySof® MA60AC) inserted in the ciliary sulcus. These clinical cases suggest that the development of ND are related to the positioning of IOL inside the capsular bag rather than the refractive index of the IOL material or the edge design of the IOL.

A more recent ray tracing study conducted by Holladay and Simpson21 suggested that the edge design and high refractive index are only secondary contributing factors of ND formation, which essentially revised their original theory. These results suggest additional factors play an important primary role in the etiology of ND. With their new ray tracing study, Holladay and Simpson21 proposed that ND is present when there is gap the retinal images formed by limiting light rays missing the optic of the IOL and maximum limiting rays that are refracted by the IOL (Figure 2).

**Figure 2: Pupil Size - A.** In a small pupil, a gap is formed between the most anterior ray refracted by the IOL and the most posterior ray. **B.** In a large pupil, there is overlap in the area between the most anterior ray refracted by the IOL and the most posterior ray missing IOL. (Modified based on Holladay & Simpson’s paper21)

Any factors that affect the width and location of the gap will contribute to the patient’s complaint of ND. One of the primary factors proposed is the optical surface design of IOL, which can be briefly categorized into three types: convex-plano, biconvex and plano-convex. The convex-plano IOL provides greatest spread and most anterior refracted rays, therefore least chance of ND formation. Any factors that may change the optical surface design of IOL such as the power of the IOL and asphericity of the IOL may subsequently change the size and location of the gap and therefore, ND symptoms. Makhotkina et al reported that ND was associated with short axial length and high IOL power in their study.22 Davidson reported Dysphotopsia (PD+ND) appears to be generated in eyes that require IOL powers in the mid to high 20s.23 Of course, patients with short axial length are also often associated with large angle Kappa, which will be discussed later as another important factor in leading to ND formation. Again, multiple factors may work simultaneously in ND formation, and more clinical data is necessary to validate these proposed factors.

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IOL size and posterior chamber depth

Supposition 2: ND is induced by expanded depth of posterior chamber after cataract surgery

After cataract surgery, the iris moves posteriorly due to the fact that IOL is much smaller in diameter and significantly thinner than the natural crystalline lens. A gap is usually formed between the iris and the IOL surface. It was proposed that ND is induced by the expanded depth of the posterior chamber after cataract surgery. However, Vamosi et al measured iris-optic distance with Ultrasound Biomicroscopy (UBM) in patients with severe symptoms of ND. The data was not statistically significantly different from those from normal pseudophakic population. Masket and Fram also reported ND cases with in-the bag-IOL despite shallow posterior chamber depths (UBM measurement). They also reported one case in which ND persisted even after iris suture fixation of the bag-IOL complex was employed to reduce the posterior chamber depth. However, in cases in which the IOL was placed in the sulcus, a secondary piggyback IOL was used, or reverse optic capture techniques were used, ND symptoms can be relieved or improved. Most of time in these cases, the iris-optic distance was reduced. These clinical data indicate that the development of ND is not simply related to the depth of posterior chamber, other factors are involved.

2. ND and surgical technique

Anterior capsule overlapping the IOL

Supposition 3: ND reduces over time owing to anterior capsule haze

Capsulorhexis, also known as Continuous Curvilinear Capsulorhexis (CCC), is a technique pioneered by Drs. Howard Gimbel and Thomas Neuhann to remove the central part of the anterior capsule of the lens during modern cataract surgery in order to have a smooth capsulotomy and facilitate IOL positioning in the center of capsular bag to result in a symmetrical 360° anterior capsule overlap. Masket and Fram proposed that ND could be induced at the interface of the anterior capsulotomy and the front surface of the posterior chamber IOL, suggesting that a reflection of the anterior capsulotomy edge is projected onto the nasal peripheral retina. Supporting evidence for this includes 1) the reverse optic capture technique innovated by Masket resulting in a high success rate reducing ND symptoms in his practice; 2) Nd:YAG laser removal of a translucent anterior peripheral capsule resolving persistent ND symptoms as reported by Cooke et al.; Folden also reported success with YAG laser anterior capsulectomy, with a complete resolution in 3 out of 6 cases and partial success in 2 out 6 cases; 3) in-the-bag nasal IOL optic/overlapped capsular bag truncation led to resolving of ND symptoms reported by Alapati et al. Points 2 and 3 also suggest that the opacification of anterior capsule cannot explain the self-recovery of ND in most patients. Additionally, a recent ray tracing study by Holladay and Simpson also supported the theory that the anterior capsule serves as an additional primary factor by significantly reducing the intensity of the maximum limiting refracted ray.

IOL haptic junction position

The results of a clinical study by Henderson et al. inferred that the position of a single piece IOL haptic junction may play a role in reducing ND formation in some patients. When the haptic junction is positioned slightly towards the superior nasal (Figure 3), ND shadow is reduced or eliminated, possibly due to the limiting ray missing the IOL optic now will pass through the haptic of the IOL. Theoretically, simply placing the haptic junction at horizontal or slightly superior nasal position will refract the ray slightly posterior compared to when the haptic junction are placed in a different position, thus reducing or possibly eliminating the gap or shadow. This simple and easy maneuver by the surgeon was proposed to reduce the chance of ND. However, this maneuver did not reduce the incidence of persistent ND when compared to the control group, eyes with IOL haptic junction placed vertically.
Figure 3: IOL Positioning - The superior-nasal positioning of IOL optic-haptic junction reduced the incidence of ND after cataract surgery compared with vertical positioning of IOL optic-haptic junction on the first postoperative day. However, no significant difference of ND incidence was observed between two groups at 1 month post-surgery (Henderson et al.30)

Temporal clear corneal incisions

Supposition 4: early transient ND is induced by temporal clear corneal incision

Another hypothesis posited that the exposed corneal edema associated with a beveled temporal incision, which creates a broad surface area in contrast to the minimal surface area created with a thin perpendicular keratotomy incision, may contribute to transient ND. Contradictory clinical evidence includes a case reported by Cooke in which complaints of bilateral ND occurred with superior scleral incisions. It should be noted that in the case of this patient, the ND symptoms could have been considered at persistent. However, ND was reported with superior scleral incisions and were effectively treated with IOL exchanges performed through temporal incisions. In addition, there are no reports of ND occurring after radial keratotomy, LASIK or other cornea surgeries that involve corneal incisions.

3. Patient predisposing anatomy and neuro-adaptation ability

Pupil size

Clinically, it has been reported that ND is often associated with small size pupil in photopic conditions and dilation of the pupil can alleviate ND symptoms. A theoretical ray tracing calculation by Holladay and Simpson (Figure 2B) showed that a large pupil can create an overlapping area between the most anterior ray refracted by IOL and most posterior ray missing the IOL resulting in no ND formation. Hong et al. also used ray tracing to show that smaller pupils increase the potential of developing ND symptoms.
Angle Kappa (κ) and Angle Alpha (α)

Angle Kappa is the angle between the visual axis and the pupillary axis. It represents the decentration of pupil center from the visual axis and can be clinically identified by what is normally a nasal displacement of the corneal light reflex from the pupil center. The normal Angle Kappa is slightly positive due to the fact that the fovea lies slightly temporal to the point at which the pupillary axis intersects with the posterior pole of the globe. Hyperopes tend to have large positive Angle Kappa. Holladay and Simpson showed the close relationship of size of Angle Kappa and the size of ND: the larger the Angle Kappa, the larger the potential of the gap to form ND.21 As stated previously, Makhotkina et al.22 reported eyes with ND were significantly shorter and had implanted IOLs of higher powers than control eyes, although no Angle Kappa data were presented. Large Angle Kappa has also been shown to contribute to decentration of the IOL and subsequent positive dysphotopsia such as glare and halo in multifocal patients.32

Angle Alpha is the angle between the visual axis and optical axis. An Angle Alpha ≥ 5.2° may increase the exposure of the nasal peripheral retina, and hence be associated with ND as suggested by Holladay et al.4

Neuroadaptation

As discussed previously, in most cases, ND is transient in nature for the majority of patients. Coroneo33 has proposed neuroadaptation where the brain over time adapts to ND and any shadows may no longer be perceived.

Other anatomical features

Other anatomical features in patients that have been associated with the occurrence of ND are 1) having a prominent globe or a shallow orbit; 2) the presence more functional retinal tissue in the anterior nasal quadrants than in the anterior temporal quadrants; 3) a greater preponderance of ND in left eyes.10,13,22,26
Summary

Although modern cataract surgery is extremely successful, patient satisfaction can sometimes be affected by the occurrence of negative dysphotopsiae. Clinical investigation has indicate that ND is not induced solely by square edged IOL designs or high index of refraction acrylic materials such as AcrySof® IOLs. Although ND is relatively rare, the accumulated number of severe cases are significant enough to warrant continuous effort to understand the etiology, to help to improve IOL design and to guide surgeons on preoperative considerations in order to continue to improve patient satisfaction after cataract surgery.

Disclosures: SM and NF are paid Alcon consultants.
References


AcrySof® Family of Single-Piece IOLs
Important Product Information

CAUTION: Federal law restricts these devices to sale by or on the order of a physician.

INDICATIONS: The family of AcrySof® single-piece intraocular lenses (IOLs) includes AcrySof® UV-Absorbing IOL, AcrySof®IQ, AcrySof®IQ Toric® and AcrySof IQ ReSTOR® and AcrySof IQ ReSTOR® Toric IOLs. Each of these IOLs is indicated for visual correction of aphakia in adult patients following cataract surgery. In addition, the AcrySof toric IOLs are indicated to correct astigmatism at the time of cataract surgery. The AcrySof IQ ReSTOR IOLs are for cataract patients with or without presbyopia, who desire increased spectacle independence with a multifocal vision. All of these IOLs are intended for replacement in the capsular bag.

WARNINGS AND PRECAUTIONS:
GENERAL CAUTIONS FOR ALL ACRYSOF® IOLS: Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk/benefit ratio before implanting any IOL in a patient with any of the conditions described in the Directions for Use that accompany each IOL. Caution should be used prior to lens encapsulation to avoid lens decentration or dislocation. Viscoelastic should be removed from the eye at the close of surgery.

CAUTIONS ASSOCIATED WITH ACRYSOF® IQ RESTOR® IOLS: Some patients may experience visual disturbances and/or discomfort due to multifocality, especially under dim light conditions. Visual symptoms may be significant enough that the patient will request explant of the multifocal IOL. Spectacle independence rates vary with all multifocal IOLs; as such, some patients may need glasses when reading small print or looking at small objects. Clinical studies indicate that posterior capsule opacification (PCO), when present, may develop earlier into clinically significant PCO with multifocal IOLs.

CAUTIONS ASSOCIATED WITH ACRYSOF® IQ TORIC AND RESTOR® TORIC IOLS: Optical theory suggests that, high astigmatic patients (i.e. > 2.5 D) may experience spatial distortions. Possible toric IOL related factors may include residual cylindrical error or axis misalignments. Toric IOLs should not be implanted if the posterior capsule is ruptured, if the zonules are damaged, or if a primary posterior capsulotomy is planned. Rotation can reduce astigmatic correction; if necessary lens repositioning should occur as early as possible prior to lens encapsulation.

Prior to surgery, physicians should provide prospective patients with a copy of the appropriate Patient Information Brochure available from Alcon informing them of possible risks and benefits associated with the AcrySof® IQ Toric, AcrySof® IQ ReSTOR® and AcrySof IQ ReSTOR® Toric IOLs.

Do not resterilize. Do not store at temperatures over 45° C. Use only sterile irrigating solutions to rinse or soak IOLs.

ATTENTION: Refer to the Directions for Use labeling for the specific IOL for a complete list of indications, warnings and precautions.

See product instructions for complete wear, care and safety information.