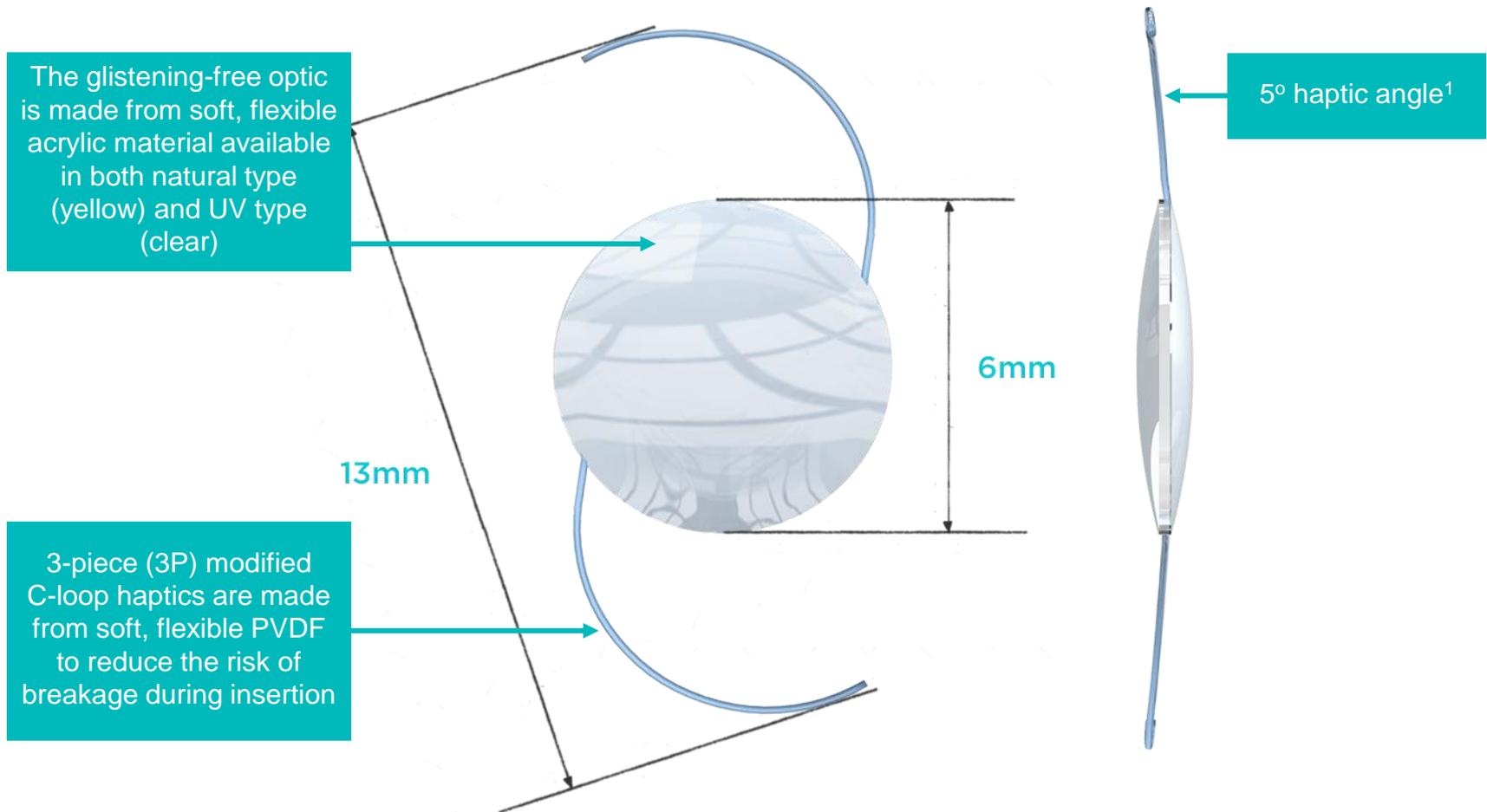




AvanseePreset

Technical deck

Avansee is a foldable posterior chamber aspheric hydrophobic monofocal intraocular lens (IOL)



1. Data on file.
Avansee™Preset package insert.

Avansee technical specification: General

Model	PN6AS and PN6A (natural type), PU6AS and PU6A (UV type)
Recommended incision size	PN6AS and PU6AS: 2.4 mm PN6A and PU6A: 2.75 mm
Overall length	13mm
A-constant* (ultrasound)	118.7
A-constant* (optical)	119.0 (SRK/T) 119.3 (SRKII)
Predicted anterior chamber depth	5.3mm

*The A-constant is presented as a starting point (reference value) for the lens power calculation. When calculating the exact lens power, it is recommended that calculations should be performed individually, based on the equipment used and the operating surgeon's own experience.

Avansee™Preset package insert.

Avansee technical specification: Optic

Material	Hydrophobic soft acrylic (UV-absorbing acrylic resin; natural type also contains proprietary blue-light filtering)
Design	Aspheric, asphericity: $-0.04\mu\text{m}$
Colour	Natural (PN6AS and PN6A), Clear (PU6AS and PU6A)
Length	6mm
UV cut off at 10% T	405nm (+20.0 dioptre lens)
Refractive index	1.519 (35°C)
Configuration	Biconvex
Power range	+6.0 through +26.0 dioptre: +6.0 to +10.0 dioptre (1.0D increments) +10.0 to +26.0 dioptre (0.5D increments)

Avansee technical specification: Haptic

Material¹	Polyvinylidene fluoride (PVDF)
Colour¹	Blue
Configuration¹	Modified C-loop
Angle²	5°

1. AvanseePreset package insert.
2. Data on file.

Avansee effectively corrects visual acuity in the majority of aphakic eyes

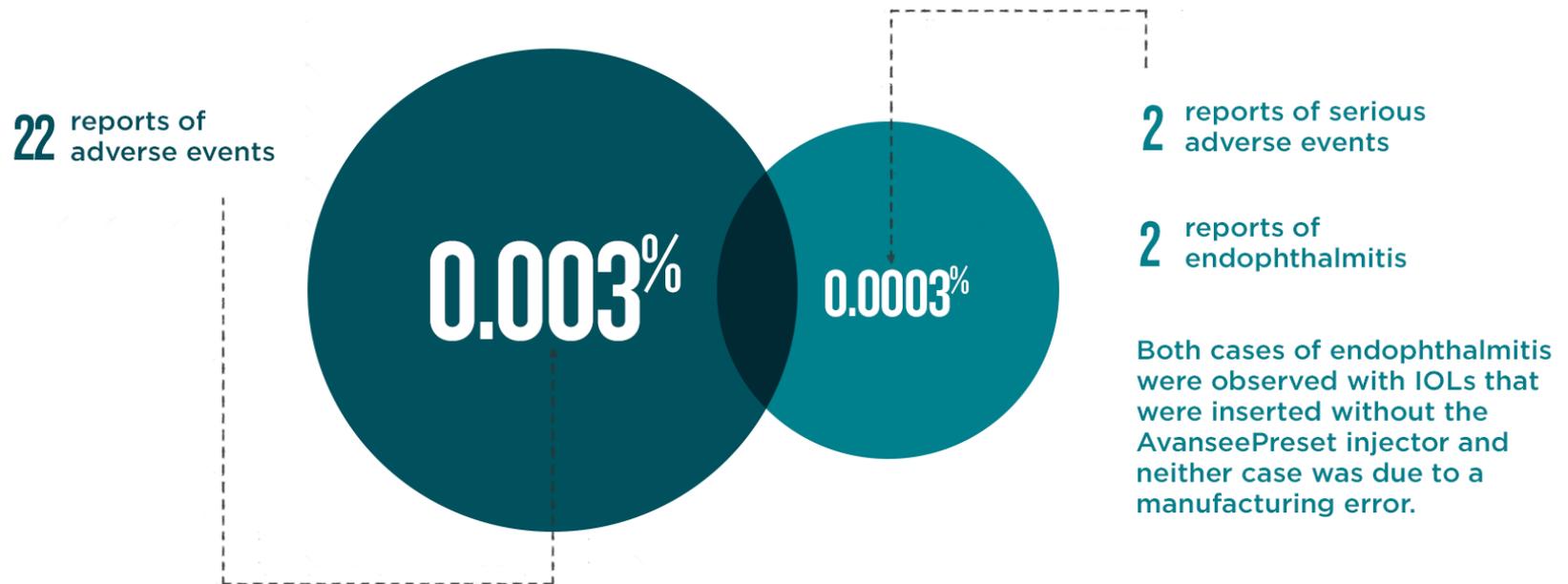
Study details	Study duration	CVA 0.7+ (% of eyes)	CVA 1.0+ (% of eyes)
70 patients* aged 42+ years undergoing surgery for senile cataract ^{1,2}	1 month	94	82
	1 year	96	85
71 eyes aged 40+ years undergoing surgery for uncomplicated senile cataract ^{2,3}	1 month	92.9	70.4
	1 year	92.5	69.8

*100 eyes

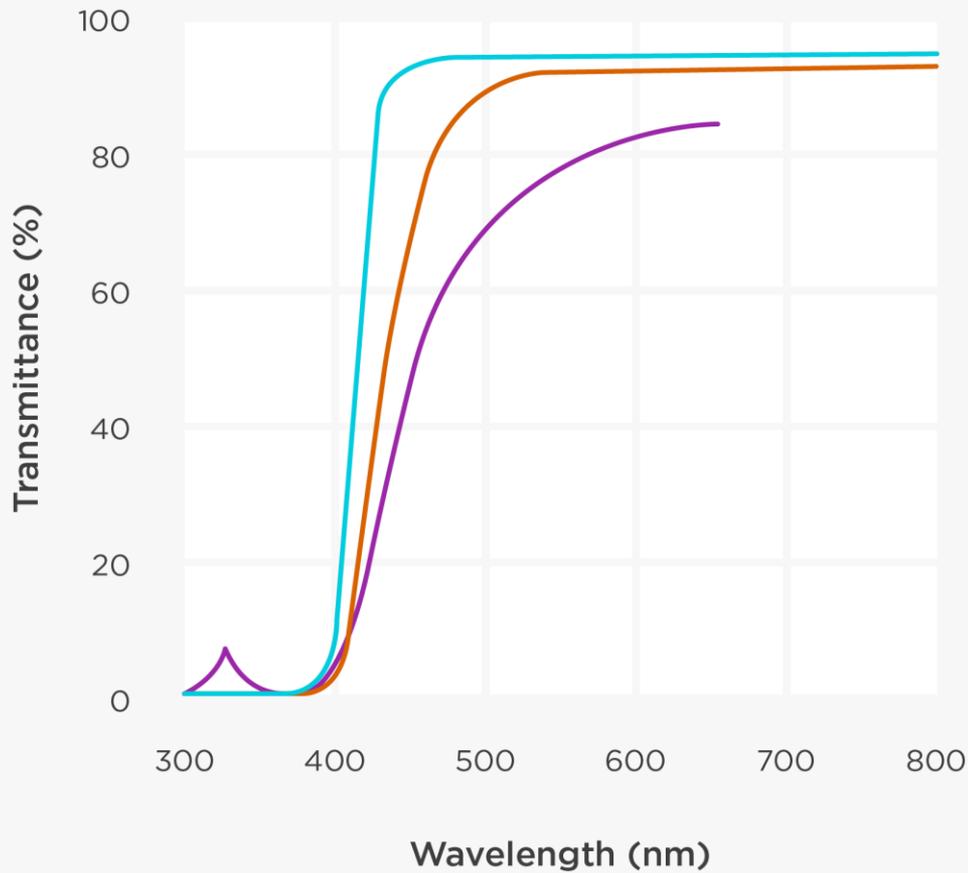
1. Data provided by K Miyake.
2. Miyake K, *et al. EuroTimes Suppl.* Sept. 2014.
3. Adapted from Kurosaka D, *et al. IOL&RS* 2005;19:331-338.

The number of adverse effects reported for Avanse is low

Over 600,000 Avanse lenses have been sold since its launch in 2007.



Spectral transmittance closely replicates that of a phakic eye of a 53-year-old patient



PU6AS, PU6A = UV-type (untinted)¹

PN6AS, PN6A = Natural-type (yellow-tinted)¹

- PU6AS, PU6A +20.0 D
- PN6AS, PN6A +20.0 D
- Crystalline²

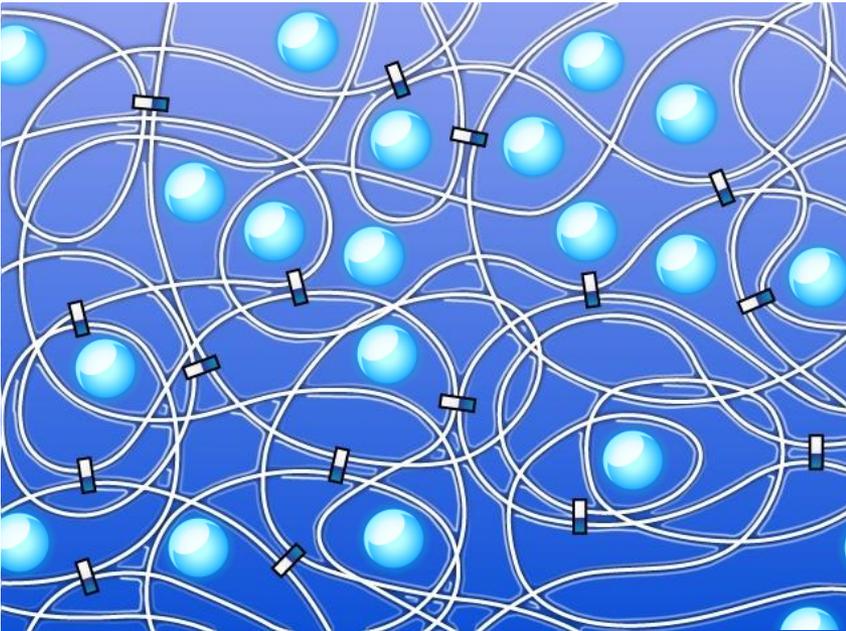
1. Avanse™ Preset package insert.

2. Boettner EA and Wolter JR. *Invest Ophthalmol* 1962; 1(6): 776-783.

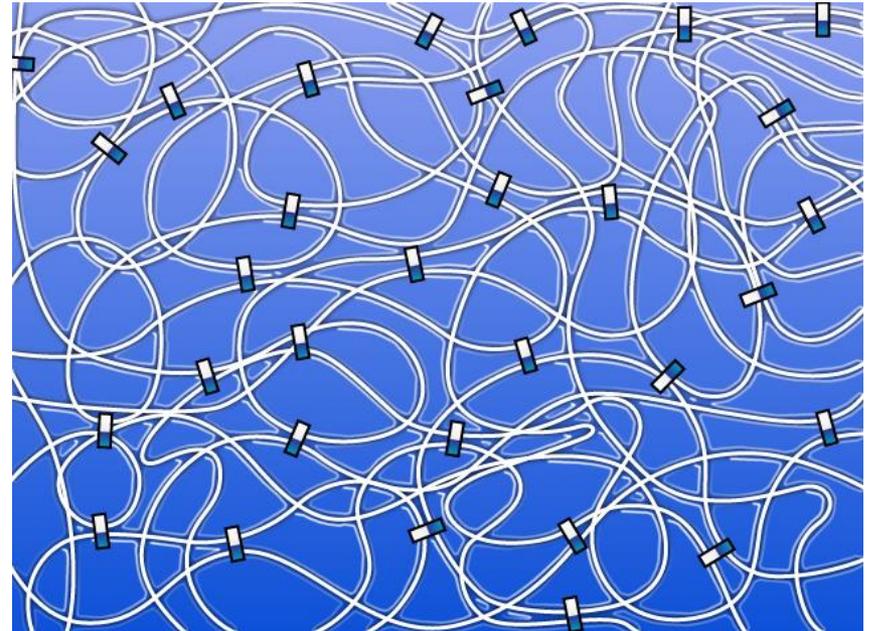
Avansee optics are made using a stringently-controlled cast-moulded method

Avansee's cast-moulded optics are made from a stable, uniform and highly cross-linked polymer, which prevents water molecules gathering in the microvoids of the material, thereby reducing the risk of glistenings.

Past cast-mould method



Current cast-mould method

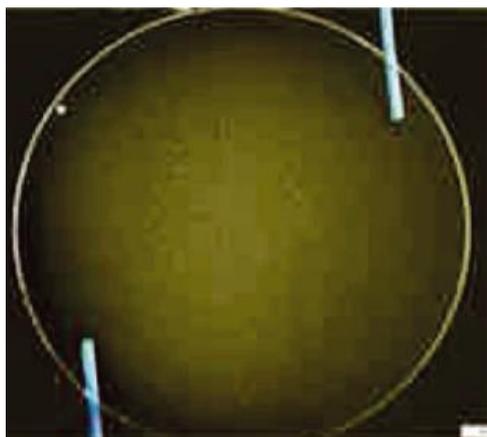


 Accumulated water molecules

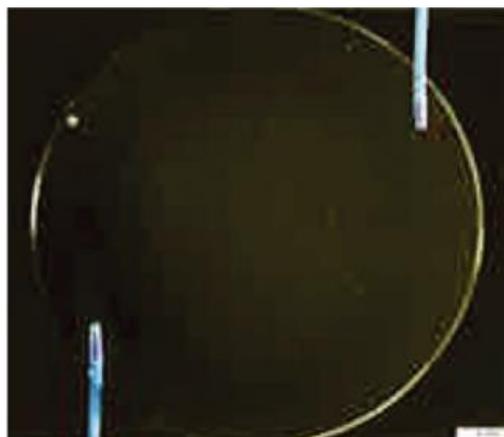
 Bridge molecule

The risk of glistenings is inversely proportional to the density of cross-linkages in the optic polymer

Density of cross-linkages in the optic polymer:



$\frac{1}{4}$



$\frac{1}{2}$

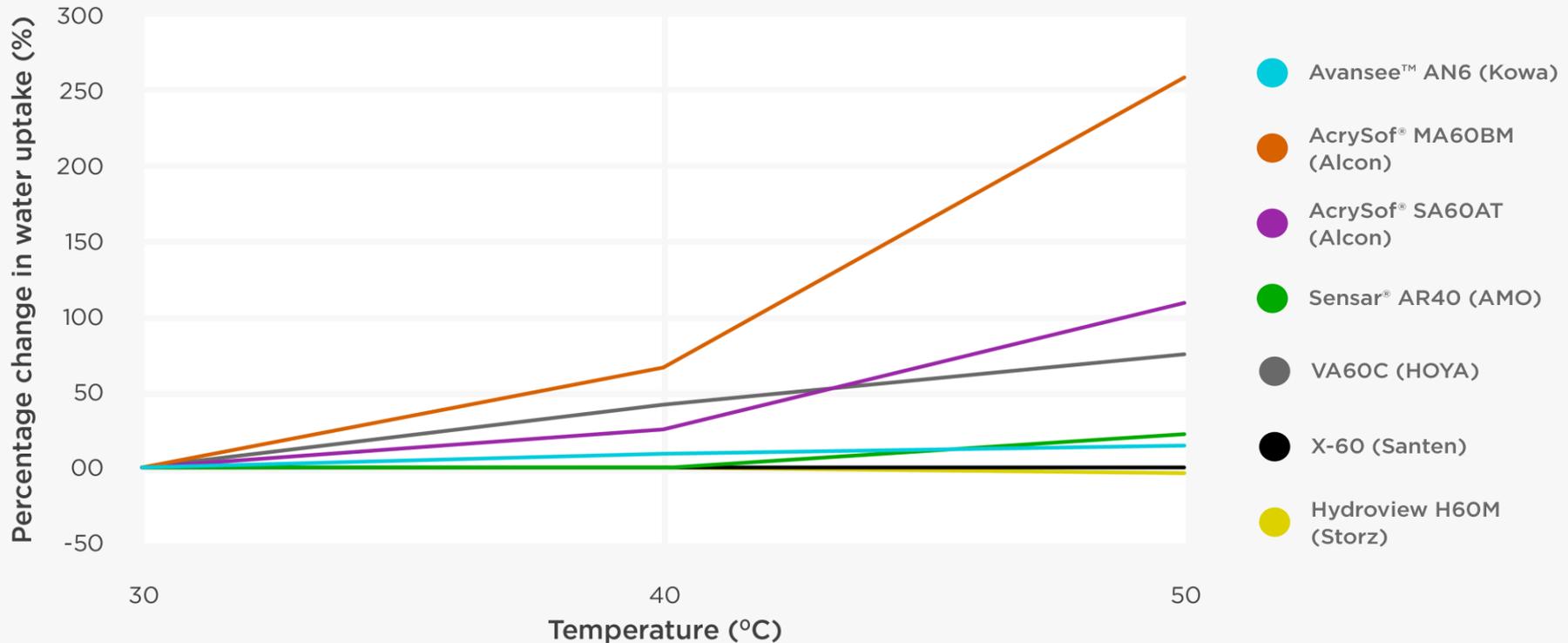


1 (e.g. Avanse)

- IOLs were incubated in a 35°C water bath for 24h and then at 25°C
- IOLs with a high density of cross-linkages in the optic polymer (e.g. Avanse) were not associated with glistenings

Avansee optics demonstrate a significantly lower, more stable change in water uptake than other dry-packaged IOLs

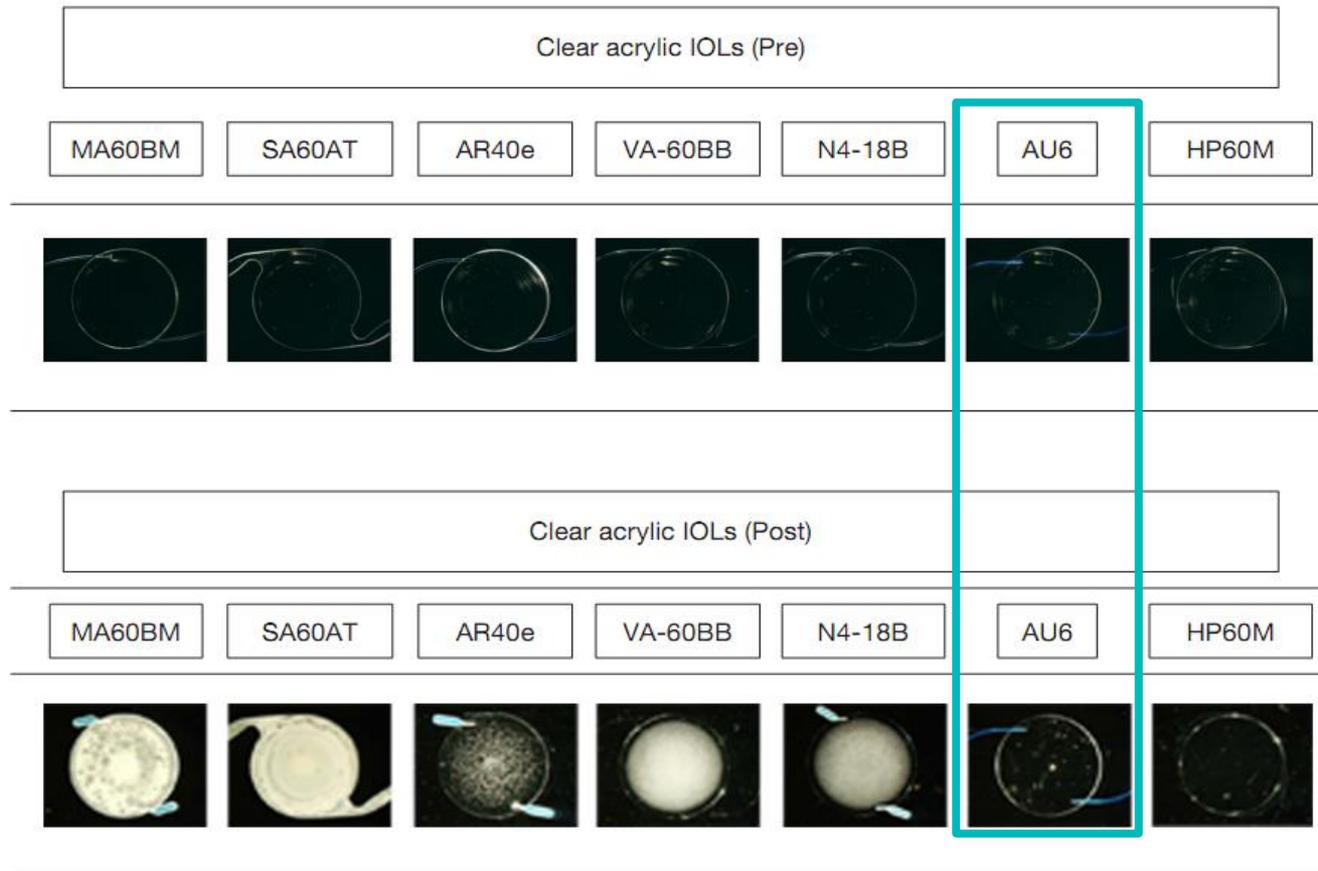
Change in water uptake at different temperatures^{1,2}



1. Miyata A. In Ooshika T, *et al.* Ganka Sinryo Kuorifai 20 Ed. Nakayama Shoten Co., Ltd. 1-25-14 Hakusan, Bunkyo-Ku, Tokyo To, Japan 113-8666;2014:367-370.
2. Miyake K, *et al.* EuroTimes Suppl. Sept. 2014.

Unlike other hydrophobic acrylic IOLs, Avanse does not show glistening-like opacity *in vitro*¹

IOLs underwent severe accelerated deterioration tests simulating 20 years of wear.²



1. Kawai K, et al. *J Exp Clin Med.* 2012;37:62–65.

2. Thomes BE, Callaghan TA. *Clin Ophthalmol.* 2013;7:1529-34.

Avansee has a high level of optical purity *in vitro*¹

IOLs underwent severe accelerated deterioration tests²

	Optical purity	Microvacuoles/ Mm ²	Glistening severity grade*
Alcon MA60AC		251	3
Hoya PC-60AD		883	3
Bausch & Lomb Envista		15	0
Avansee AU6KA		21	0

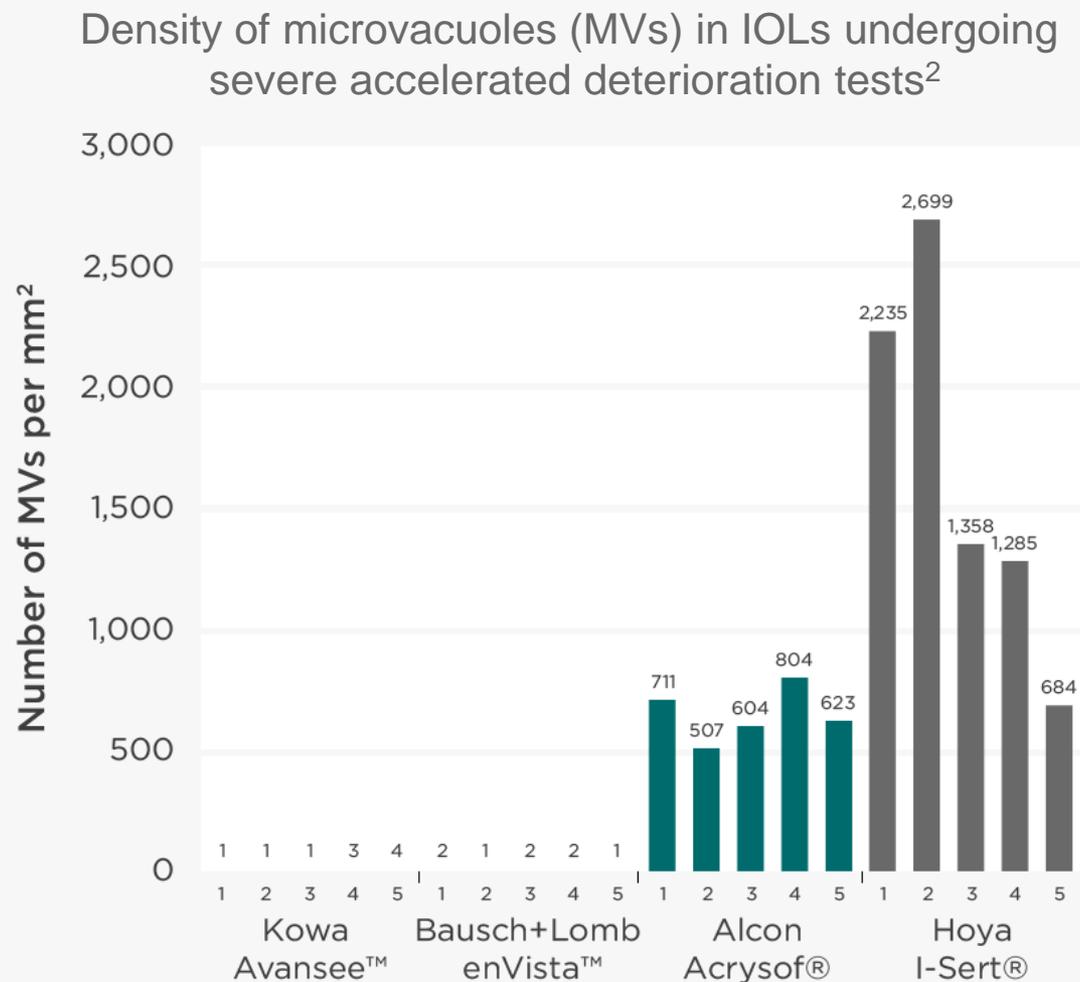
*Graded 0 to 3 using the method described by Miyate *et al.*³

1. Auffarth GU, *et al.* Data presented at DGII; February 2015, Karlsruhe, Germany.

2. Thomes BE, CaMiyata A, *et al. Jpn J Ophthalmol.* 2001;45(6):564–9.

3. Ilaghan TA. *Clin Ophthalmol.* 2013;7:1529-34

Avansee is glistening free *in vitro*¹



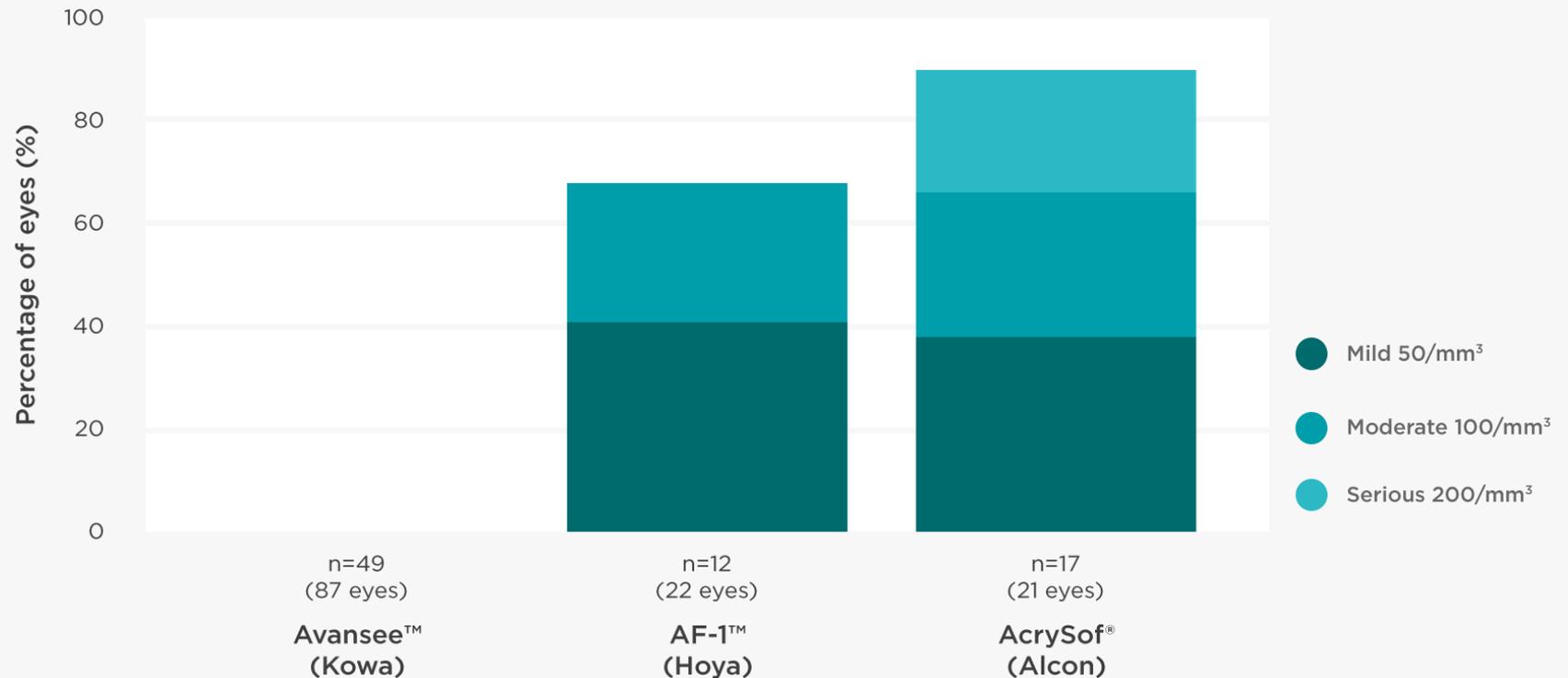
IOL	Glistening severity code*
Avansee AU6KA	0
Bausch+Lomb enVista	0
Alcon AcrySof	3
Hoya I-sert	3

*Graded 0 to 3 using the method described by Miyate *et al.*³

1. Auffarth GU, *et al.* Data presented at DGII; February 2015, Karlsruhe, Germany.
2. Thomes BE, CaMiyata A, *et al.* *Jpn J Ophthalmol.* 2001;45(6):564–9.
3. Ilaghan TA. *Clin Ophthalmol.* 2013;7:1529-34

Avansee is glistening-free *in vivo*

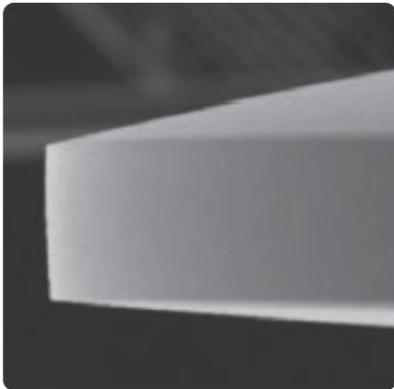
Glistening reported for 3 different IOLs in a 4-year observational study



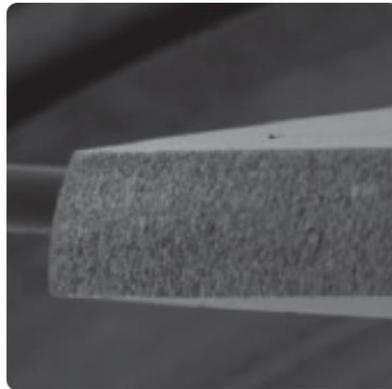
Avansee is carved without grinding to provide a squarer edge than other IOLs¹

Compared to round-edged IOLs, those with a square edge to their posterior surface are more likely to induce a sharp bend in the capsular bag, thereby preventing lens epithelial cell migration and posterior capsule opacification (PCO) formation.²

Moulded process



Avansee™ AN6K
(Kowa)

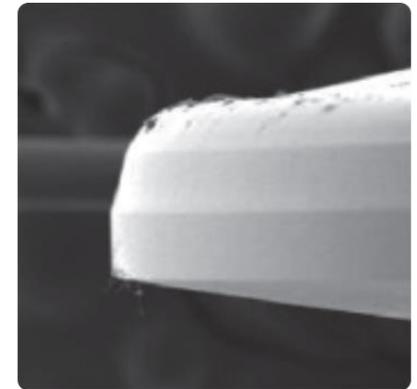


AcrySof® MA60AC
(Alcon)

Lathe-cut process



Acryfold UY60BBR
(Hoya)



Sensar® AR40e
(AMO)

Scale x100

1. Miyake K, et al. *EuroTimes Suppl.* Sept. 2014.
2. Morgan-Warren PJ, Smith JA. *Clin Ophthalmol.* 2013;7:1661-1667.

Avansee is associated with a low PCO rate

Retrospective study in 4,862 eyes.

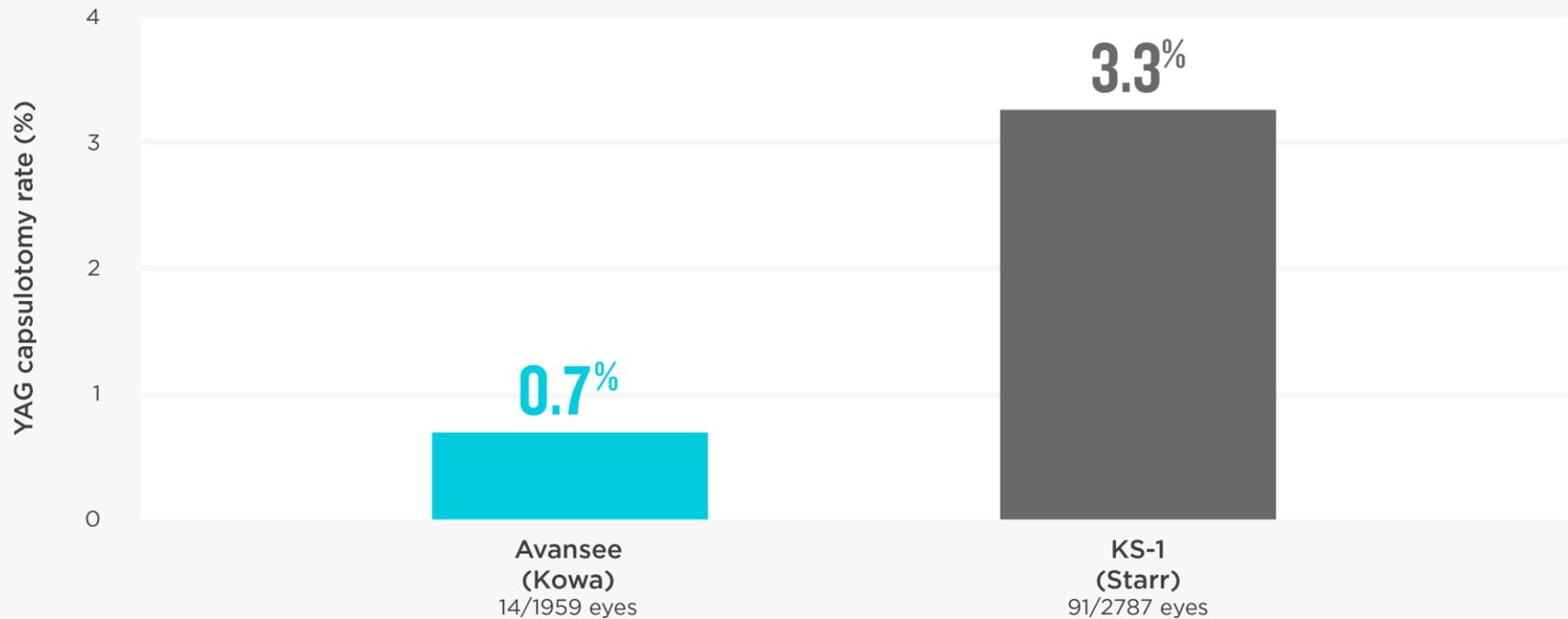
Company	Model	Number of PCO cases	Number of cases requiring Nd:YAG
Kowa	Avansee AN6, AN6K, AN6M, AN6MK	2,206	38 (1.7%)*
Alcon	Acrysof® SA60AT, SN60AT, SN60WF	1,604	39 (2.5%)*
Hoya	YA-60BBR	1,052	76 (7.2%)

Nd:YAG, neodymium-doped yttrium aluminium garnet; PCO, posterior capsule opacification

p<0.0001 vs. Hoya.

Avansee is associated with a low rate of YAG capsulotomy in clinical practice

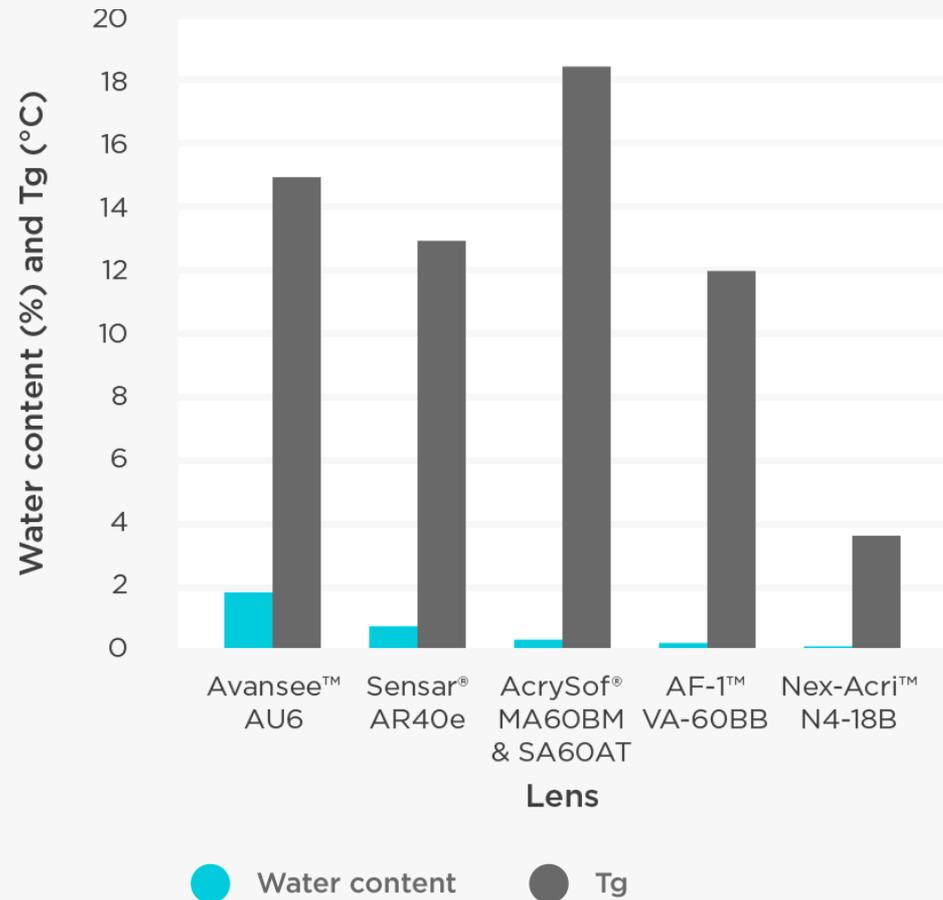
January-June 2011, within 2 years after operation.



Avansee is likely to be at least as flexible as other dry-packaged IOLs

IOLs with a high water content and a low glass transition temperature (Tg) are generally more flexible than other IOLs, meaning they are:

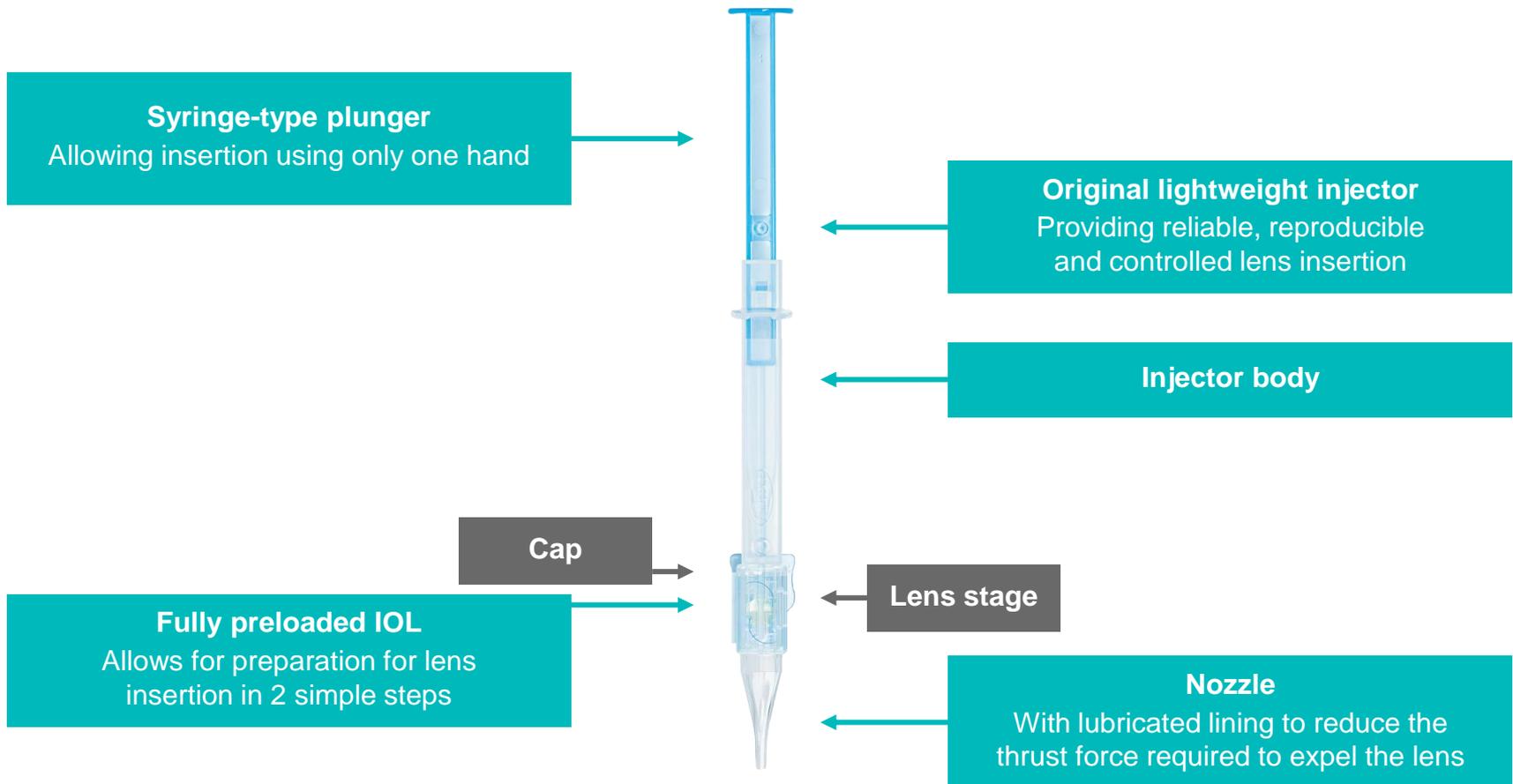
- Less likely to be damaged during folding and insertion
- More likely to quickly and fully regain their shape



Avansee™ Preset is a fully preloaded, single-use injector system

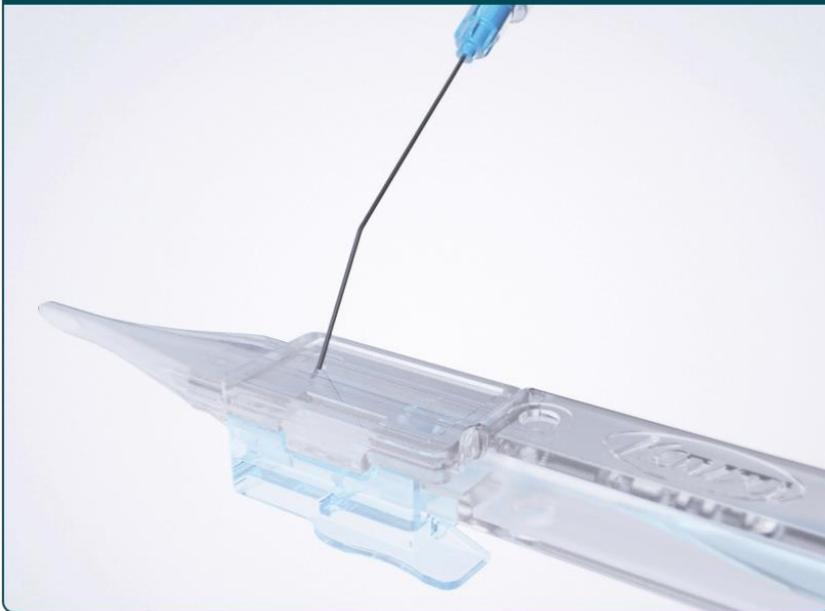
AvanseePreset

Offering optimal visual acuity with minimal post-operative complications.

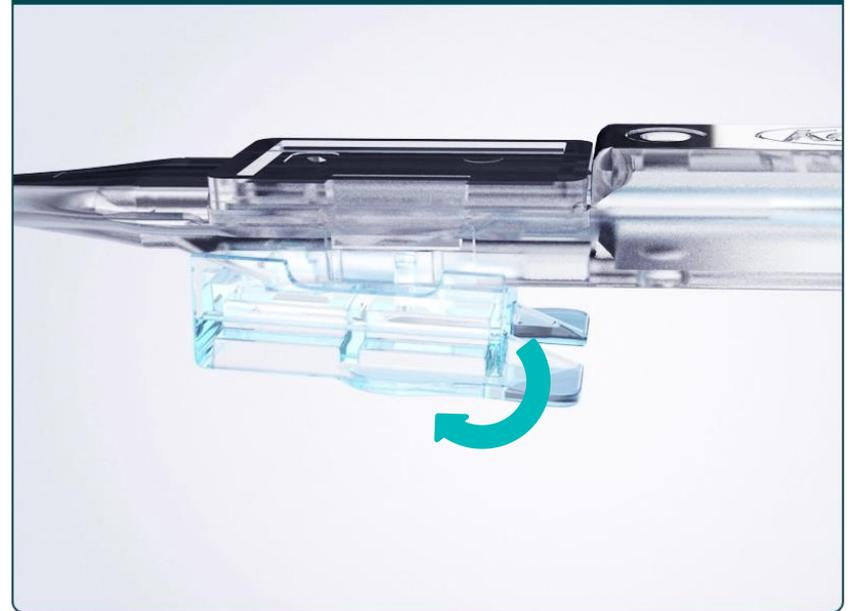


Avansee™Preset allows preparation for IOL insertion in 2 simple steps

1. Inject the ophthalmic viscosurgical device (OVD)



2. Remove the lens stage



The temperature of the device and the OVD should be kept between 21°C and 25°C during use.

Avansee™ Preset: Recommended ophthalmic viscoelastic devices (OVDs)

- Most OVD's are suitable for use with AvanseePreset, however the following are not recommended:
 - High viscosity OVDs, such as Healon 5 (the IOL may get stuck in the nozzle)
 - Dispersive OVDs that include chondroitin sulphate, such as Viscoat and DisCoVisc (these may not cover the lens properly or may cause the lens to rotate in the nozzle)
 - Hydroxypropyl methylcellulose, due to a lack of experience with this OVD
- At least 0.15ml OVD should be used when inserting Avansee using AvanseePreset
- Insufficient OVD may result in damage to the lens

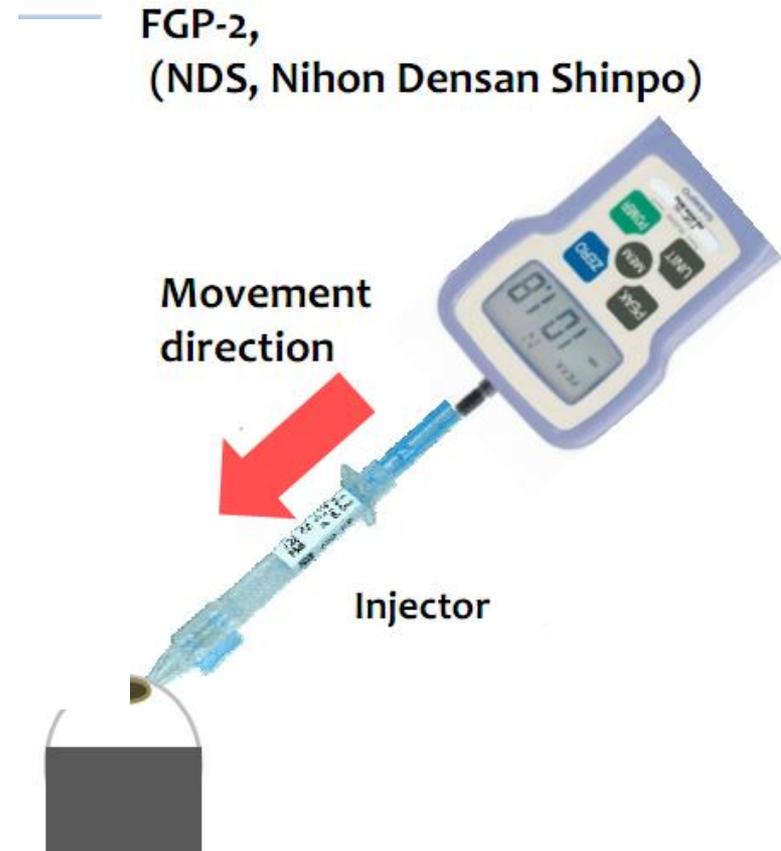
Avansee™ Preset allows smooth and controlled IOL delivery

- A major challenge for injectors is the gliding ability of the cartridge
- Friction between the polypropylene cartridge and the IOL can increase the thrust force required to expel a lens from its injector
- Excessive pressure may cause the IOL to stick to the cartridge wall resulting in lens damage or crimping, haptic breakage, and/or cartridge damage
- To avoid this, the inside of some injectors (including AvanseePreset) are lubricated to facilitate gliding and reduce thrust force
- Forces vary within each IOL class according to the IOL and injector characteristics

Methods

Surgery	0.5 ml of OVD was injected after phacoemulsification of porcine eyes and IOLs were inserted through a 3mm corneal incision
System	FGP-2 (digital force gauge; NDS)
OVD	1% OVD, KOWA Co. Ltd., Japan
Conditions	23.3°C; 52.4% humidity
Samples	IOLs (n= 5/6; +25.0D) were tested per injector

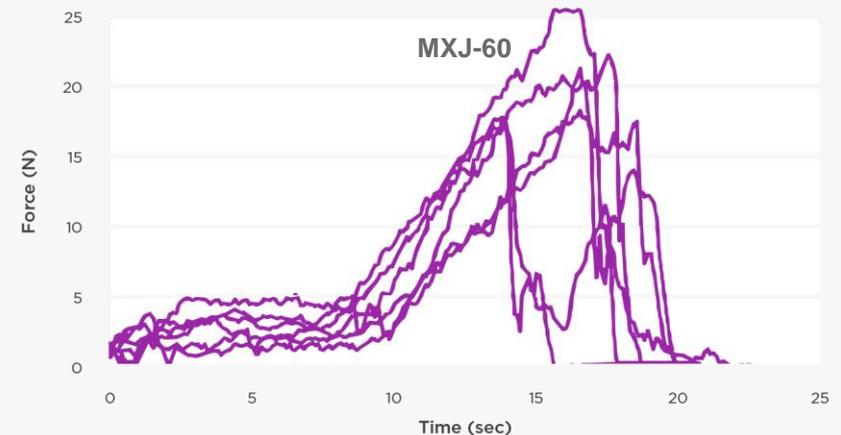
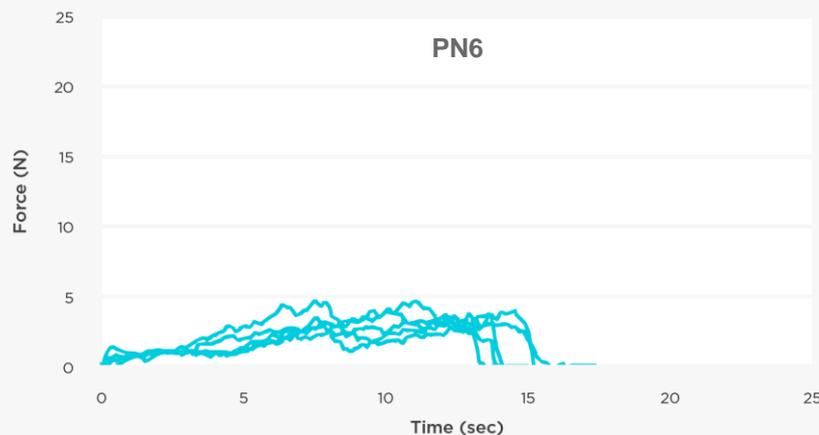
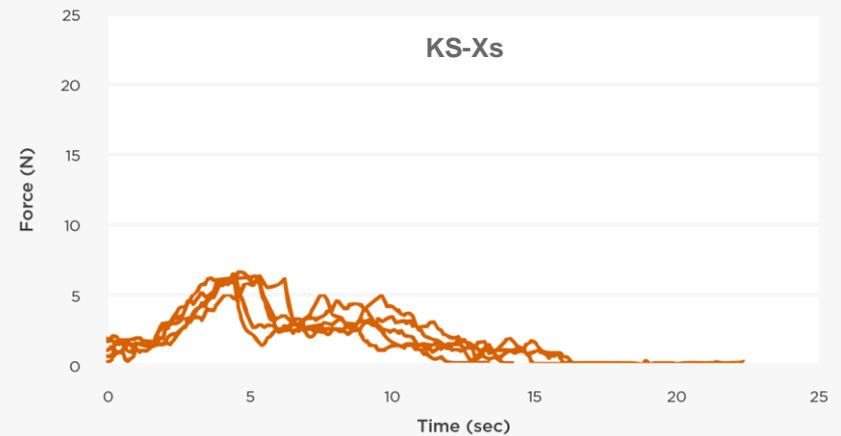
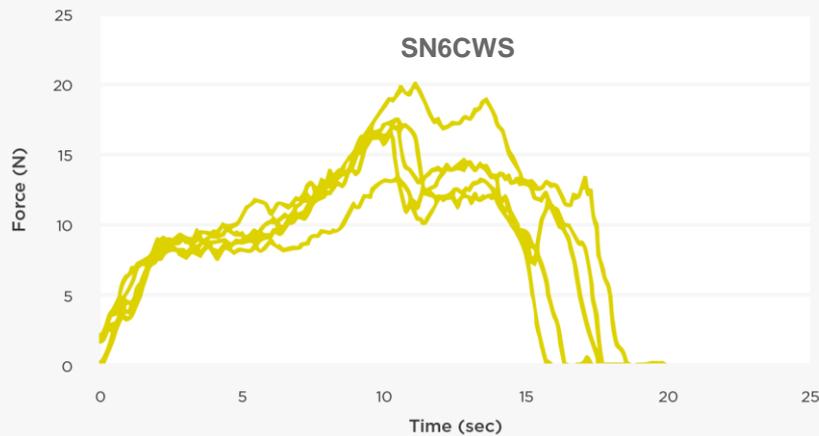
OVD, ophthalmic viscoelastic device



EYE fixation system (Neitz Co.)

The design of the lens together with a lubricated injector facilitates a consistent and low thrust force for Avanse

Compared to other IOL injectors, the thrust force required to expel Avanse into phacoemulsified porcine eyes is consistent and low.



Avansee™Preset provides smooth and controlled IOL insertion



Approximately 0.2 million units of AvanseePreset were supplied to surgeons in Japan between 2010 (when AvanseePreset was first launched) and March 2014, with only 122 complaints about movement abnormalities.*

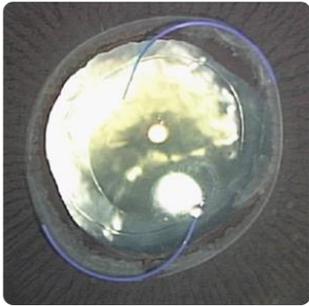
- Minimises IOL damage or deformation during insertion
- Facilitates accurate and stable IOL insertion within the capsular bag
- Reduces the risk of complications during surgery
- Reduces the risk of infection
- Increases the speed and reliability of surgery

*Trauma to the optic or haptic, incorrect optic or haptic movement, trapped lens in the nozzle, abnormal resistance force during injection and failure of lens implantation.
AvanseePreset package insert

Avansee is associated with a low risk of misalignment

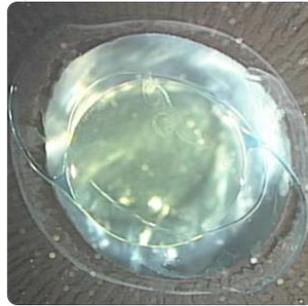
Posterior Miyake apple views showing the effects of five different IOLs on the capsular bag.

Avansee™



No zonular stress or transformation of the capsular bag, soft haptics are unlikely to damage the eye

AF-1™ FY-60AD



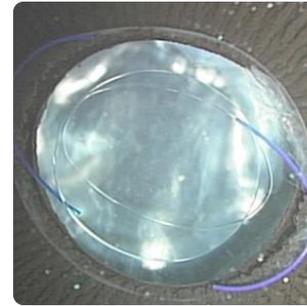
The hard haptics have grown into the capsular bag

AcrySof® IQ



The shape of the capsular bag is good but the contact area between the IOL and the capsular bag is small. This can lead to IOL misalignment

Eternity X-70



The IOL has caused transformation of the capsular bag

Tecnis®



The hard haptics have grown into the capsular bag

Avansee adopts a stable position in the eye

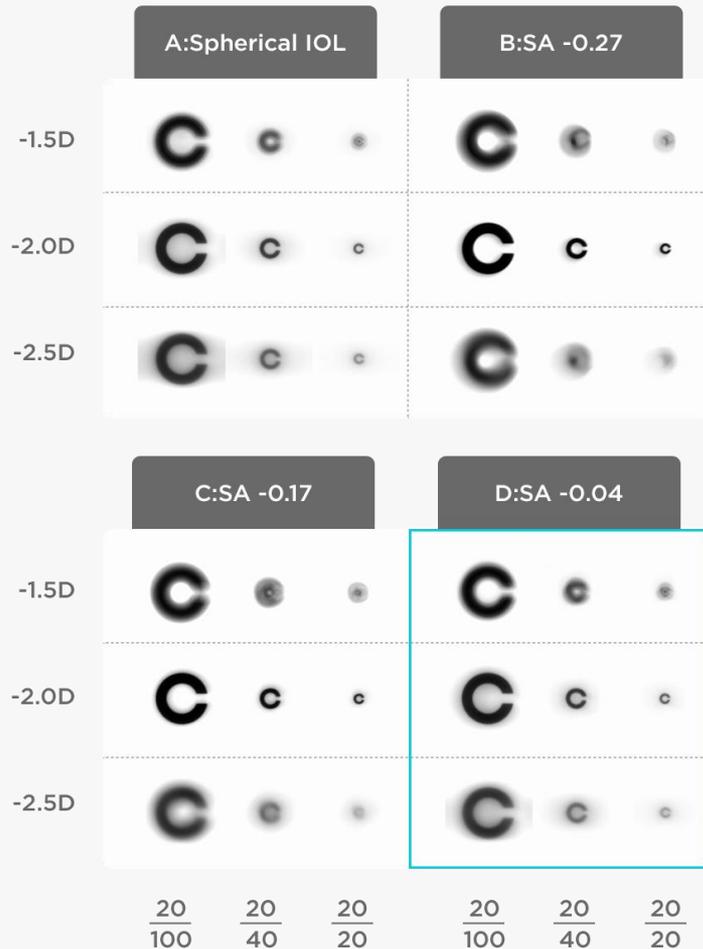
- IOL stability increases as the angle of contact between the loop and the lens capsule gets larger
- Compared to some IOLs, the angle of contact for Avansee is relatively large, suggesting it may be more stable and less prone to misalignment

IOL	Angle of contact (°)
Avansee	75.8
Acrysof® IQ	59.6
Tecnis®	64.6
AF-1™ FY-60AD	81.1
Eternity X-70	97.5

Avansee retains the spherical aberration (SA) of the eye

- IOLs have the potential to modify the spherical aberration (SA) of the eye
- Misalignment of IOLs in postoperative eyes is common
- IOLs that have little effect on the SA of the eye can potentially improve the quality of vision by reducing the risk of coma aberration associated with IOL misalignment (decentration and tilt)
- Avansee retains the SA of the eye, and is therefore less affected by decentration or tilt than IOLs with a greater SA corrective power

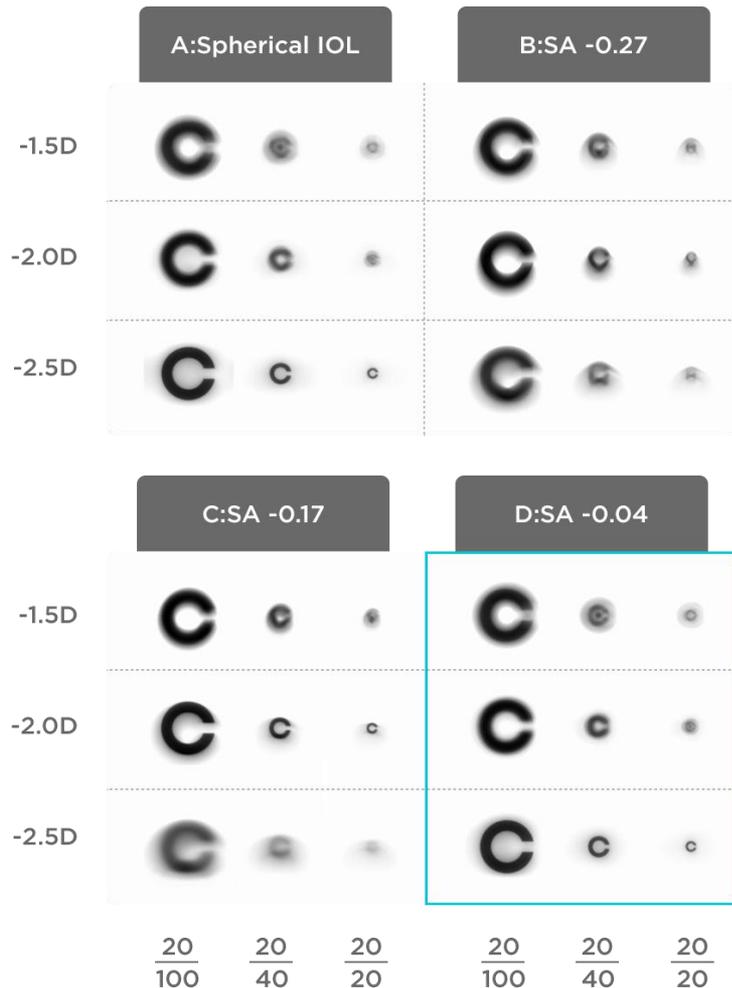
Landolt ring simulations corresponding to IOLs in a model eye: Without misalignment



A water-immersed model eye was developed and the retinal images produced by IOLs with various degrees of SA correction were assessed under conditions of alignment and misalignment

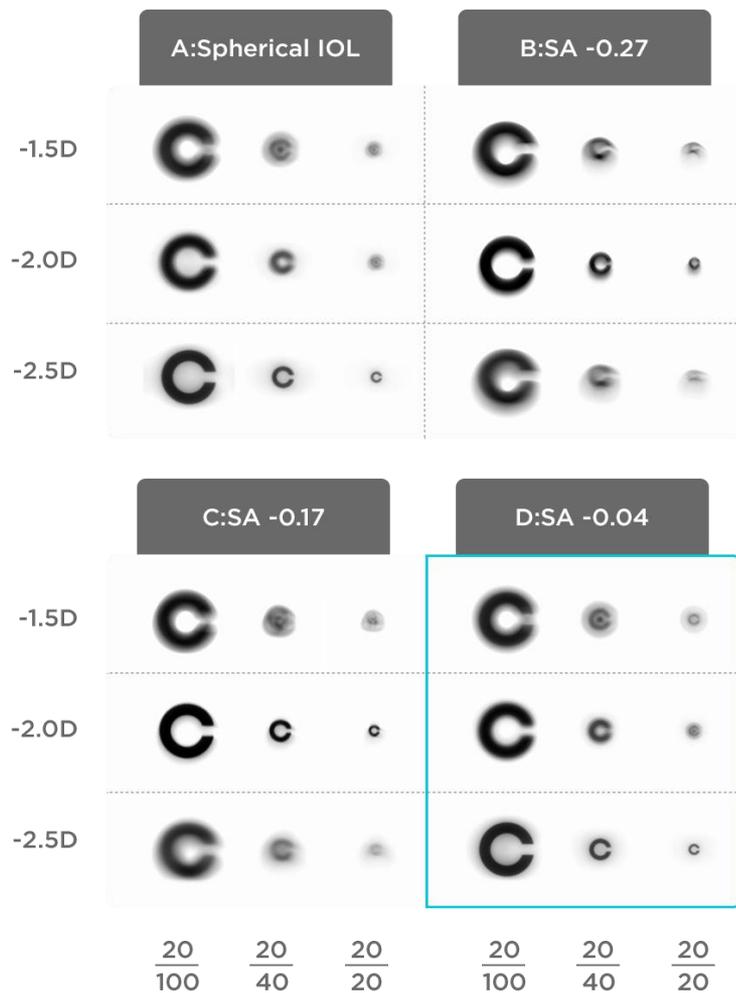
Avansee D:SA = -0.04 μ m

Landolt ring simulations corresponding to IOLs in a model eye: Tilted by 5.0 degrees



Compared to IOLs with a greater SA corrective power, the retinal image produced by Avanse (D:SA -0.04 μ m) is minimally affected by tilt

Landolt ring simulations corresponding to IOLs in a model eye: Decentred by 0.5mm



Compared to IOLs with a greater SA corrective power, the retinal image produced by Avanse (D:SA -0.04 μ m) is minimally affected by decentration

Avansee/Avansee™ Preset: Technical summary (1)

- Avansee's optics are made from soft, flexible, hydrophobic acrylic material available in both natural-type (yellow) and UV-type (clear)
- Optics are made using a stringently-controlled cast-moulded method resulting in a uniform and highly cross-linked polymer, which eliminates the risk of glistenings
- 3-piece (3P) modified C-loop haptics are made from soft, flexible PVDF to reduce the risk of breakage during insertion
- The recommended incision size for Avansee is 2.4 mm for PN6AS and PU6AS and 2.75 mm for PN6A and PU6A
- Doptres range from +6.0 to +26.0
- Avansee effectively corrects visual acuity in the majority of aphakic eyes

Avansee/Avansee™Preset: Technical summary (2)

- Avansee is carved without grinding to provide a squarer edge than IOLs produced using the lathe-cut method, thereby reducing the risk of PCO
- Compared to other dry-packaged IOLs, Avansee has a high water content and a low Tg. It is therefore likely to quickly and fully regain its shape after insertion
- AvanseePreset (the fully-preloaded, single use injection system) provides simple, reliable, reproducible and controlled lens insertion with minimal post-operative complications
- Avansee adopts a stable position in the eye and is associated with a low risk of misalignment
- Avansee retains the SA of the eye; optical performance is minimally affected by tilt or decentration