Avansee™ Preload1P

Technical Slide Kit

April 2017

avansee™ preload1P

UIN: IOL17 00011 Date of Prep: April 2017

Agenda

1. **Avansee™ Preload1P: Summary of product characteristics**

2. **Excellent IOL characteristics**

    2.1 Glistening-free optic

    2.2 360 degree square edge

    2.3 Smooth lens opening

    2.4 Original asphericity

3. **Avansee Preload1P: Small incision, fully preloaded, plunger-type inserter**

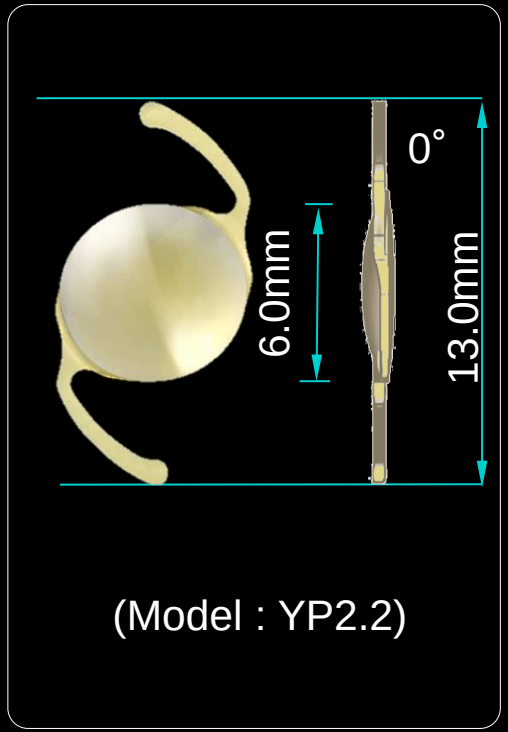
    3.1 Smooth, low resistance IOL insertion

4. **Summary and conclusions**

1. Avansee™ Preload1P: Summary of product characteristics

Avansee™ Preload1P: Summary of product characteristics

Model		YP2.2 (yellow type) CP2.2 (clear type)
Material		Hydrophobic soft acrylic (UV-absorbing acrylic resin; yellow type also contains proprietary blue-light filtering)
Overall / Optic length		13mm / 6mm
Configuration of lens		Biconvex
Configuration of haptic		Modified C-loop
Asphericity		-0.04m
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)
Recommended incision size		2.4mm (through cornea) 2.2mm (through sclera cornea)
A-constant*	**Ultrasound**	118.6
	Optical (SRK/T)	119.0



(Model : YP2.2)

*The A-constant above is presented as a reference value for lens power calculations. 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 experience.

Avansee™ Preload1P package insert.

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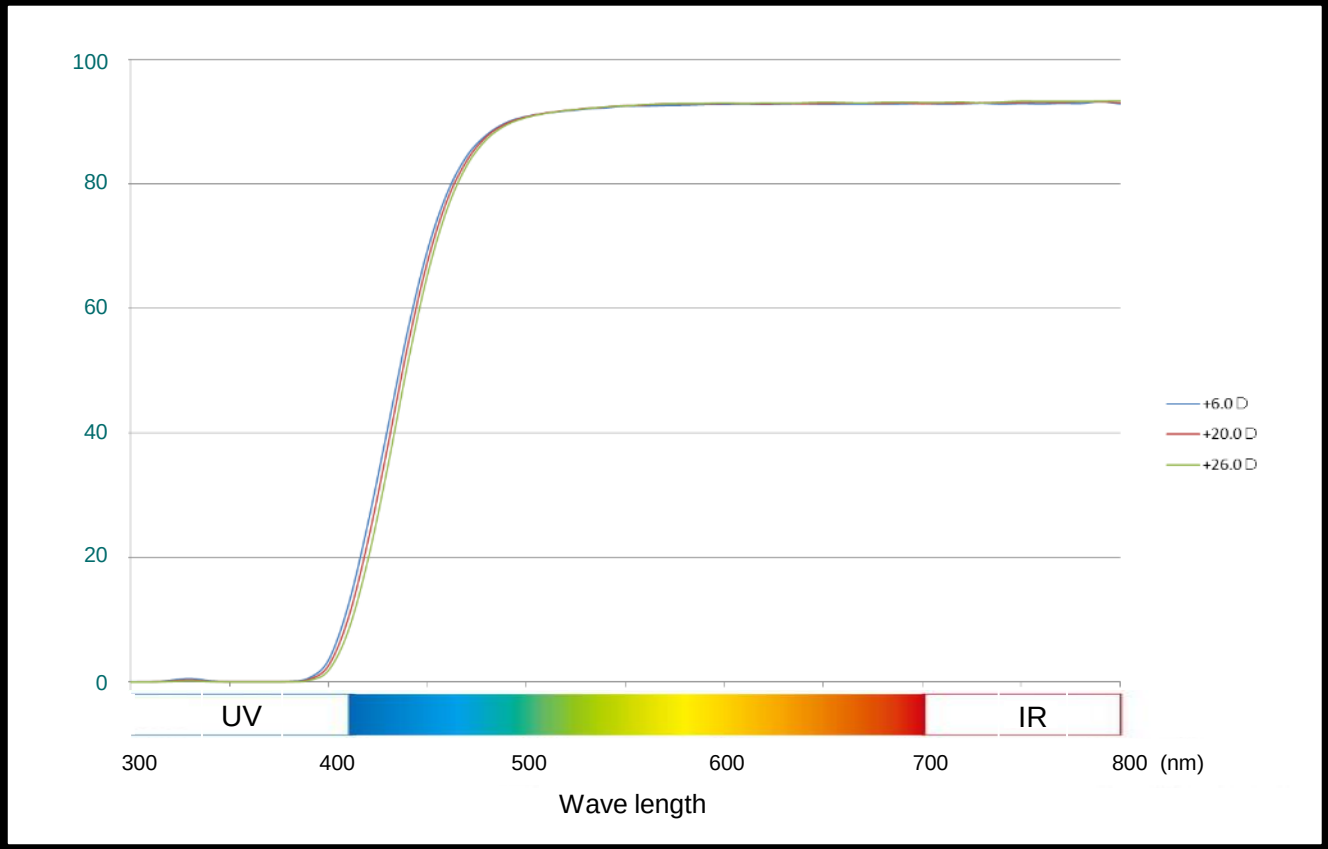
Avansee™: Spectral transmittance

Controlled concentration of chromophore provides consistent spectacle transmittance curve irrespective of dioptric power

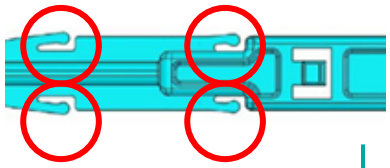


Small incision, plunger-type inserter

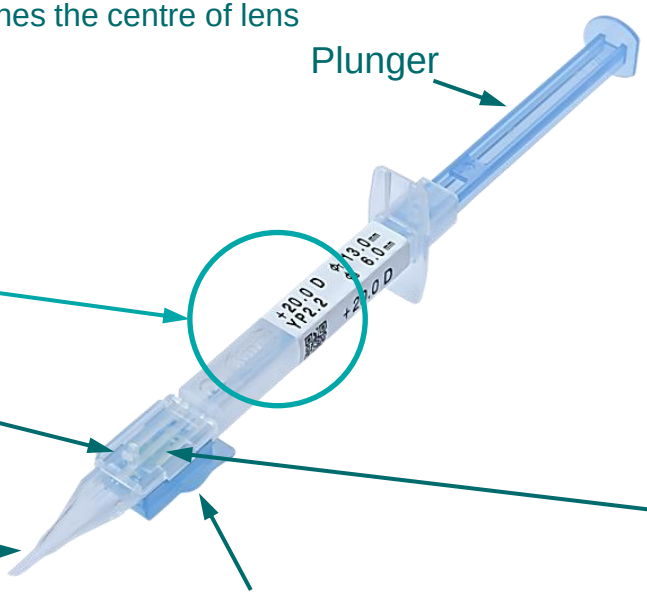
Four stabilisers, angled nozzle and unique plunger provide more controlled lens insertion

Four stabilisers

to make sure the head of plunger pushes the centre of lens



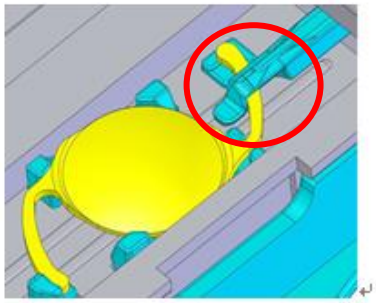
Plunger



Unique plunger (scoop-shaped plunger)

to control the attitude and the movement of lens during insertion

OVD inlet



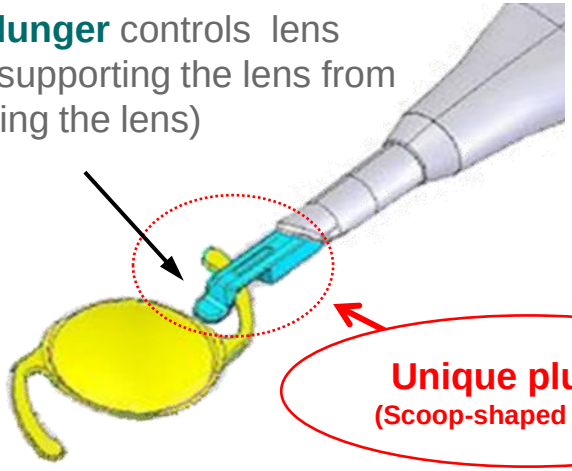
Angled nozzle

to control the movement of lens during insertion

Lens stage

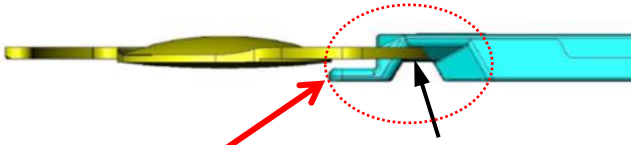
Unique plunger ensures accurate and consistent lens placement during insertion

The unique plunger controls lens placement by supporting the lens from behind (scooping the lens)



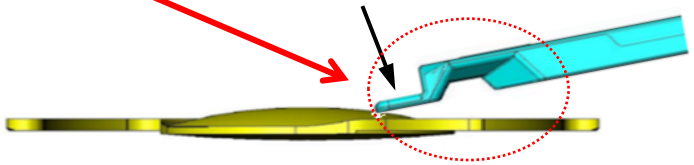
Unique plunger
(Scoop-shaped plunger)

This is an example of a scoop shape



The unique plunger prevents the trailing haptic from sticking to the optic

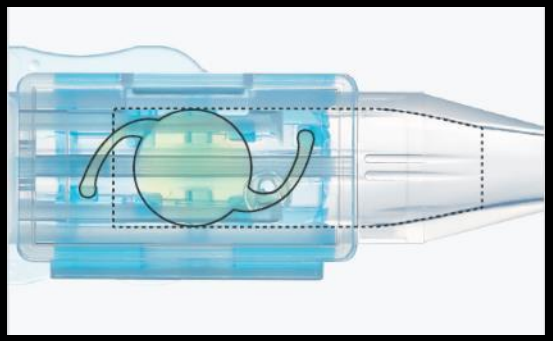
It is easy to adjust the lens position with **the unique plunger** after releasing the lens in the capsular bag



Avansee™ Preload1P allows preparation for insertion in 3 simple steps

Step 1: Injecting the OVD

- **OVD is inserted through the inlet** up to the dashed line, filling the nozzle and **covering the entire lens optic**.



OVD, ophthalmic viscoelastic device

Avansee™ Preload1P package insert.

Avansee™ Preload1P: Recommended OVDs

- Most OVD's are suitable for use with Avansee Preload1P, 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)
- At least 0.17ml of OVD should be injected, using an OVD needle with 25 gauge or greater[1]
- Insufficient OVD may result in damage to the lens[1]

OVD, ophthalmic viscoelastic device

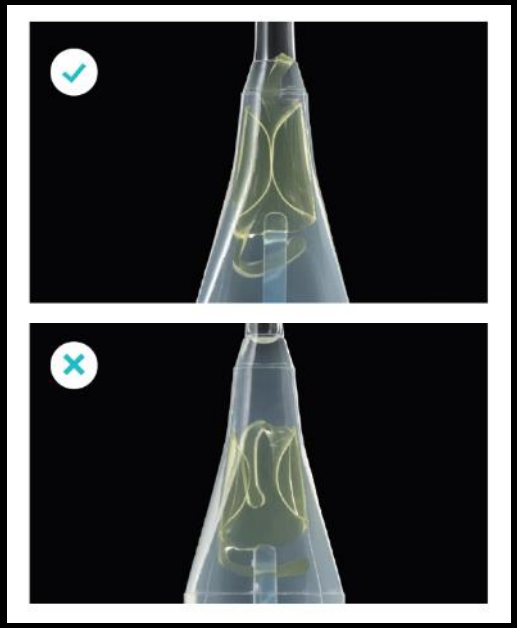
Avansee™ Preload1P allows preparation for insertion in 3 simple steps (contd.)

Step 2: Removing the lens stage

- The main inserter body should be supported, and the lens stage slowly removed towards the nozzle tip

Step 3: Positioning the lens for insertion

- The plunger should be pushed at a slow, constant rate to move the IOL forward, **stopping when the IOL optic is rolled and its edges make secure contact.** Failure to stop at the correct point will increase the likelihood of unsuccessful lens insertion.



Avansee™ Preload1P package insert.

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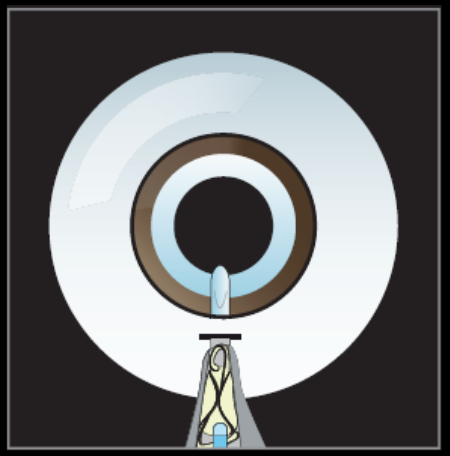
Avansee™ Preload1P insertion

The bevel of the nozzle must always point downwards until the nozzle is removed from the eye

Insertion

Insert the nozzle tip **with the bevel facing down** through the incision to just before the central pupillary area. **While the bevel is down, the inserter will be leaning towards the left.**



Release

Advance the plunger at a slow, constant rate, **inserting the IOL into the eye within 20 seconds.** Once the IOL is inside the capsular bag, continue to push the plunger **until the trailing haptic is completely released.**

Completion

Check the lens positioning and remove the nozzle from the eye. **Ensure the bevel continues to face downwards** until the nozzle has been removed from the eye.

Avansee™ Preload1P package insert.

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Helpful hints (1)

1. Preventing the sudden release of IOLs from the inserter

- Always follow the 3-step preparation process
  - Stop the plunger at the correct point and insert the IOL into the eye within 20 seconds
  - Always use the enough amount of OVD
  - Check the resistance force while pushing the plunger

2. Ensure the lens stage is removed prior to pushing the plunger

- If the lens stage is not removed at the correct time, the inserter should be discarded and replaced with a new one

This lens must not be used

The procedure must immediately be discontinued if any problems are encountered.

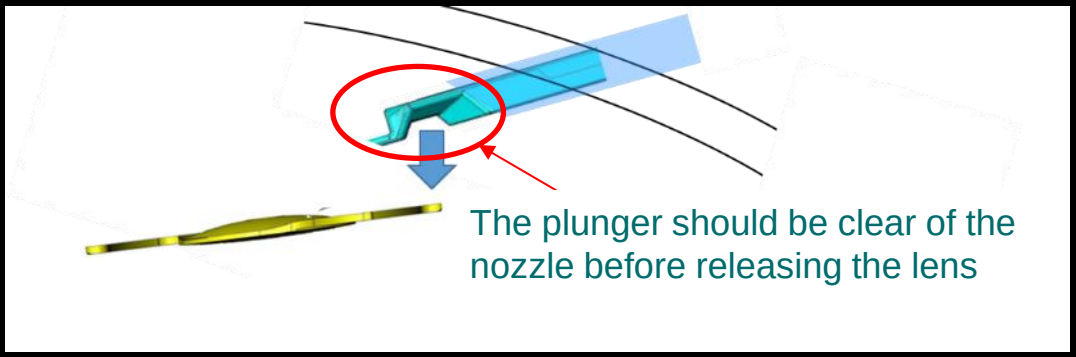
Helpful hints (2)

3. Problems removing the plunger from the eye

- Reinsert the plunger keeping the bevel down; try removing the plunger again.

4. The trailing haptic is not released in the eye

- Further push the plunger, otherwise the haptic will be stuck between the unique plunger and the nozzle.



5. Ensure the plunger is not inadvertently pulled backwards

- If this occurs, the inserter should be discarded and replaced with a new one.

A guide to using Avansee™ Preload1P, the fully preloaded intraocular lens system from Kowa

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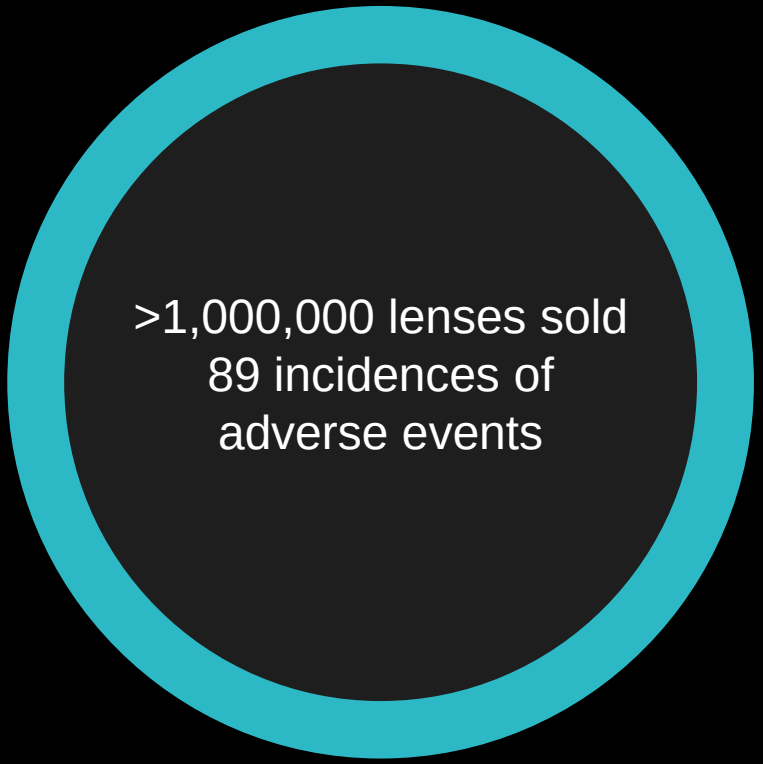
The number of adverse events reported for Avansee™ is low

Over 1 million units of Avansee lenses have been sold in Japan since 2007, with very low incidences of adverse events (0.009%) and serious adverse events (0.0009%).



Data on file

2. Excellent IOL characteristics

2.1 Glistening-free optic

2.2 360 degree square edge

2.3 Smooth lens opening

2.4 Original asphericity

2.1 High quality, glistening-free optic with no evidence of deterioration over time

Advanced optical purity

- The optical purity of IOL optics can potentially deteriorate after implantation due to glistening*
- If present, glistening is typically observed within a few months of surgery and appears as small bright spots across the optic
- The impact of glistening on visual function is controversial; some studies report **significant increases in light scatter and decreases in contrast sensitivity, modular transfer function, and/or visual acuity** that can only be corrected by IOL replacement
- The formation of glistening is influenced by **manufacturing technique, IOL packaging**, postoperative inflammation, ocular diseases, ocular medications and the **duration of IOL use**.

*Fluid-filled, light-reflecting microvacuoles 1 to 20µm in diameter, formed by the absorption and subsequent condensation of water within the matrix of the optic material.7-10

Schmickler S, Auffarth GU. A Perfect Partnership: The Avansee Preloaded IOL System *EuroTimes Suppl.* Sept 2016.

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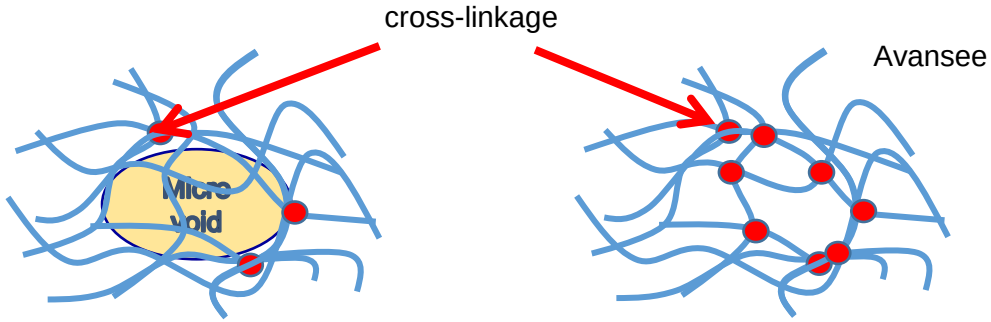
The risk of glistening is reduced by increasing the density of cross-linkages in the optic

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 glistening



<appropriate density of cross-linkage>

Low density ⟷ **High density**

The lens is soft and flexible but is likely to develop glistening

Avansee: Soft, flexible lens; no glistening

Unlikely to develop glistening but the lens is too hard

Miyake K, Rosen E, Ota I, *et al.* Emerging Monofocal Intraocular Lenses in Europe: Potential Role for AvanseePreset. *EuroTimes Suppl.* Sept. 2014.

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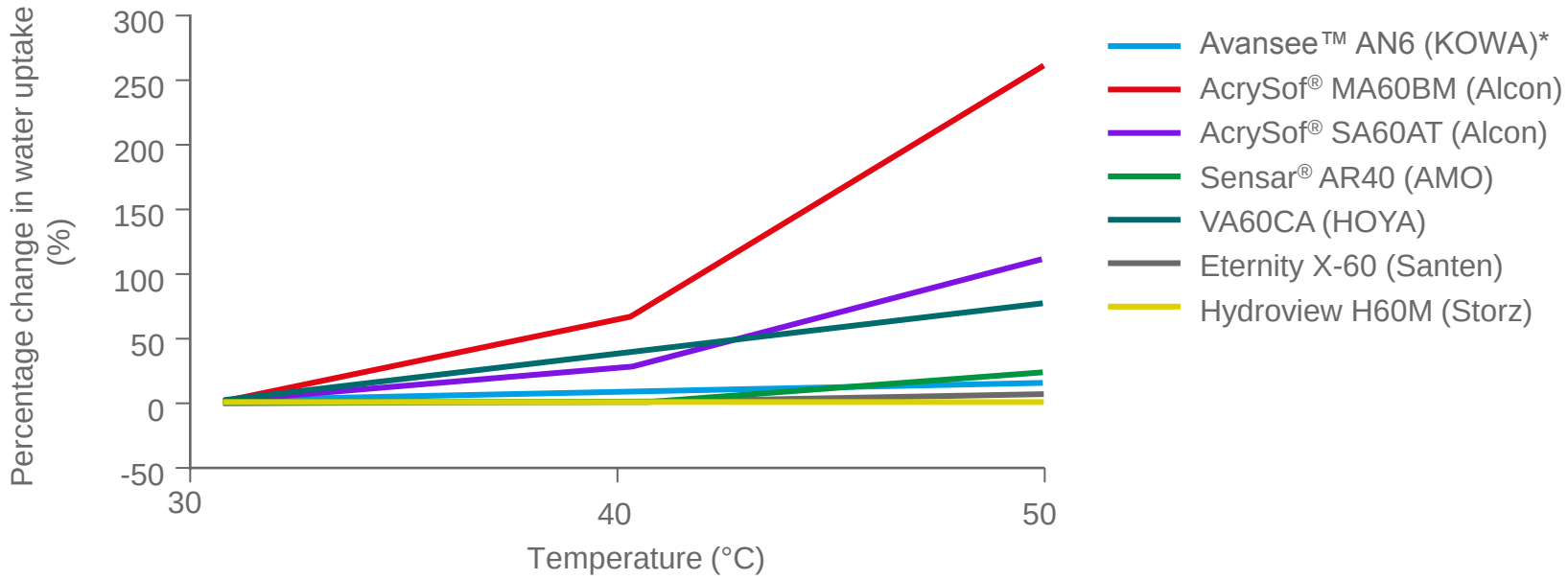
Avansee™ optics show a significantly lower, more stable change in water uptake than other dry-packaged IOLs

Change in water uptake at different temperatures[1,2]



*The optic for both 1P and 3P lenses are produced using the same materials

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, Rosen E, Ota I, *et al.* Emerging Monofocal Intraocular Lenses in Europe: Potential Role for AvanseePreset. *EuroTimes Suppl.* Sept. 2014.

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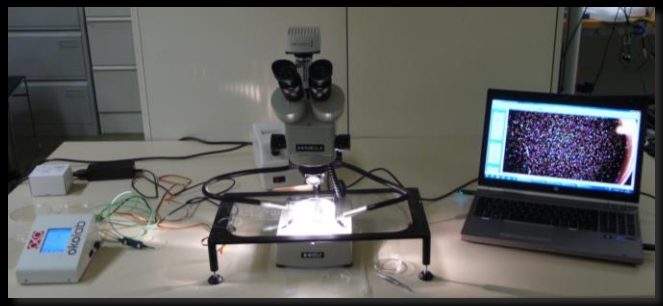
In vitro accelerated deterioration: Study 1

- Step 1 : IOLs (5 lenses per model, +20.0D) were incubated in saline at 45°C for 24 hours

- Step 2 : Reducing the temperature to 37°C for 2.5 hours using a water bath

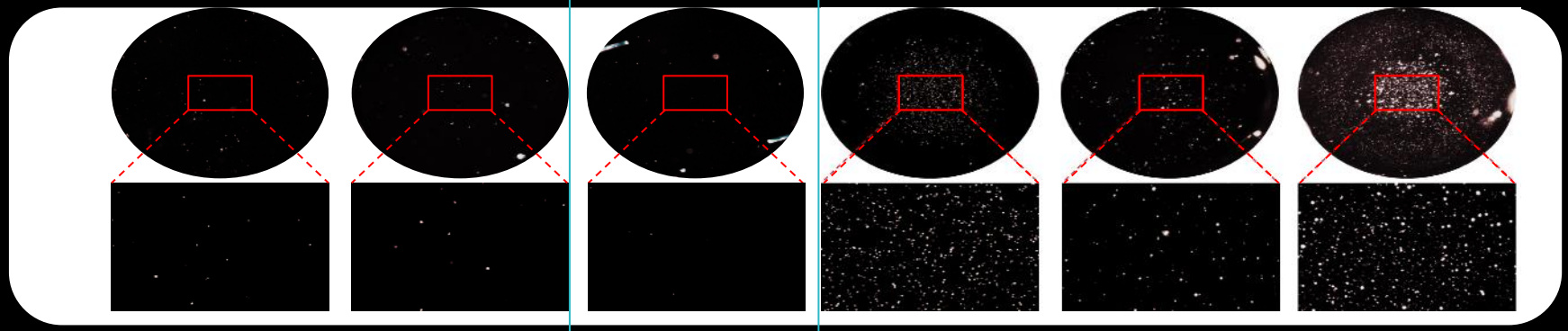
- Step 3 : Analysis of the samples and evaluation using a dedicated software



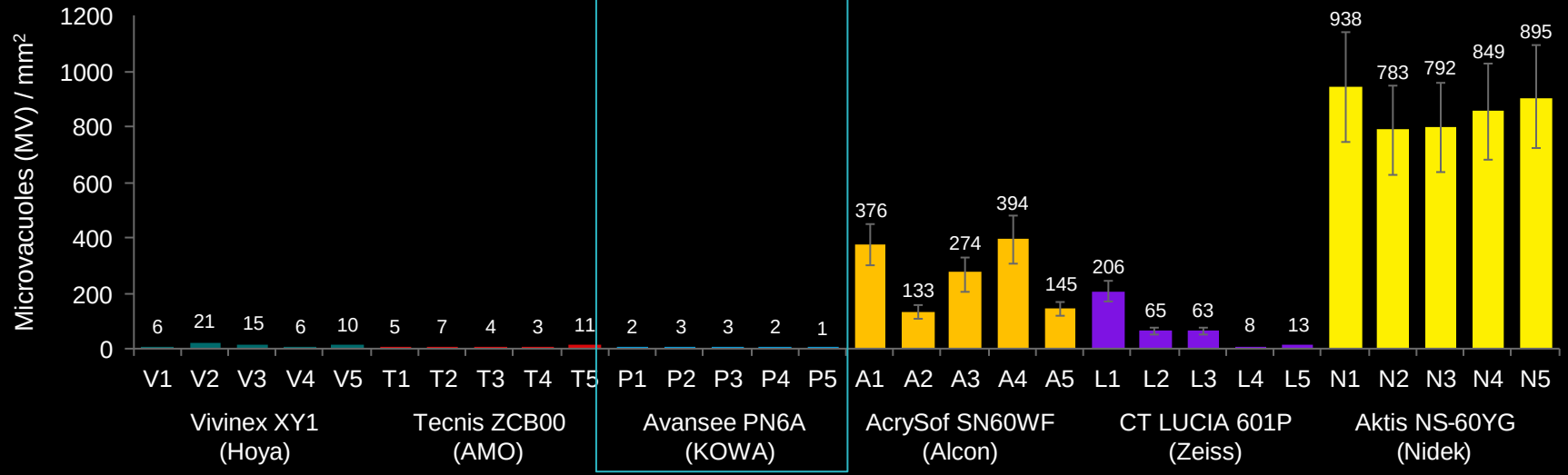
Data provided by Auffarth GU

Thomes BE, Callaghan TA. Evaluation of in vitro glistening formation in hydrophobic acrylic intraocular lenses. Clin Ophthalmol. 2013;7:1529-34.

Study 1: Avansee™ is glistening-free *in vitro*



Glistening grade:	0	0	0	2.6	1	3+
Average MV/mm^2:	11.6	6	2.2	264.4	71	851.4



*The optic for both 1P and 3P lenses are produced using the same materials

Data provided by Auffarth GU

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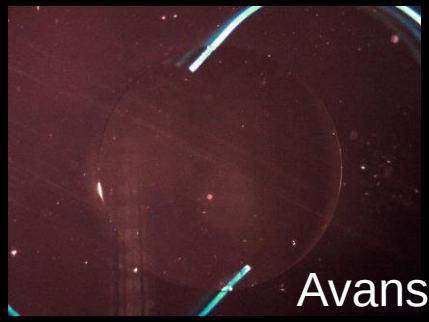
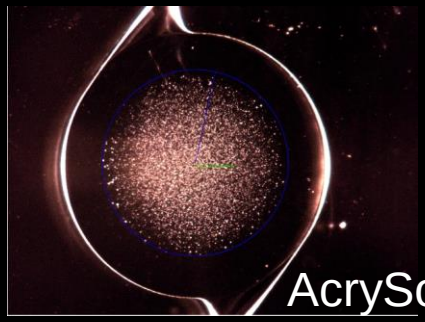
In vitro accelerated deterioration: Study 2

- 100 Avansee Preset PU6A IOLs with a labelled power of +21.0 D were immersed in an oven at 45°C to perform accelerated material deterioration tests. The standard experimental method was extended for continuous data production over a time period of 100 days to observe the glistening formation and development. No glistening formation was observed in the Avansee Preset PU6A IOLs.



Avansee



AcrySof

- With 20 AcrySof SA60AT IOLs extensive measurements with the same experimental procedure were performed. Here, the formation and development of severe glistening could be observed. The glistening start to appear between 5-24 hours at 45°C. Their number increases over time up to 60 days. After 60 days a plateau could be observed where the IOL optic area appeared saturated with the microvacuoles.

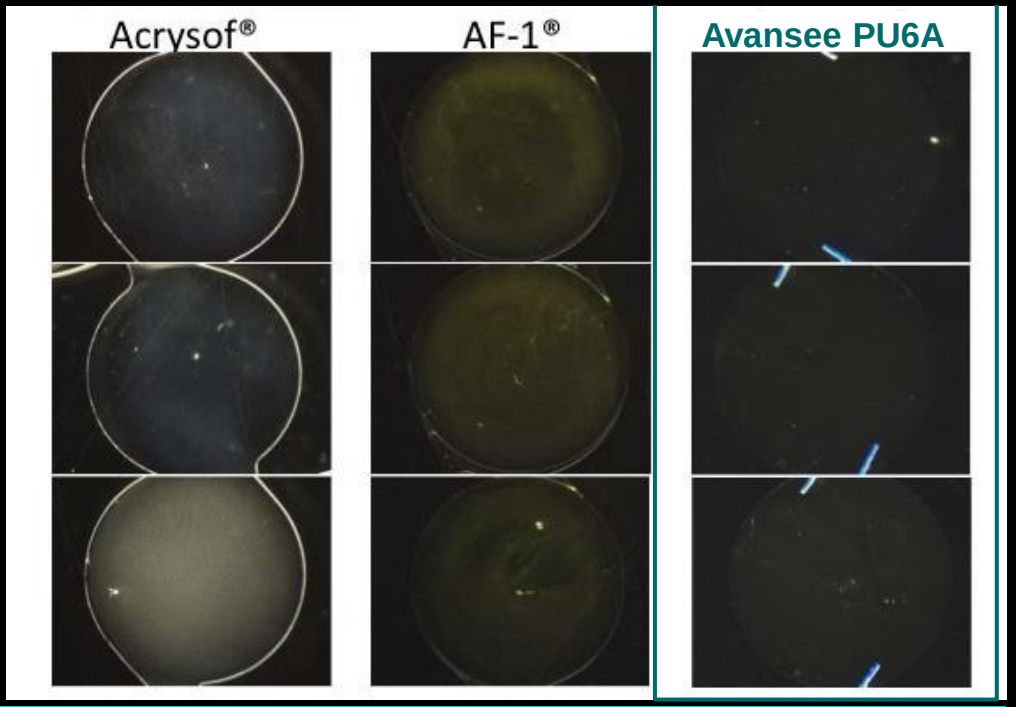
*Both 1P and 3P lenses are manufactured using the same materials

Data provided by Auffarth AU

Avansee™ is glistening free *in vivo*

Preclinical study in rabbits

- IOLs were implanted into aphakic eyes of white domestic rabbits
- IOLs were surgically removed after 8 months and stored in 33°C saline to prevent the post-surgical separation of the water phase
- IOLs were examined under a microscope at constant temperature



- Glistening was observed on Acrysof IOLs and, to a lesser extent, on AF-1; **Avansee was glistening free**

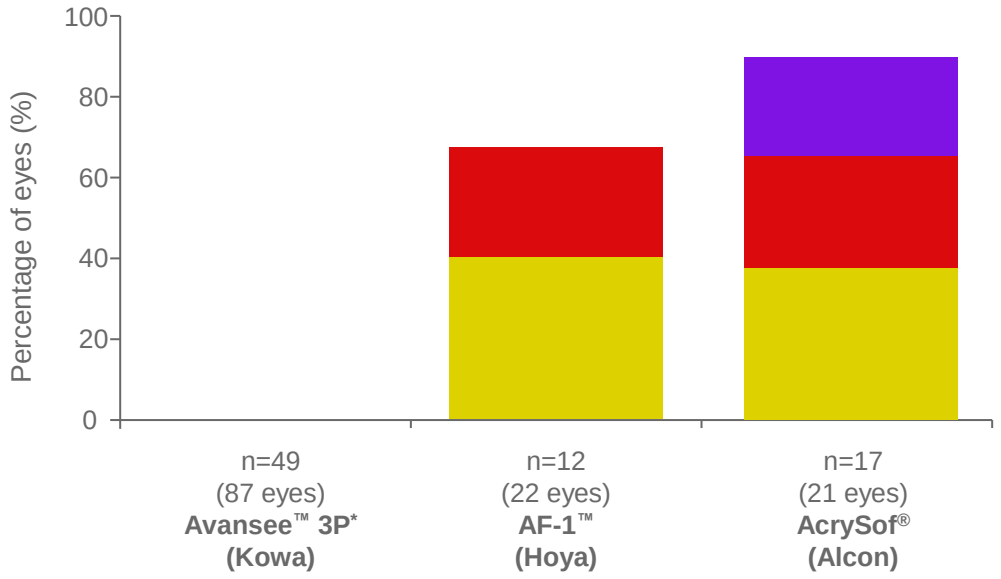
*Both 1P and 3P lenses are produced using the same materials

Matsushima H. Whitening. 2014. http://www. iolsafety.com/ issues-under-discussion/glistenings/letter-ofopinion/146-hiroyuki-matsushima-md-phd-on-whitening.html. Accessed January 2017

Avansee™ is glistening-free *in vivo*

Real-life observational study in humans

4-year observational study in 130 human eyes undergoing cataract surgery



There have been no reports of glistening with Avansee since its launch in Japan in 2007

*Optics both 1P and 3P lenses are produced using the same materials

Miyake K, Rosen E, Ota I, *et al.* Emerging Monofocal Intraocular Lenses in Europe: Potential Role for AvanseePreset. *EuroTimes Suppl.* Sept. 2014.

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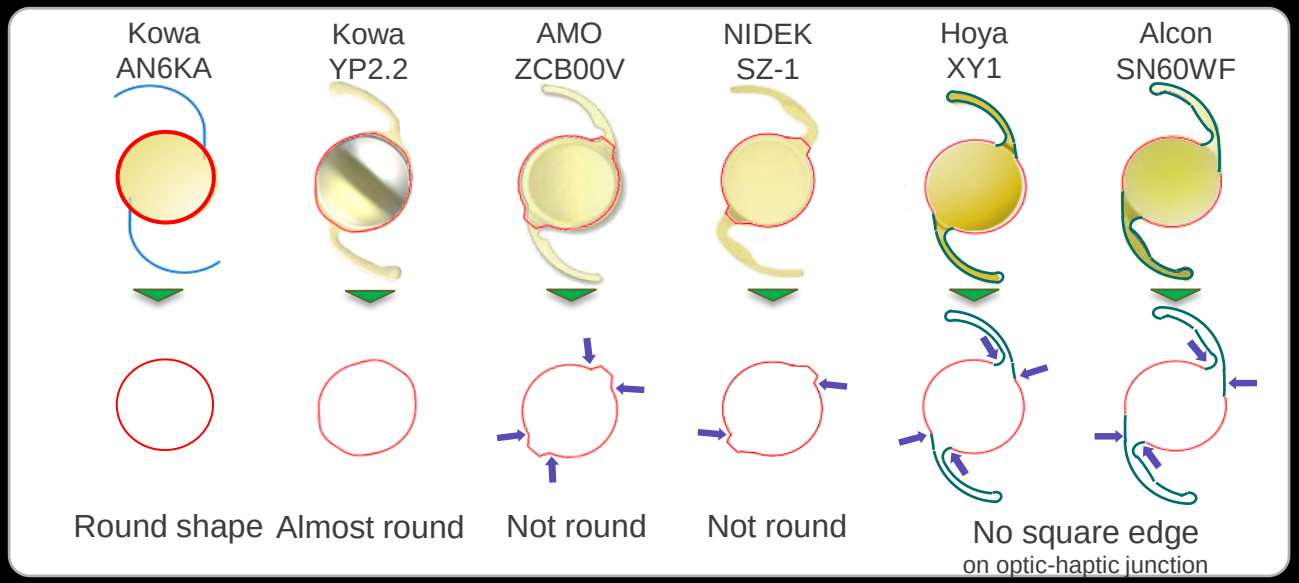
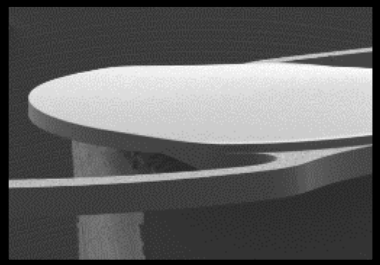
2.2 360 degree square edge designed to reduce the risk of PCO

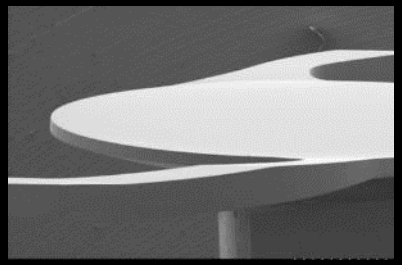
Unlike other IOLs, Avansee™ has a 360 degree posterior square edge that extends to the optic-haptic junction



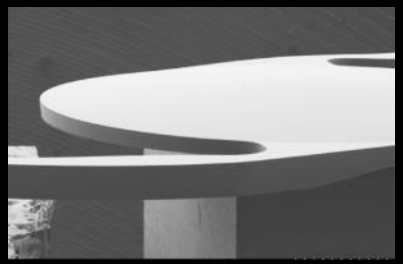
Avansee YP2.2



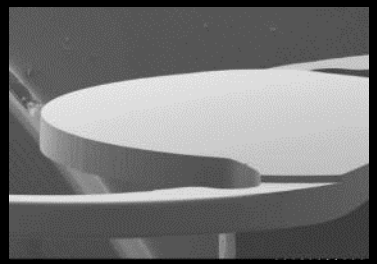
Hoya Micro255



Alcon SN60AT



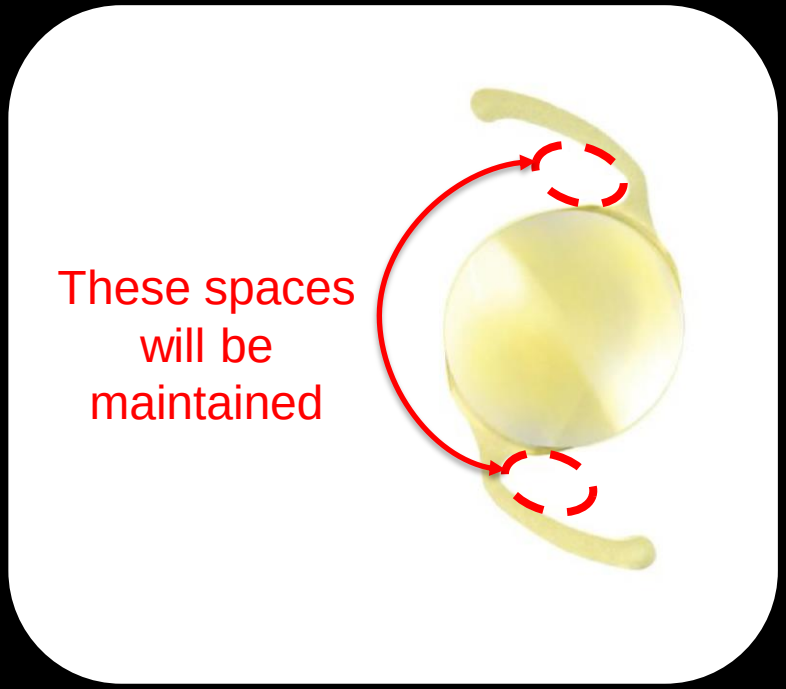
AMO ZCB00V



Data on file

Unique haptics maintain space and aid adhesion between the anterior and posterior capsules

- The unique haptic' shape maintain some space for aid adhesion between the anterior and posterior capsules, which will maximize the effect of 360 degree square edge in order to reduce the risk of POC.

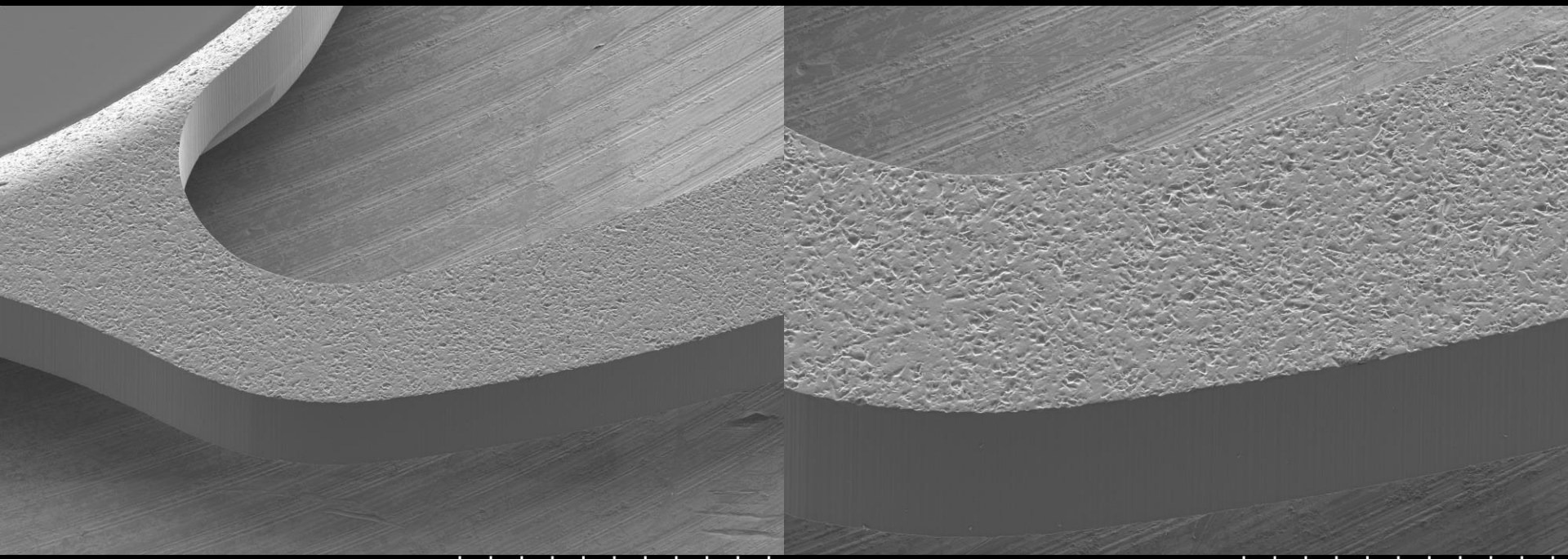


360 degree square edge + Unique haptics = to reduce the risk of PCO

2.3 Smooth IOL unfolding

Avansee™ 1P haptic is designed to facilitate smooth IOL unfolding after insertion with stable implantation

- The indented haptic tends not to stick to the optic after the IOL is released from the inserter

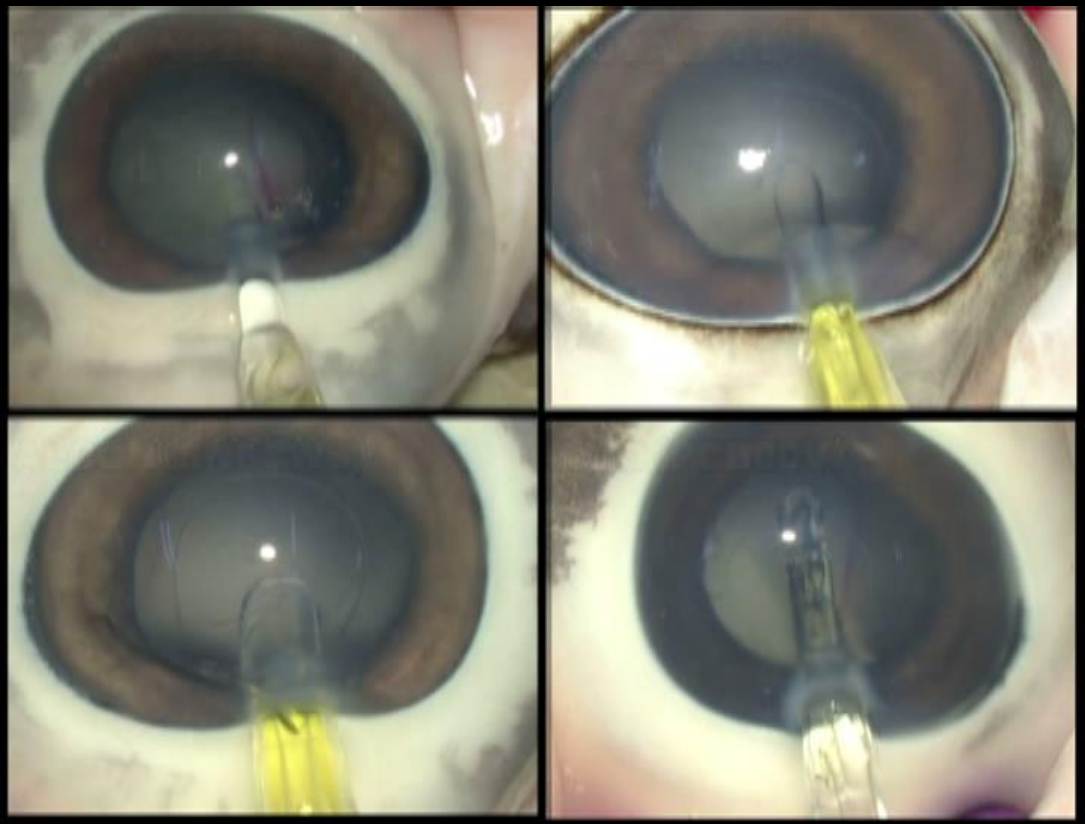


Data on file

Smooth IOL unfolding after insertion

Indented haptic surface prevents sticking to the optic after release.

Optimal water content (≤2.0%) provides good flexibility and shape regain after insertion.



http://avansee.eu/en/preload1p/control/

2.4 Abberation-neutral – visual acuity largely unaffected by decentration or tilt

IOLs (e.g. Avansee™) that retain or minimally affect the SA of the eye are less affected by misalignment

- Aspherical IOLs have the potential to improve visual function by modifying the SA of the eye, either by:
  1. Nullifying the SA of the eye, thereby focusing an image at the plane of focus with good contrast
  2. Reducing the SA of the whole eye to approximately 0.1µm (pupil diameter 6mm; a value typically found in healthy young people)
  3. Decreasing the SA of the IOL to approximately 0, thereby retaining the SA of the whole eye
- Misalignment of IOLs in postoperative eyes is common; average levels of decentration and tilt can sometimes reduce the visual performance of the IOL
- Compared to IOLs with a greater SA corrective power, IOLs (e.g. Avansee) that retain or minimally affect the SA of the eye are less affected by misalignment

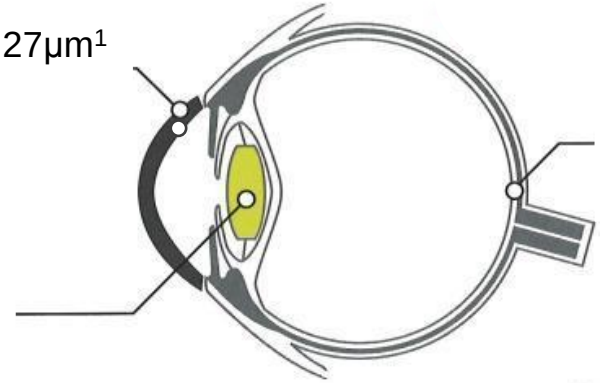
SA, spherical aberration

Fujikado T, Saika M. Evaluation of actual retinal images produced by misaligned aspheric intraocular lenses in a model eye. *Clin Ophthalmol*. 2014:8 2415–2423

Unlike other IOLs, Avansee™ minimally affects the SA of the eye

Long depth of focus; less affected by decentration or tilt than IOLs with a greater spherical aberration corrective power

Corneal aberration
- spherical aberration = +0.27µm[1]
- (+ coma aberration)



Residual ocular spherical aberration
+0.23µm

Avansee's asphericity
-0.04µm

SA, spherical aberration

1. Wang L, Dai E, Koch DD, *et al.* Optical Aberrations of the Human Anterior Cornea. *J Cataract Refract Surg*. 2003;29(8):1514-21.

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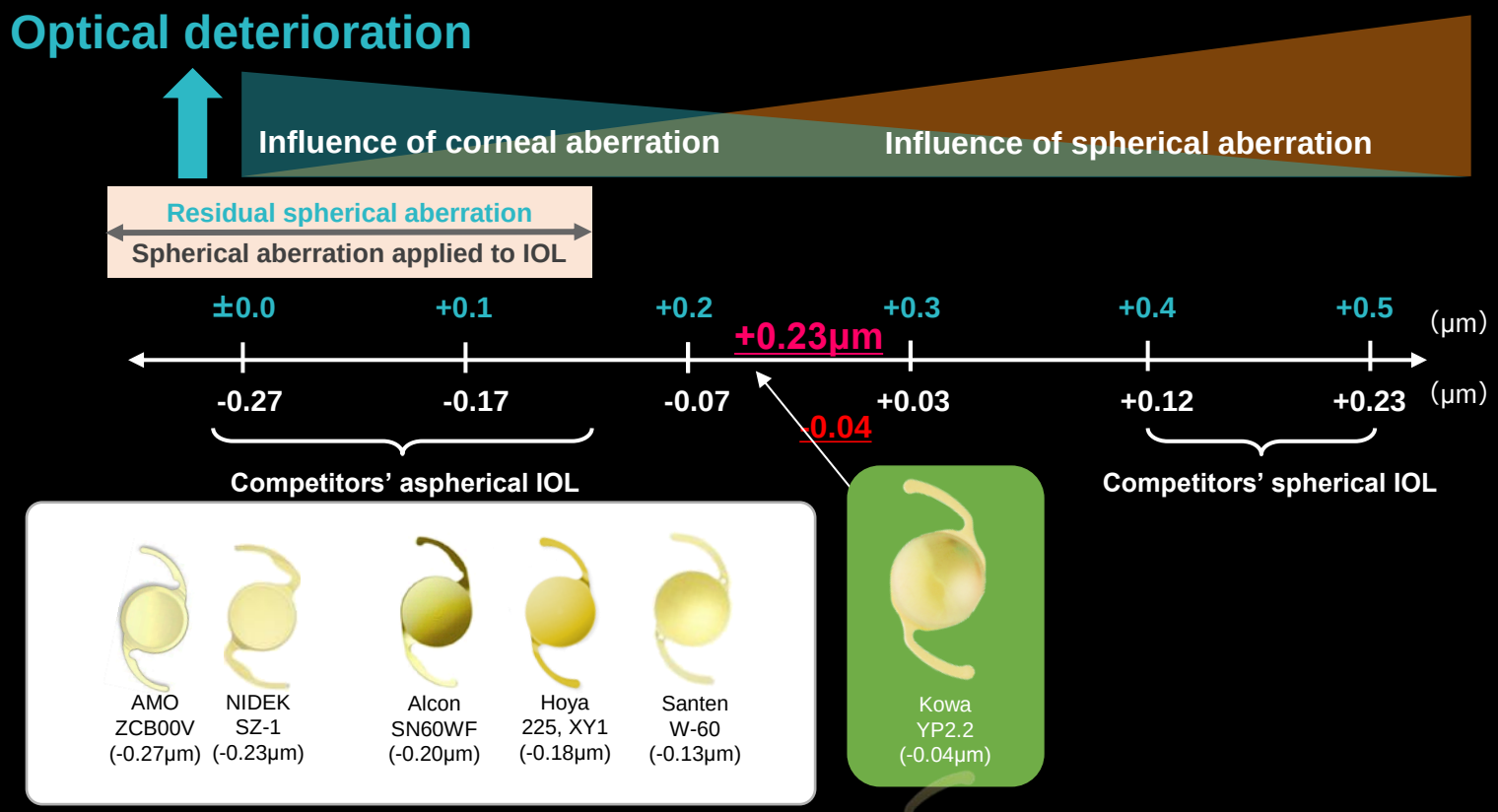
Avansee™ has optimised neutral asphericity

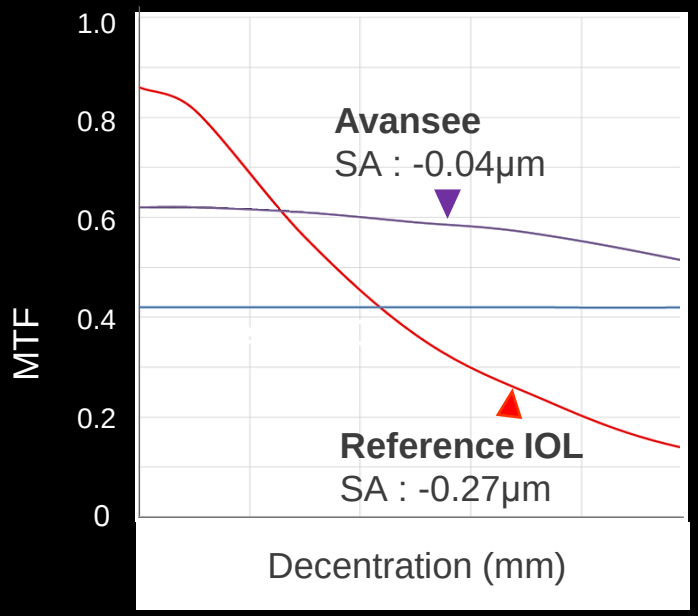
Avansee has optimised neutral asphericity

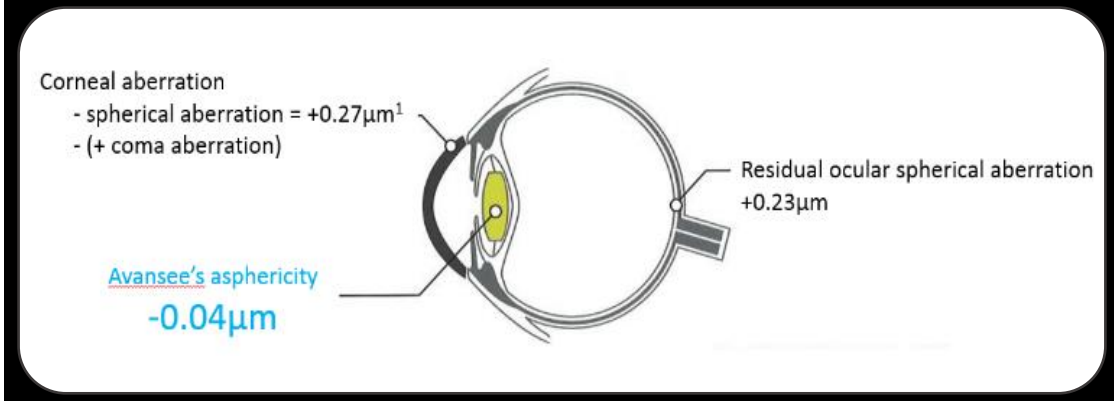


Based on Rinsho Ganka, Junya Kisawa 70(1):16-23,2016

Unlike IOLs that correct the SA of the eye, decentring errors have less effect on modular transfer function for Avansee™

- MTF was calculated based on the design value for a 4mm pupil size



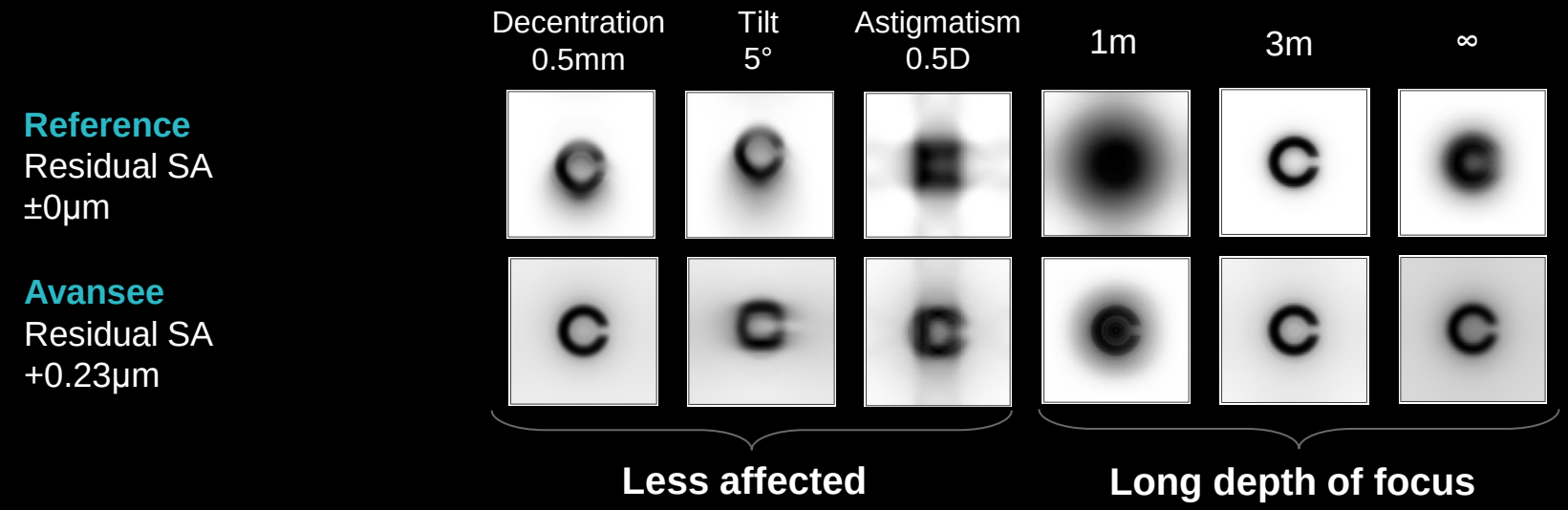


SA, spherical aberration; MTF, modulation transfer function

Fujikado T, Saika M. Evaluation of actual retinal images produced by misaligned aspheric intraocular lenses in a model eye. *Clin Ophthalmol.* 2014; 8: 2415–2423.

Avansee™ provides long depth of focus and is less affected by misalignment than IOLs that correct the SA of the eye

- 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



Abberation neutral concept provides long depth of focus and is less affected by decentration and tilt

SA, spherical aberration; MTF, modulation transfer function

Fujikado T, Saika M. Evaluation of actual retinal images produced by misaligned aspheric intraocular lenses in a model eye. *Clin Ophthalmol.* 2014; 8: 2415–2423.

UIN: IOL17 00011 Date of Prep: April 2017

3. Avansee™ Preload1P: Small incision, fully preloaded, plunger-type inserter

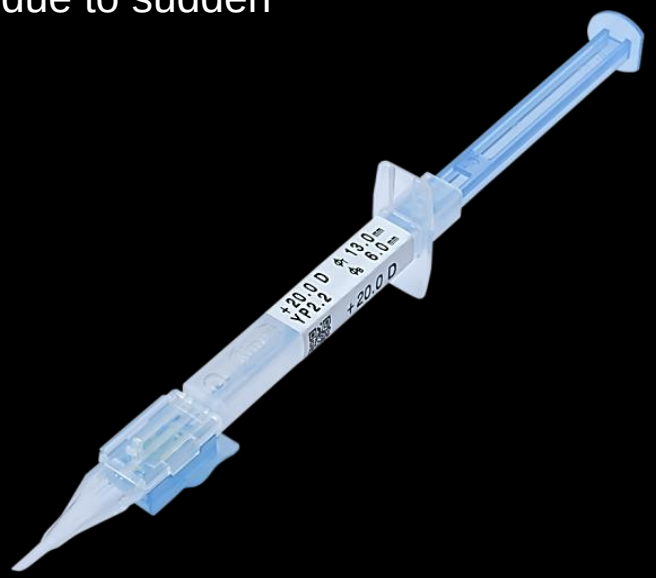
3.1 Smooth, low resistance IOL insertion

3.1 Smooth, low resistance IOL insertion

The success of IOL insertion largely depends on the quality of the IOL inserter

- A major challenge for IOL inserters 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 inserter
- Excessive pressure may cause the IOL to stick to the cartridge wall resulting in lens damage or crimping, haptic breakage, and/or cartridge damage
- Inconsistent pressure may damage intraocular tissues due to sudden IOL release.

- To avoid these, the inserter of Avansee Preload1P is specifically designed for Avansee 1P.

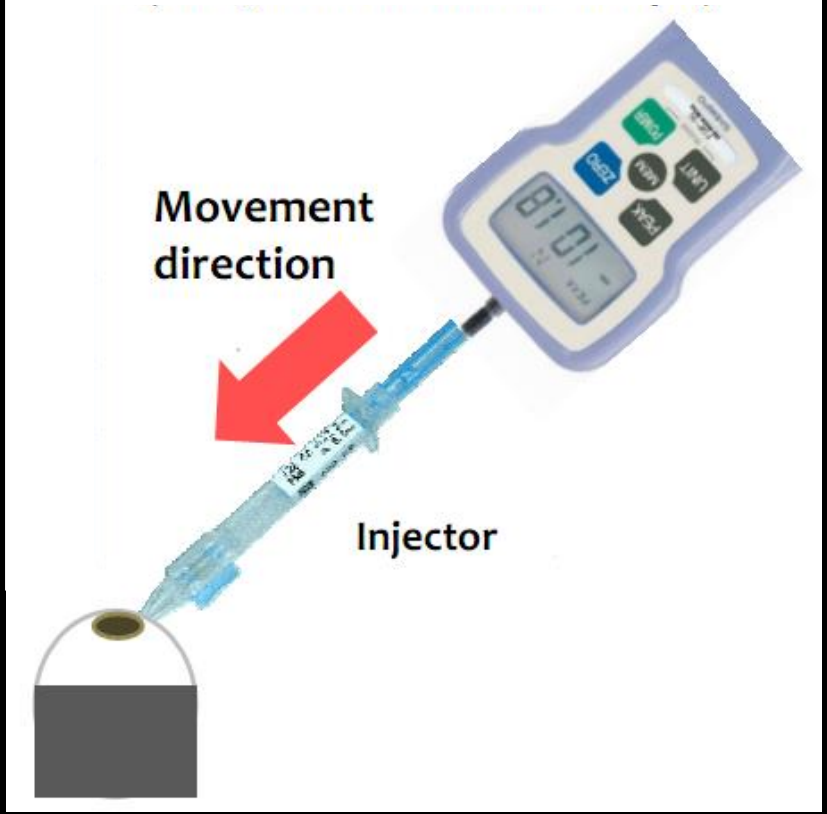


Schmickler S, Auffarth GU. The Perfect Partnership: A review of European clinical and laboratory data on Kowa's Avansee™Preset. *EuroTimes Suppl.* Sept 2016.

Avansee™ Preload1P resistance study

Surgery	0.5 ml of OVD was injected into the anterior chamber and capsular bag of porcine eyes after phacoemulsification. Syringe-type inserters were used according to the manufacturer's instructions to insert IOLs through a 1.8-2.5 mm corneal incision
System	FGV-10XY (automated digital force gauge meter; Shimpo Instruments)
Control	IOL delivery into a plastic petri dish, without an eye
Conditions	Temperature 22°C to 25°C; 50% humidity
Samples	10 IOLs (+26.0D) were tested per inserter (N = 60 in total)

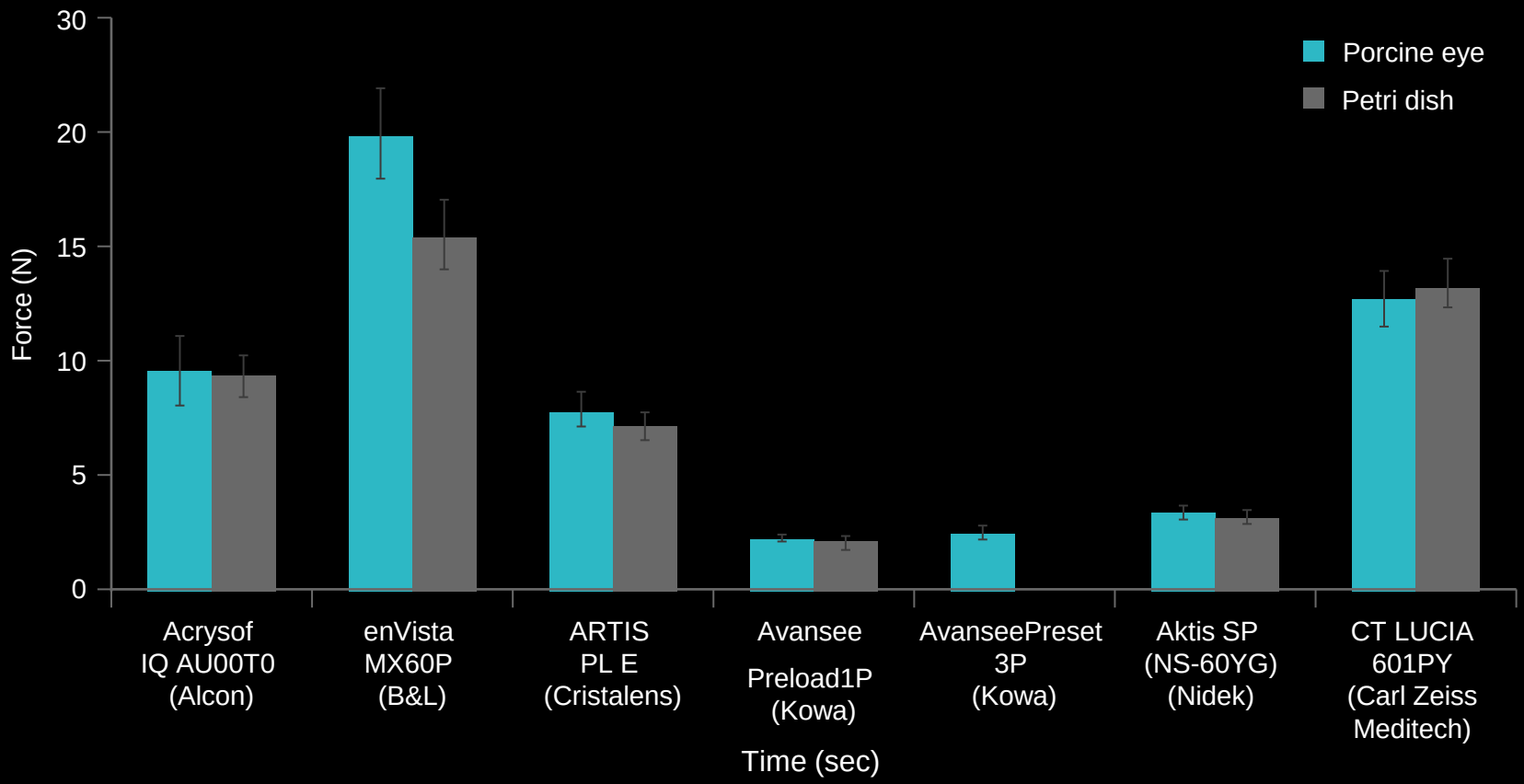
FGV-10XY (automated digital force gauge meter; Shimpo Instruments)



OVD, ophthalmic viscoelastic device

Method based on Usui M, Tanaka T. Resistance force for intraocular lens insertion through lens cartridges and syringe-type injectors. *J Cataract Refract Surg* 2015;41:1745-1751

Avansee™ Preload1P demonstrates a lower resistance force than other IOL inserters

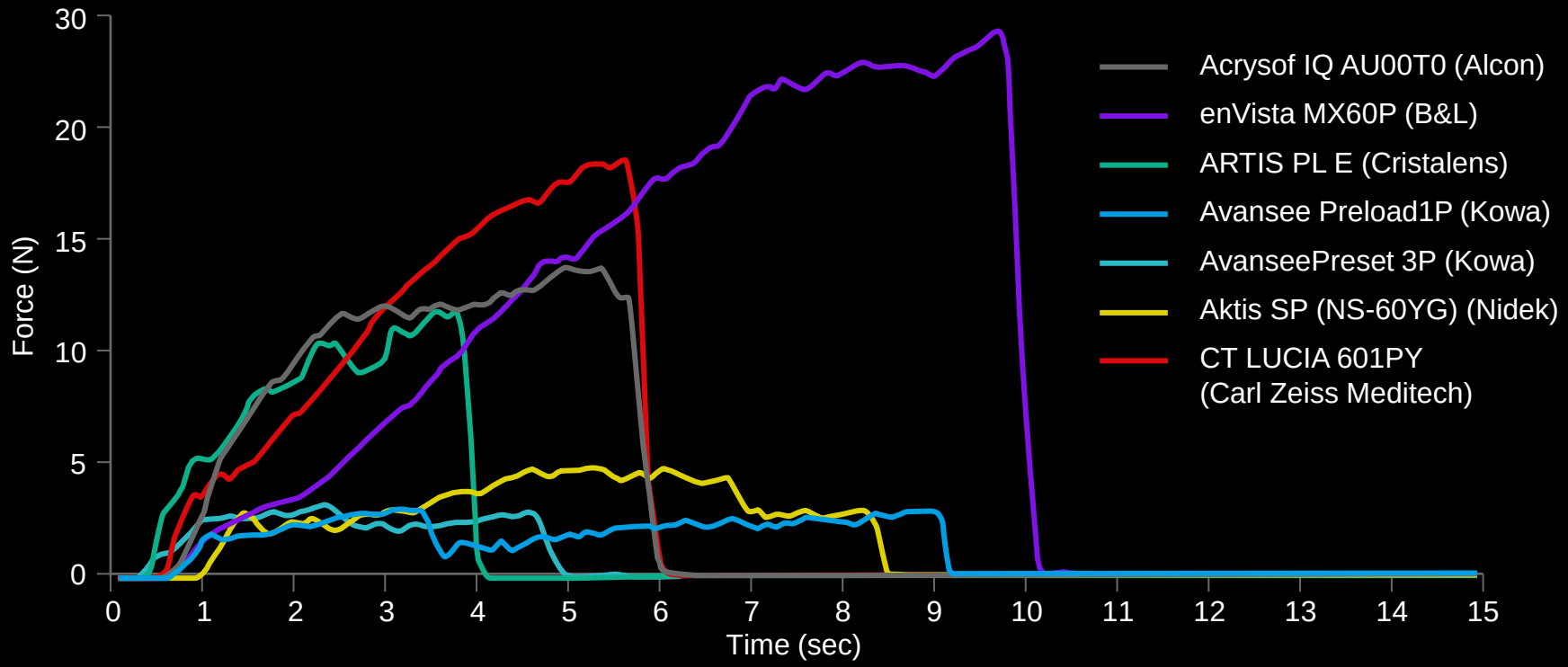


Lower resistance force = lower thrust force and reduced hand stress

Data provided by Auffarth GU

UIN: IOL17 00011 Date of Prep: April 2017

Avansee™ Preload1P provides smoother, more controlled IOL insertion than some other IOL inserters

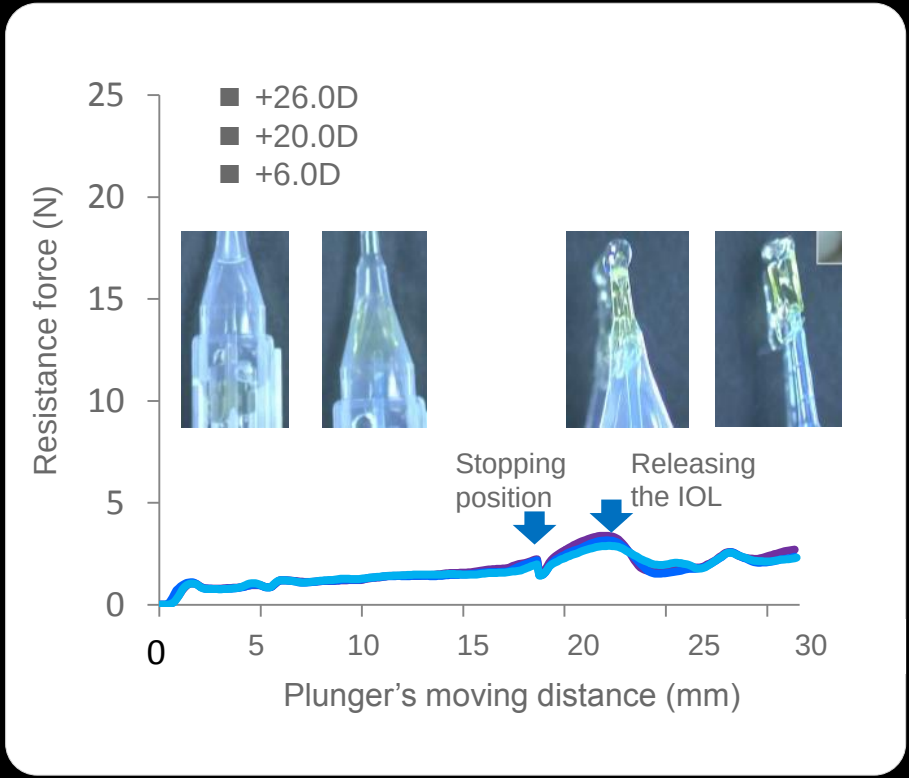


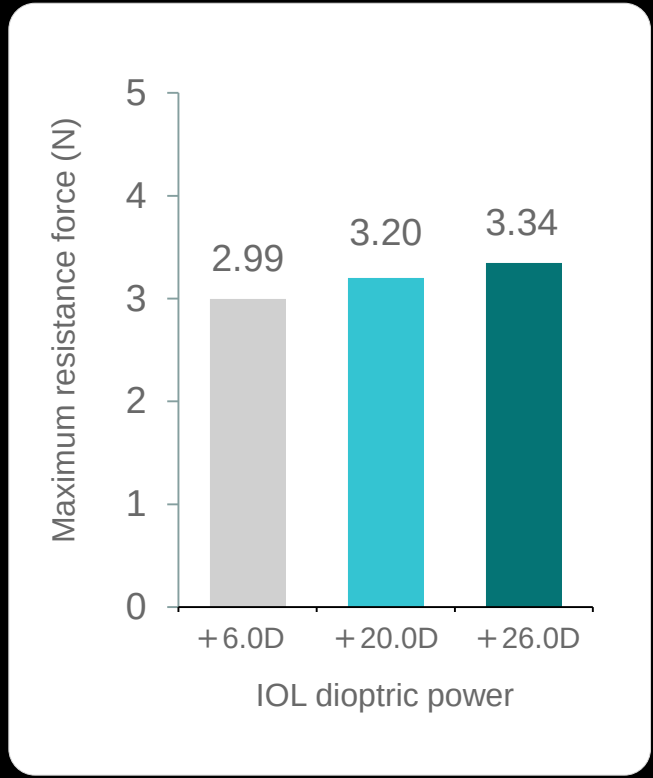
Smooth, controlled IOL insertion = improved safety and reliability

Data provided by Auffarth GU

UIN: IOL17 00011 Date of Prep: April 2017

Avansee™ Preload1P provides smooth, controlled IOL insertion irrespective of IOL dioptre





[Method] Resistance forces were measured by Table-top Material Tester EZ-S (Shimadzu) when the plunger was depressed at 15mm/min. (n=1 per dioptre)

Data on file

4 Summary and conclusions

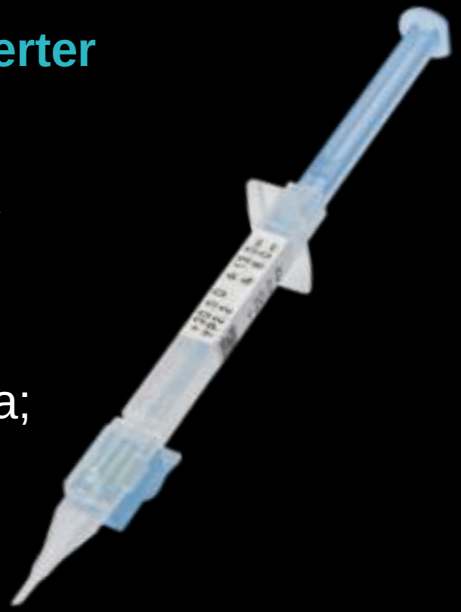
1. Convenience

Wide range of available IOLs

- Soft, flexible hydrophobic acrylic IOL available in both natural-type (yellow with proprietary blue-light filtering; YP2.2) and UV-type (clear; CP2.2)

Fully preloaded, small incision, plunger-type IOL inserter

- Ensures optimal IOL folding every time
- No IOL handling - ensures sterility and reduces the risk of infection
- Preparation for IOL insertion in only 3 simple steps
- Allows insertion through a small incision (2.4mm cornea; 2.2mm sclera cornea)



2. Control

Simple, reliable, controlled lens insertion

- Unique plunger stabilises the lens attitude and movement during IOL insertion
- Angled nozzle consistently releases the lens in the correct position
- Avansee Preload1P ensures a low delivery force across the full range of dioptres
  - Can be used with one hand
  - Minimises the risk of IOL damage

Smooth, controlled lens unfolding after insertion

- 1-piece (1P) modified C-loop haptic with an indented surface prevents the haptic sticking to the lens
- Smooth lens unfolding after insertion

3. Confidence (1)

Glistening-free optics

- Advanced-design optics made using a stringently-controlled cast-moulded method resulting in a uniform and highly cross-linked polymer
  - Glistening-free optic both *in vitro* and *in vivo*
  - Optical purity unlikely to deteriorate over time

Low risk of PCO

- 360 degree square edge extending to the optic-haptic junction designed to reduce the risk of lens epithelial cell migration and PCO
- Unique haptics maintain space and aid adhesion between the anterior and posterior capsules

3. Confidence (2)

Visual acuity largely unaffected by misalignment

- Retains the spherical aberration of the eye

Proven long-term safety

- Used extensively in Japan with a very low incidence of adverse events (0.009%) and serious adverse events (0.0009%)

Advanced design ensures correct lens placement, every time