Smart PLUG™

The Intelligent Solution to Dry Eye

Using innovative technology to set a new standard in Punctal Occlusion Devices

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Professor Weber earned his BS degree from the University of Chicago in 1963 and his PhD in Chemistry from Harvard University in 1968. He joined University of Southern California as an Assistant Professor in 1968 and has been a full Professor since 1978.

Professor Weber's main research area includes synthesis of stereo-regular polycarbosilanes, functional polysiloxanes, and copolymers thereof as well as their applications as ceramic precursors and functional silicones. Both of them have been extensively studied as medical implant materials. He is the author or co-author of approximately 250 publications, nine patents, and two books.

Professor Weber believes the use of the thermosensitive hydrophobic acrylic polymer for SmartPlug is just a beginning of an era where an increasing number of smart materials find their uses in the medical field. The advances in smart material research have resulted in numerous medical devices, which in one way or another have a smart function – sensing a stimulus and responding accordingly to give a useful function.

Inventor, Stephen Zhou, Ph.D.

Dr. Stephen Zhou earned his BS and MS degrees in Organic Chemistry in China, and a Ph.D. in Polymer Material Sciences from the University of Southern California, USA. Following a period as Director of Research for Pharmacia Corporation, Dr. Zhou joined Medennium in 1999 as Vice President of Research. Since 1990 Dr. Zhou has received patents for a high refractive index silicone material, heparin surface modification, hydrogel materials, and several patents in the area of "smart" materials; notably drug delivery devices, accomodative lenses and SmartPlug.

Clinical Investigator, Christian Spaleck, M.D.

Christian Spaleck, M.D., did his medical training and residency at the University of Munich, Germany. Dr Spaleck is in group practice in Eichstätt and in private practice at the Ambulatory Surgery Center in Ingolstadt, Germany; where he specializes in cataract and refractive surgery. Dr Spaleck is an active member of the European Society of Cataract and Refractive Surgery (ESCRS) presenting several papers at their annual meeting and a member of the American Society of Cataract and Refractive Surgery (ASCRS), with specific involvement in the ASCRS Special Interest Group for Intraocular Lenses. He has coauthored "The Atlas of Cataract Surgery", (Martin Dunitz, 1999). Dr Spaleck is a clinical investigator for the SmartPlug.

Introduction

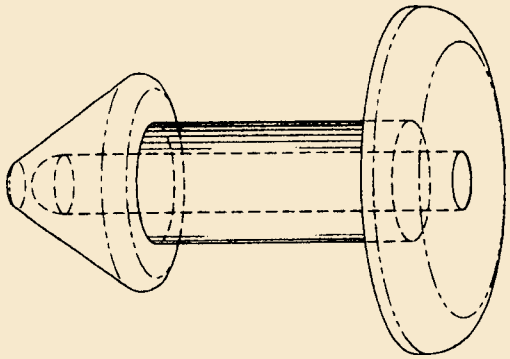
Dry Eye Syndrome

The causes of dry eye syndrome are varied and complex, however the symptoms of dryness, redness, grittiness or related ocular sensations derive from an imbalance in the quantity or quality of tears. The incidence of dry eye syndrome is expected to increase substantially as a consequence of nerve damage due to LASIK procedures[1] and cosmetic eyelid surgery (i.e. blepharoplasty). Treatments include use of artificial tear eyedrops, in which effectiveness is limited by patient compliance, or physically plugging the punctum, the lacrimal drain, thereby increasing the residence time of the tear film[8]. The punctum can be plugged irreversibly by cautery or laser treatment, or reversibly by a device called a punctum plug[6]. Insertion of punctum plugs has been demonstrated to be an effective treatment for dry eye syndrome[2, 3, 4, 5, 12].

Currently used punctum plugs

Punctum plugs have been in use for more than 20 years, during which time their design has changed little[3, 6]. Usually made of silicone, they consist of a conical head, a cylindrical body which is sometimes ribbed, and a cap. The plug is inserted head-first into the punctum with the cap exposed. Some patients experience irritation from the protruding cap as they blink. The conical head and ribs or other similar features are intended to resist extrusion of the plug, which can occur within 3 months in up to 50% of cases[2].

A conventional punctum plug



To insert a conventional punctum plug, the physician or optometrist first must use a gauging device to measure the patient's punctum, and based on the measurement, chooses one of 5 plug sizes from inventory. Because these plugs are made of flexible silicone, which is not rigid enough to simply insert directly into the punctum, the punctum must be dilated. This allows about 30 seconds to insert a punctum plug before the punctum closes and grips the plug.

Silicone punctum plugs can migrate downstream in the lacrimal drain system and become irretrievable, in rare cases causing inflammation, dacryocyctitis, or canaliculitis[7, 9, 11]. Growth and adherence of tissue around the very design features intended to help resist extrusion of the traditional punctum plug from its normal, intended location complicate its removal, sometimes necessitating surgery.

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A "Smart" Material Allows an Advanced Punctum Plug Design

SmartPlug employs a novel design (US Patent No. 6,234,175B1) to greatly simplify insertion of the device while eliminating the possibility of ocular irritation due to cap protrusion. The technological leap that made SmartPlug possible was development of a new "smart" material by polymer scientists at Medennium. A "smart" material can be defined as a material that alters its physical properties in response to an external stimulus. The recent emergence of various "smart" materials and their diverse applications represent the cutting edge of materials science[10].

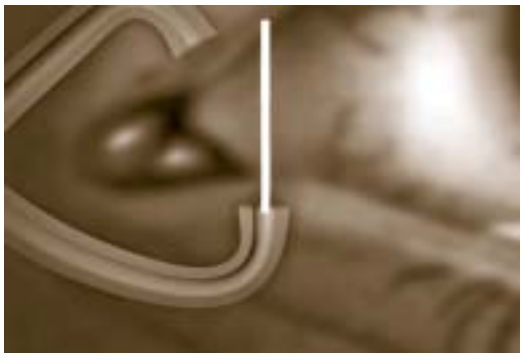
The "smart" material developed for SmartPlug alters its physical state between a rigid solid and a soft gel in response to temperature changes in its environment. This thermosensitive hydrophobic acrylic material is solid at room temperature but becomes a soft gel at body temperature (or at any temperature above 30°C). The rigidity of the "smart" material at room temperature allows insertion of the rod shaped SmartPlug without prior dilation of the punctum.

After insertion, as SmartPlug equilibrates to body temperature, the "smart" material softens and expands to fit the patient's punctum. This expansion force fixates the SmartPlug in the vertical portion of the punctum.

The thermosensitive hydrophobic acrylic material of SmartPlug has two "smart" properties. The first "smart" property is its transition from rigid solid to soft gel at around 30°C. The second "smart" property manifests itself while it is expanding in diameter from 0.4 mm up to 1 mm during the temperature induced solid to gel transition. This expansion in diameter is accompanied by a decrease in the length of SmartPlug.

When the force exerted by the expansion of SmartPlug equals the force of resistance of the surrounding tissue of the punctum, expansion ceases. This second "smart" property of the thermo sensitive hydrophobic acrylic material causes SmartPlug to conform to the shape of the patient's punctum.

The rigidity of the "smart" material at room temperature allows insertion of the rod shaped SmartPlug without prior dilation of the punctum. After insertion, as the SmartPlug equilibrates to body temperature, the "smart" material softens and expands to fit the patient's punctum. This expansion in diameter is accompanied by a decrease in the length of the SmartPlug.



SmartPlug Before Insertion

SmartPlug In Final Position and Shape

Medennium

Insertion of SmartPlug™

SmartPlug is packaged in a silicone carrier which prevents premature expansion due to elevated temperature. Removal from its carrier is simplified by using forceps with a central groove (Medennium Model 502). SmartPlug is a rigid solid at room temperature, formed in a prestretched slender rod ready for immediate insertion. The rod is approximately 0.4 mm in diameter and rigid, allowing insertion without prior punctual dilation. Because SmartPlug expands in diameter once inserted into the patient's punctum, one size SmartPlug fits a range of punctum sizes, thus measurement of the patient's punctum is unnecessary.

Centrally grooved forceps (Medennium Model 502), may also be used for insertion. Since the SmartPlug is longer than a collagen plug (9 mm as compared to 2 mm for collagen plugs), it is designed to be easier to see and to grasp. Two-thirds of SmartPlug is inserted into the punctum and one-third is left protruding from the punctum. Immediately following insertion, body heat causes SmartPlug to expand in diameter, conforming to the patient's punctum. A concomitant decrease in length "draws in" the portion of SmartPlug left outside the punctum. There is no protruding cap left externally. SmartPlug in its final position is completely contained within the lower vertical punctum.

Removal of SmartPlug is via irrigation. Simply introduce a cannula into the lower punctum and irrigate using a syringe of saline solution. The downward pressure of the saline on SmartPlug overcomes the expansion force that is holding SmartPlug in place. In addition, SmartPlug's hydrophobic material becomes slippery when bathed in the irrigating solution to eliminate tissue adhesion. This property combined with the uniform shape of the plug and gel-like consistency is designed to facilitate the complete passage through the lacrimal system. The small size and gel like nature of the plug means that it may not always be identified.

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Biocompatibility

The thermosensitive hydrophobic acrylic material used in SmartPlug was tested as recommended in ISO 10993 *Biological Evaluation of Medical Devices* and the FDA Blue Book Memorandum material biocompatibility matrix. The results *(Table 1)* indicate that the material used in SmartPlug is safe and fully biocompatible.

Table 1. Biocompatiblity of Smart Plug™ Material[13]

Test	Result
ISO Agarose Overlay (extract and direct)	Non-toxic
ISO MEM elution	Non-toxic
Ames Assay (mutagenicity)	Non-Mutagenic
ISO Implantation Test	Acceptable
Maximization Sensitization	0% Sensitization
Exhaustive Extraction - Non-Polar	0.2% Extractables
Exhaustive Extraction - Aqueous	0.0% Extractables
Acute Systemic Toxicity	Non-toxic
Subchronic Toxicity Assay	Non-toxic

The results of the study suggest that SmartPlug is a safe and effective treatment for dry eye syndrome.

Human Clinical Study of SmartPlug™ [13]

A prospective, randomized, open-label evaluation of SmartPlug and a commercial silicone punctum plug was performed in a clinical study of 31 patients with dry eye syndrome in Bellflower, California, USA. SmartPlug was inserted in the lower punctum of one eye and a silicone punctum plug in the other eye. Patients were evaluated for 3 months, after which SmartPlugs were removed by irrigation and the conventional silicone plugs were removed directly. Patients were further evaluated at 2 weeks post-removal.

Data from both plugs show increased basal tear secretion as determined by objective measurement, and decreased itching, blurring, dryness, and soreness, as evaluated subjectively. Eyes treated with SmartPlug showed less erosion and surface defects as determined by fluorescein staining, whereas eyes treated with silicone punctum plugs showed more devitalized tissue as determined by Rose Bengal staining.

In addition, SmartPlug treated eyes (but not the silicone punctum plug treated eyes) were evaluated as having decreased burning and stinging, foreign body sensation, tearing, discharge and photophobia symptoms.[13]

No unusual findings were observed by slit-lamp microscopy. Notably, 6 silicone punctum plugs were extruded during the study and had to be replaced. No SmartPlug was extruded.

Removal of SmartPlugs consisted of irrigation with an isotonic saline solution. A lower punctum irrigation test of each subject established a patent lacrimal system.

Following the 2-week period without punctum plugs at the end of the study, all patients reverted to their previous dry eye symptoms.

The results of the study suggest that SmartPlug is a safe and effective treatment for dry eye syndrome.

Treatment of dry eye syndrome by insertion of SmartPlug into the punctum offers several advantages over currently available silicone punctum plugs *(Table 2)*. Because the one size of SmartPlug is designed to fit a range of puncta, an inventory of multiple sizes of plugs need not be maintained. Measurement of the patient's punctum is no longer necessary, nor is the gauging device used for this purpose. Because SmartPlug is designed to expand after insertion to fit the contours inside the punctum, dilation of the punctum (necessary to insert silicone punctum plugs) is eliminated. SmartPlug is a rigid rod at room temperature, simple to insert with grooved forceps – a specialized inserter is not required. Once inserted, no cap protrudes to potentially irritate or scratch the patient's cornea. SmartPlug is to be removed by simple irrigation with isotonic saline.

Table 2. Comparison of SmartPlug™ with silicone punctum plugs

	SmartPlug™	Silicone plugs
Gauging patient's punctum	Not necessary	Required
Sizes	One size	5 to 7 sizes
Dilation of punctum	Not necessary	Required
Insertion device	Forceps	Specialized inserter
Protruding cap	None	Yes

Conclusion

SmartPlug represents an intelligent application of materials technology setting a new standard in punctal occlusion devices. SmartPlug offers real benefits over currently used silicone punctum plugs both to physicians and to patients suffering from dry eye syndrome.

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A New Way of Seeing

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Approved for sale in Canada.
Limited by Federal law to investigational use in the USA.

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