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A PERFECT PARTNERSHIP: THE AVANSEE PRELOADED IOL SYSTEM

A review of European data

avansee[™] preset



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Abstract

Cataract surgery has dramatically evolved over recent years due to the development of injectors that insert a folded intraocular lens (IOL) into the eye through a small incision. A number of IOLs and IOL injector systems are currently available, some of which are more reliable than others. This review compares the quality, reliability and ease-of-use of the more common IOLs/IOL injectors with the three-piece (3P) Avanse™ IOL/Avanse™Preset injector (Kowa Co., Ltd., Japan) – one of the most commonly used injector systems in Japan and available for use in Europe since 2014.

Unlike some IOL injectors, the AvansePreset lens and injector have been designed to perfectly partner each other to provide an injector system that is quick, easy and reliable to use, with more controlled, more stable IOL insertion than some other systems. Compared to many other IOLs, the optical purity of the Avanse lens is unlikely to be compromised during insertion and is also unlikely to deteriorate over time. This suggests that Avanse 3P insertion using the AvansePreset injector system is a useful option for the treatment of aphakia during cataract surgery.

Introduction

The development of foldable IOLs that can be injected through small incisions has enabled ophthalmologists to perform minimally invasive cataract surgery without the need for suturing. This reduces the risk of infection, minimises induced corneal astigmatism, and improves patient recovery time. The ideal IOL should gently unfold after injection and fully regain its mechanical and optical properties to replace the natural lens of the eye. It should assume a stable position in the eye without exerting zonular stress or causing transformation of the capsular bag, provide high levels of corrected visual acuity (CVA), retain its optical purity over time, and be associated with a low risk of postoperative complications, such as posterior capsule opacification (PCO) and endophthalmitis.¹ Whereas the overall stability and quality of an IOL largely depends on the design, material, and processes used to manufacture the lens, the success and safety of IOL insertion are related to the ease-of-use, reproducibility and reliability of the injector system.

The ideal injector system should be single-use to avoid the need for cleaning and sterilisation, be fully preloaded to provide accurate and reproducible lens-loading without the need for an expert and should be designed to specifically partner an appropriate lens. The required incision should be as small as possible to reduce the risk of infection and astigmatism and the injector should provide smooth, controlled and accurate delivery without damaging the IOL.

A number of IOLs and IOL injector systems are currently available, including Avanse™/Avanse™Preset (Kowa Co., Ltd., Japan), AcrySof™/UltraSert™ (Alcon, USA), TECNIS®/TECNIS iTec® (Abbott Medical Optics, USA), enVista™/BLIS™ (Bausch + Lomb Inc., USA), and Vivinex®/iSert (HOYA Surgical Optics, Japan). The aim of this review is to examine the evidence for the long-term quality and stability of the Avanse IOL, together with the ease of use and reliability of the fully preloaded, advanced design AvansePreset injector system.

Avansee/AvanseePreset

Avansee is a posterior chamber IOL with three-piece (3P) modified C-loop haptics made from soft, flexible polyvinylidene fluoride (PVDF) that are designed to reduce the risk of breakage during insertion (see Figure 1A).

The optic is made from a UV-absorbing hydrophobic soft acrylic material which, in the case of the yellow-type lens, closely replicates the spectral transmittance of the natural crystalline lens and contains a proprietary blue-light filter.^{2,3} The IOL is manufactured using a stringently-controlled cast-moulding method and is carved after polymerisation without grinding to ensure square edges.¹ This is important because square-edged IOLs are more likely to induce a sharp bend in the capsular bag than round-edged IOLs, thereby preventing lens epithelial cell (LEC) migration from the anterior capsule to the posterior capsule and reducing the risk of PCO.⁴⁻⁶ Indeed, a retrospective study in 4,862 eyes showed that the proportion of PCO cases requiring corrective treatment after two years was significantly lower in patients receiving square-edged IOLs, including Avansee and AcrySof models, than in those receiving the rounder-edged YA-60BBR (HOYA, Japan) IOL (1.7% and 2.4% vs. 7.2%; $P<0.0001$ for both comparisons).¹

Avansee is designed for IOL implantation into the capsular bag after extracapsular cataract extraction or cataract phacoemulsification.² For best results, the IOL should be inserted using the fully preloaded, single-use AvanseePreset/AvanseePresetUV injector system (see Figure 1B).

The advanced design of this system allows fast, reliable, reproducible and controlled IOL insertion in three easy steps: one to inject the ophthalmic viscosurgical device (OVD), one to remove the lens stage and the third to push the plunger. Incision sizes of 2.4mm for sclera-corneal and 2.6mm for corneal insertion are recommended for the small incision AvanseePreset injector models PN6AS and PU6AS (2.8

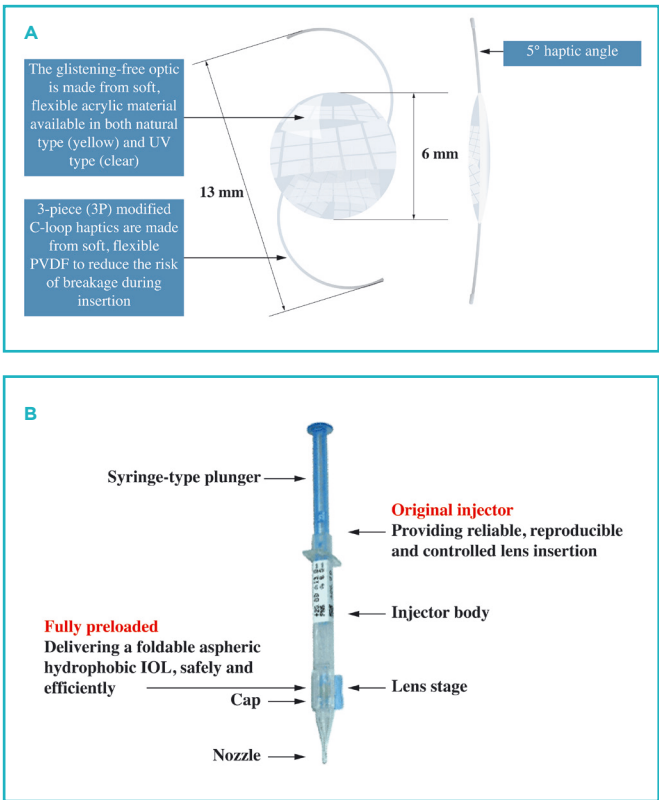


Figure 1: Key characteristics of Figure 1A: Avansee™ IOL; Figure 1B: Avansee™Preset (Kowa Co., Ltd.);UV: ultraviolet; PVDF: polyvinylidene fluoride

to 3.0mm, respectively, if using AvanseePreset PN6A/PU6A injector systems). Avansee 3P spherical models (AN6K, AU6K and AN6MK) were launched in Japan in 2007 and were followed by a fully preloaded, single-use spherical AvanseePreset injector system (PN6 and PU6) in 2010. Aspheric 3P counterparts (AN6KA, AU6KA, AN6MA, PN6A, PU6A, PN6AS, and PU6AS) were launched in Japan and Europe in 2013 and 2014, respectively. A one-piece (1P) version of Avansee (Avansee Preload 1P), that can be inserted through a smaller 2.2 to 2.4mm incision is due to be launched in Japan in late 2016 and in Europe in early 2017.

Avansee provides a high quality optic with no evidence for deterioration over time

The optical purity of IOL optics can potentially deteriorate after implantation due to the formation of glistenings: fluid-filled, light-reflecting microvacuoles (MVs) 1 to 20µm in diameter that are formed by the absorption and subsequent condensation of water within the matrix of the optic material.⁷⁻¹⁰ If present, they are typically observed within a few months of surgery and appear as small bright spots across the optic. The impact of glistenings on visual function is controversial; whereas some studies report no effect,^{7,9;11-12} others report significant increases in light scatter and decreases in contrast sensitivity,¹³⁻¹⁶ modular transfer function,¹⁵ and/or visual acuity¹⁶⁻¹⁸ that can be corrected by IOL replacement.^{17;18} There is evidence to suggest that patients undergoing IOL implantation should be monitored throughout their lives in case glistenings and/or their clinical impact continue to worsen over time.^{11;16}

The formation of glistenings is influenced by a number of factors, including manufacturing technique, IOL packaging, postoperative inflammation, ocular diseases, ocular medications and the duration of use.^{11;19-21} Although glistenings have been reported for IOL optics manufactured from all materials (silicone, hydrophilic acrylic and hydrophobic acrylic), they are most frequently seen in dry-packaged hydrophobic IOLs.⁹ This is because the degree of glistening is determined by a state of equilibrium in water content within the IOL; whereas hydrophilic acrylic IOLs achieve equilibrium at 18% to 33% water content, the level is considerably lower (0.3% to 1.5%) for hydrophobic IOLs. Despite being hydrophobic, the change in water saturation following incubation over a range of temperatures in saline is considerably lower for Avansee than for other hydrophobic IOLs (MA60BM [Alcon, USA], SA60AT [Alcon, USA] and

VA60CA [HOYA Surgical Optics, Japan]).¹⁸ Indeed, the change for Avaneer is similar to that observed for some wet-packaged IOLs (e.g. X-60 [Santen Pharmaceuticals Ltd., Japan] and H60M [Storz Ophthalmics, USA]). This is because Avaneer optics are made from a stable, uniform and highly crosslinked polymer that prevents water molecules gathering in the microvacuoles of the material.¹

Differences in optical purity between hydrophobic IOLs have been demonstrated by a series of in vitro accelerated deterioration studies in which IOLs are incubated in saline at elevated temperatures before visualising under a microscope. The ‘real-time’ optical deterioration rate is usually determined using either the Arrhenius equation – an empirical equation based on the principle that chemical reactions proceed more slowly at low temperatures and vice versa – or a simplified version of the Arrhenius equation, known as the acceleration formula (Q10).²² One such study, in which four different hydrophobic acrylic IOLs were incubated in saline at 45 ± 1°C for 24 hours and then at 37 ± 1°C for a further 2.5 hours to allow glistenings to form, found that Avaneer AU6KA and enVista IOLs (n = 5 per IOL type) were almost free of glistenings, whereas AcrySof MA60AC and iSert PC-60AD IOLs showed a large number of glistenings.²³ Each of the IOLs included in this study were clear (not yellow tinted), with dioptric power +20.0 and an integrated UV inhibitor. The density of glistenings was determined by scanning the entire lens in order to identify the region of maximum glistening density. Pictures of

the worst-case location (usually the central region) were taken for analysis using a digital camera attached to a microscope (90x magnification) and the density of glistenings was calculated using i-Solution software (iMT Technology). According to the glistening scale described by Miyata et al.,²⁰ Avaneer and enVista could be classified as Grade 0 lenses (the highest grade [glistening-free]), while I-Sert and AcrySof IOLs were classed as Grade 3 (see Figure 2).

A major limitation of this study is that, despite evidence to suggest that MVs continue to develop over time,^{9,24-26} glistening density was determined at only one time point. To address this issue, Avaneer PU6A and AcrySof SA60AT IOLs (both with dioptric power +21.0D) were incubated in saline at 45 ± 1°C for 100 days, corresponding with 170 days of wear at 37°C according to the Q10-formula. Lenses were transferred to a 37 ± 1°C water bath for 2.5 hours and each IOL was analysed under a microscope and photographed using a digital camera (data on file). The number of glistenings was determined using image processing software. After analysis, each of the IOLs was immediately placed back in the oven and the accelerated deterioration test was continued with regular IOL analysis for 100 days. No glistenings were observed in the Avaneer IOLs at any point during the study. In contrast, severe glistening was observed in the AcrySof IOLs. MVs began to appear after five to 24 hours and their number increased for up to 60 days, after which the optic area appeared saturated and a plateau was observed.

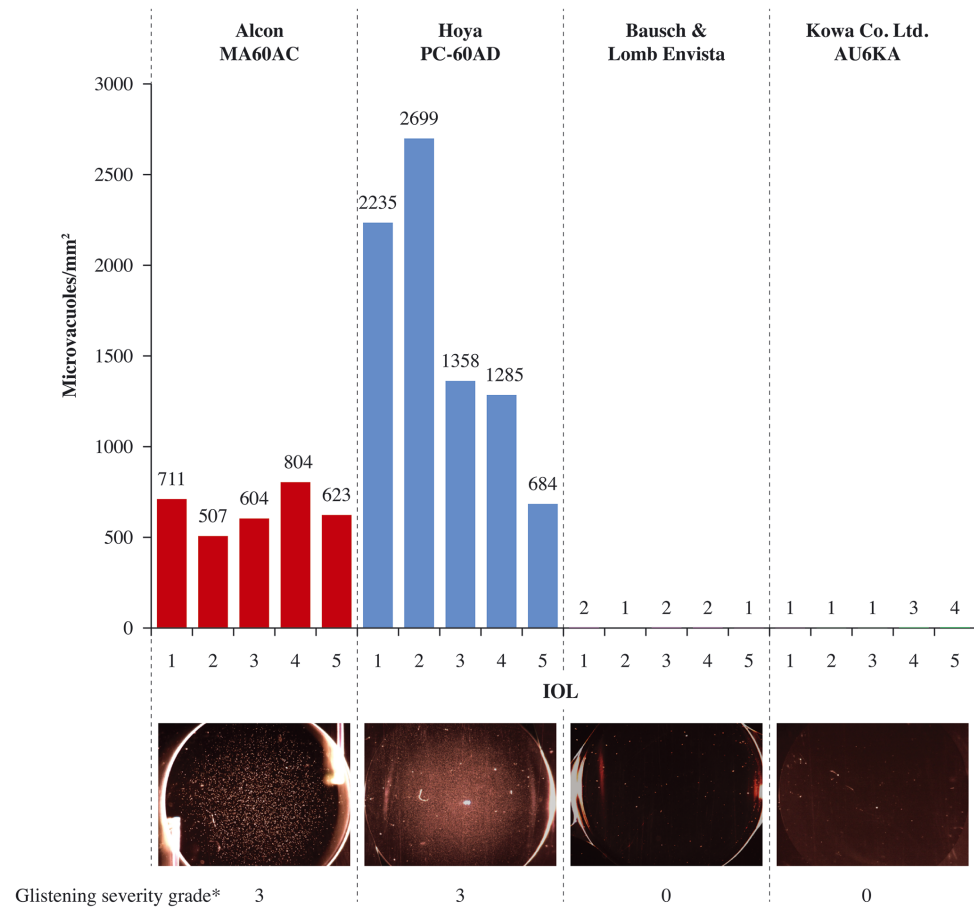


Figure 2: Density and distribution of microvacuoles in four hydrophobic IOLs.²³ *Based on the glistening scale described by Miyata et al²⁰

Although in vitro studies are considered useful tools for investigating IOL deterioration,⁹ it is not clear whether the mechanisms underlying glistening formation in vitro replicate those in vivo, or whether the characteristics of MVs are the same.²¹ A correlation between in vitro and in vivo tests has been demonstrated by an in vivo study in rabbits in which three different types of hydrophobic IOL were removed from phacoemulsified eyes six months after implantation.²⁷ In this study, significant glistenings were observed in AcrySof and AF-1 lenses,

but not in Avanssee lenses. Similarly, a four-year observational study carried out in 78 adults (130 eyes) found that both AcrySof and AF-1 IOLs were associated with glistenings in the majority of patients, whereas no glistenings were observed for Avanssee.¹ Since its launch in 2007, no significant glistenings have been reported for Avanssee¹ and Avanssee is considered to be 'glistening free'. The clinical importance of this observation will become clearer as patients undergoing cataract surgery live longer and the duration of IOL use increases.

AvansseePreset provides reliable, controlled IOL insertion with minimal damage to the optic

Although safer and more reliable than non-preloaded or partially pre-loaded injector systems, fully preloaded IOL injectors are not completely risk-free, especially if the injectors are poorly designed for the lens. Some injectors are associated with marked pushing resistance during IOL delivery, which has the potential to cause IOL damage (e.g. haptic breakage and scratches, stress fractures, cracks and/or tear lines in the optic), injection-system damage (e.g. cartridge cracking), and/or sudden IOL release leading to damaged intraocular tissues.^{28,29} The force required to expel an IOL from a cartridge partly depends on the degree of friction between the cartridge and the IOL. To facilitate gliding and reduce thrust force, the inside of some injectors (including AvansseePreset) are lubricated.¹ However, thrust force may also depend on the flexibility of the lens, the quality of lens folding, and on the ratio between the diameter of the injector tip and the folded IOL.

To compare thrust forces for different hydrophobic IOL injector systems, five different IOLs (n = 5 or 6 per IOL),

all with dioptr +25.0, were loaded into their respective manufacturer-recommended injector systems and inserted into the capsular bag of phacoemulsified porcine eyes.²⁹ Trust force was measured using an automated gauge system and resistance curves were found to be significantly lower and more consistent for KS-Xs (STAAR Surgical Co., USA), SN60WF with Royal injector (metal plunger) (Alcon), and AvansseePreset PN6 (Kowa Co. Ltd.) than for SN6CWS (Alcon) and NX-60/MXJ-60 (Santen Inc., Japan) IOLs (see Figure 3). The results suggests that some hydrophobic injector systems, including AvansseePreset, provide smoother, more controlled IOL expulsion with lower hand stress than others. The low correlation between thrust force and injector tip dimension in this study suggests that depressive forces are primarily associated with IOL features, such as flexibility, optic thickness, and haptic design, rather than the ratio between the diameter of the injector tip and the folded IOL. Consistent with this observation, Avanssee has a relatively high water content compared with other hydrophobic IOLs, suggesting good flexibility.¹

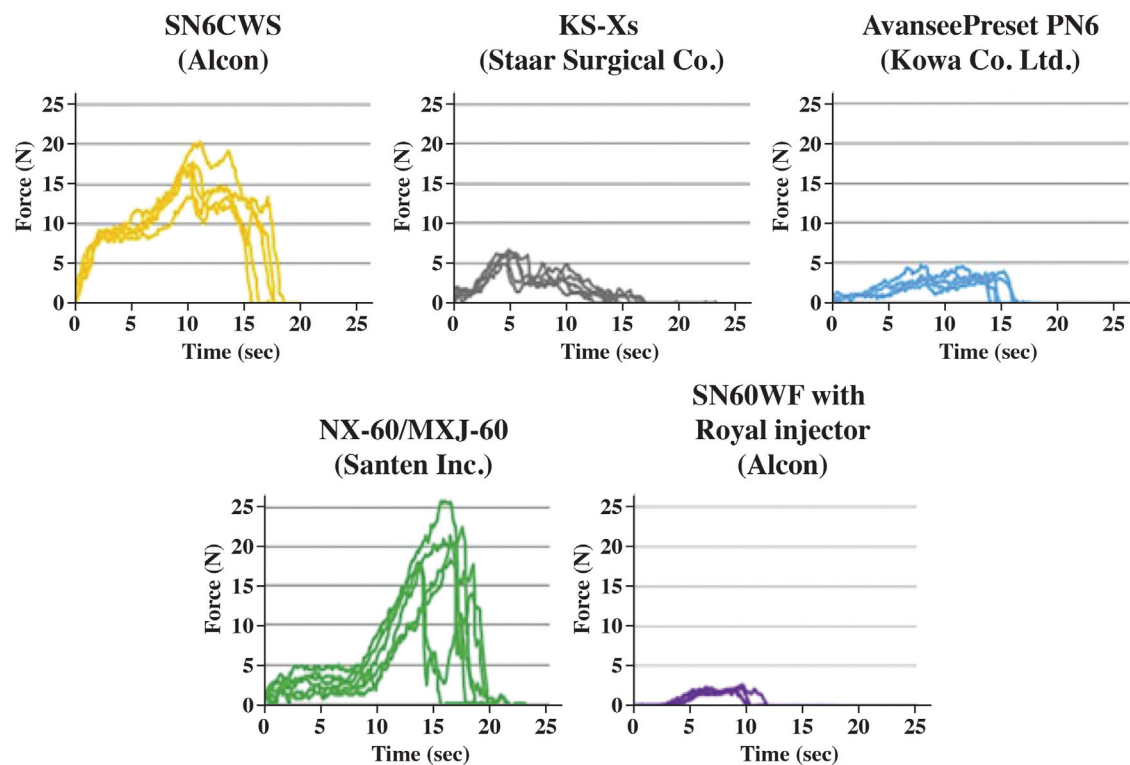


Figure 3: Trust forces required to eject four different hydrophobic IOLs from their manufacturer-recommended injector into the capsular bag of phacoemulsified porcine eyes.²⁹ Thrust force was measured using an automated gauge system

Avansee 3P, inserted using the AvanseePreset injector system, is associated with good capsular bag stability (Miyake-Apple view)

Miyake-Apple views comparing the stability of five different IOLs in a cadaver eye model show that Avansee does not cause zonular stress or transformation of the capsular bag and that, whereas some IOLs (e.g. AF-1 FY-60AD [HOYA Surgical Optics, Japan] and TECNIS [Abbott Medical Optics, USA]) have hard haptics that grow into the capsular bag, Avansee has soft haptics that are unlikely to damage the eye (see Figure 4).¹ Compared to other lenses, the angle of contact between Avansee's haptic and the lens capsule is relatively large (75.8° vs. 59.6° for AcrySof IQ [Alcon, USA], 64.6° for TECNIS [Abbott Medical Optics, USA], 81.1° for AF-1 FY-60AD [HOYA Surgical Optics, Japan] and 97.47° for Eternity X-70 [Santen Pharmaceutical

Co. Ltd., Japan]), suggesting good stability. Video analysis of AvanseePreset PU6A insertion into an eye model using Miyake-Apple view attached to a high-speed camera found controlled capsular bag implantation with simple uncomplicated IOL unfolding, smooth haptic opening, no stickiness between the optic and the haptic, and only a minor interaction between the haptics and the capsular bag (see Figure 5). The large arc of contact between the loop and the lens capsule observed in a previous study¹ was confirmed. Together, these results suggest that AvanseePreset is easy and reliable to use, provides more stable IOL insertion than some other IOLs, and may therefore be associated with a low risk of misalignment.

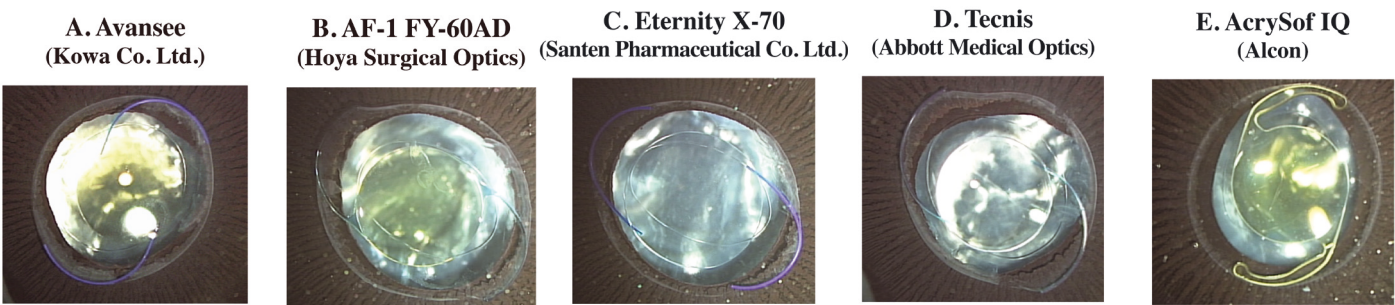


Figure 4: Miyake-Apple views showing the stability of five different IOLs in the capsular bag.¹ A - Avansee does not cause zonular stress or transformation of the capsular bag and the soft haptics are unlikely to damage the eye; B - With AF-1 FY-60AD, the hard haptics have grown into the capsular bag; C - With Eternity X-70, the IOL has caused transformation of the capsular bag; D - With TECNIS, the hard haptics have grown into the capsular bag; E - With AcrySof IQ, the shape of the capsular bag is good but the contact area between the IOL and the capsular bag is small

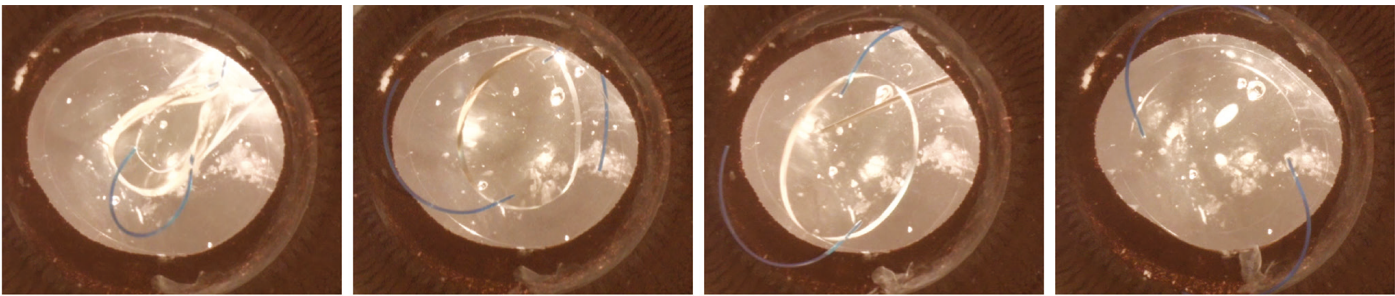


Figure 5: Sequence of events observed using video analysis of AvanseePreset PU6A insertion into a cadaver eye model using Miyake-Apple view attached to a high-speed camera

AvanseePreset is quick and easy to use in clinical practice

A retrospective, multicentre, non-randomised, uncontrolled study designed to assess the 'ease-of-use' and reliability of AvanseePresetUV (PU6A) in clinical practice was carried out at four study centres in Germany (15 patients and one surgeon per site - data on file). In all reported cases (60 implantations), surgeons felt that AvanseePreset allowed for simple two-step preparation prior to implantation (see Figure 6). Users either agreed or strongly agreed that it improved the reliability of implantation, and 98% felt that the system was reproducible. AvanseePreset appeared to reduce procedure time in approximately 75% of the cases and 85% of surgeons felt the system reduced the risk of haptic breakage. A major concern raised during the study is that the leading haptic of the lens unfolds towards the cornea which may damage the endothelial cells of the cornea. To compensate for this, surgeons may be tempted to rotate the injector during implantation, which may lead to the failure of lens implantation. However, Avansee's stable but soft haptic allows surgeons to insert and keep the injector nozzle directly towards the capsular bag during lens implantation without damaging the capsular bag with the haptic. This ensures that a

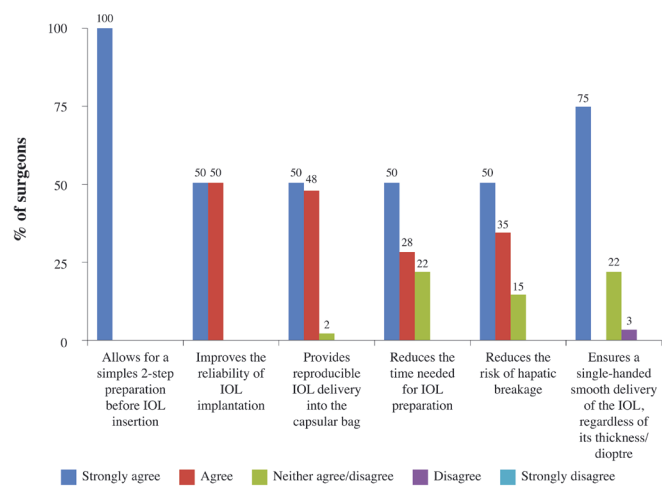


Figure 6: Results from a retrospective, multicentre, non-randomised, uncontrolled study designed to assess the 'ease-of-use' and reliability of AvanseePresetUV (PU6A) in clinical practice. The study was carried out at four study centres in Germany (15 patients and one surgeon per site)

certain distance is maintained between the leading haptic and corneal endothelial cells without rotating the injector. Together, results from this study suggest that AvanseePreset is quick and easy to use in clinical practice, as long as the system is used properly.

Conclusions

The development of injectors that insert a folded IOL into the eye through a small incision has revolutionised cataract surgery. A number of IOLs and IOL injector systems are currently available, some of which are more reliable and easy to use than others. One factor that determines the effectiveness of the preloaded injector system is whether the design of the injector has been determined by the material and design of the lens, as is the case for AvanseePreset. Studies in phacoemulsified porcine cadaver eyes show that the thrust force required to eject an Avansee IOL from its injector is consistent and low, allowing reliable, controlled IOL insertion with minimal damage to the optic.^{1,29} Miyake-Apple views comparing the stability of various IOLs in an eye model show that AvanseePreset PU6A insertion provides controlled capsular bag implantation with simple uncomplicated IOL unfolding, smooth haptic opening, no stickiness between the optic and the haptic, and only a minor interaction between the haptics and the capsular bag (data on file). Unlike some IOLs, Avansee does not cause zonular stress or transformation of the capsular bag, its soft haptics are unlikely to damage the eye,¹ and the large angle of contact between Avansee's haptic and the lens capsule suggests good IOL stability within the eye.¹ According to a survey assessing the 'ease-of-use' and reliability of AvanseePresetUV

(PU6A) in clinical practice, surgeons agreed that AvanseePreset allowed for simple two-step preparation prior to implantation and that it improved the reliability of implantation. The vast majority (98%) of surgeons also felt the system was reproducible. AvanseePreset appeared to reduce procedure time in approximately 75% of the cases, and 85% of surgeons felt the system reduced the risk of haptic breakage (data on file). Although the ease of use and reliability of the injector system is essential for safe, accurate lens delivery, the quality of the lens is also important for the long-term success of the procedure. Whereas the optical purity of some IOLs deteriorate over time due to the formation of glistenings, Avansee provides a high quality, 'glistening-free' optic with no evidence for deterioration over time.^{1,7,23,27} Current evidence suggests that glistenings may have an adverse effect on visual performance and contrast sensitivity and may continue to develop/worsen over time. Consequently, the clinical importance of glistening-free lenses, such as Avansee, is likely to become clearer as the population ages and the duration of IOL wear per patient increases. Overall, results suggest that AvanseePreset is quick, easy and reliable to use, provides more stable IOL insertion than some other IOLs, and that the purity of the Avansee optic is unlikely to deteriorate over time.

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