

# Polyethylene Glycol Hydrogel Polymer Sealant for Vitrectomy Surgery

## An In Vitro Study of Sutureless Vitrectomy Incision Closure

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**Objective:** To test a novel hydrogel sealant to secure sutureless sclerotomies under variable intraocular pressure conditions.

**Methods:** In cadaver eyes, 23- and 20-gauge (G) sclerotomies were constructed. Sixteen 23-G beveled sclerotomies were constructed in 4 eyes: 8 of the incisions were treated with hydrogel sealant, while 8 were left bare. All sclerotomies were monitored for leaks while the intraocular pressure was elevated. The pressure on incision leakage was recorded as the leak pressure (maximum tested=140 mm Hg). Additionally, sixteen 20-G sclerotomies were constructed in 4 other eyes: 8 of the incisions were treated with hydrogel sealant, while 8 were sutured. These incisions were similarly pressure tested.

**Results:** Among the 23-G incisions, hydrogel sealant application to the incisions significantly increased the leak pressure relative to bare incisions: mean (SE), 131.8 (8.2)

vs 39.5 (5.2) mm Hg, respectively ( $P < .001$ ). Only 1 of the 8 sealant-treated 23-G incisions leaked below 140 mm Hg, compared with all of the 8 bare incisions. Among the 20-G incisions, there was no difference in leak pressure among sealant-treated and sutured incisions: mean (SE), 140.0 (0.0) vs 136.3 (3.8) mm Hg, respectively ( $P = .35$ ). None of the 8 sealant-treated 20-G incisions leaked below 140 mm Hg, compared with 1 of the 8 sutured incisions.

**Conclusions:** Hydrogel sealant significantly increased the leak pressure among 23-G incisions relative to 23-G bare incisions and was equivalent to suturing among 20-G incisions.

**Clinical Relevance:** Hydrogel sealants effectively close vitrectomy incisions and may decrease the incidence of postoperative endophthalmitis and hypotony.

*Arch Ophthalmol.* 2011;129(3):322-325

**M**ICROINCISIONAL VITRECTOMY surgery (MIVS) techniques have gained acceptance by vitreoretinal surgeons worldwide. In the 2008 Preferences and Trends survey conducted by the American Society of Retina Specialists,<sup>1</sup> approximately 71% of respondents used a MIVS system (23 or 25 gauge [G]) 80% to 100% of the time when managing an epiretinal membrane without any other co-existent retinal abnormalities.

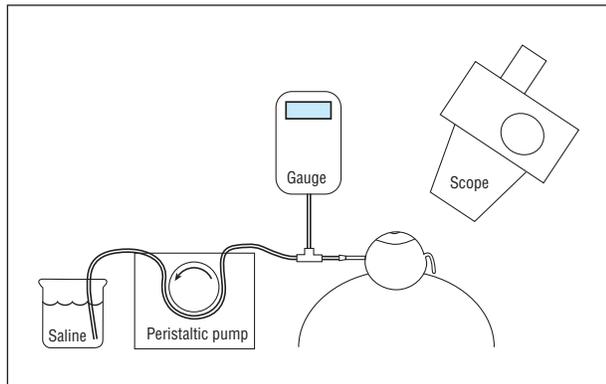
Microincisional vitrectomy surgery procedures do not routinely require sutures, and they have the advantages of improved patient comfort, reduced operating times, decreased incidence of surgically induced corneal astigmatism, and rapid visual rehabilitation. Despite these advantages, concerns regarding the safety of the procedures related to postoperative endophthalmitis and early postoperative hypotony still remain.<sup>2-7</sup>

Following MIVS procedures, hypotony may occur as a result of outflow

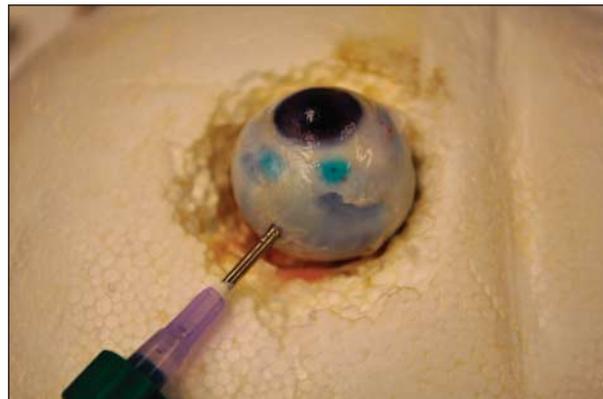
of fluid from the vitreous cavity, whereas endophthalmitis may occur as a result of inflow of ocular surface fluid. As an intervention to reduce the incidence of these complications, wound closures with sutures, cyanoacrylate glue, tissue fibrin glue, and other complex adhesives have been suggested.<sup>8,9</sup> According to the 2009 Preferences and Trends survey conducted by the American Society of Retina Specialists,<sup>10</sup> approximately 64% of respondents sutured at least 1 of the sclerotomies in 23-G MIVS.

These interventions have their limitations. Suture application prolongs operative time, may require conjunctival incisions, and induces corneal astigmatism. Furthermore, suture sensation compromises patient comfort. Cyanoacrylate glue produces heat and settles rapidly into an inflexible and friable material. Patients experience discomfort from the rough and dry surface of cyanoacrylate glue, and cyanoacrylate glue has to be used in conjunction with a bandage contact lens when used for corneal indications. The method of cya-

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**Figure 1.** Schematic of test apparatus used. Following appropriate incision treatment, the intraocular pressure was slowly increased until incision leakage was noted with a surgical microscope.



**Figure 2.** Cadaver eye with conjunctiva removed and side-inserted pressure cannula. The blue colorant in the synthetic hydrogel ocular bandage allows for visualization following application over 23-gauge incisions.

noacrylate glue application can be cumbersome and requires careful placement of a precise amount of adhesive on a dry surface to seal ocular incisions. Tissue fibrin glue (Tisseel; Baxter AG, Vienna, Austria) has been used as an alternative to sutures in a small surgical case series for closure of MIVS and 20-G vitrectomy incisions.<sup>8</sup> Fibrin glue carries the theoretical risk of anaphylaxis and disease transmission.<sup>11</sup>

Synthetic polymers such as polyethylene glycol (PEG) hydrogel polymers are safe and biocompatible. These compounds can be engineered to form hydrogels of varying absorption, consistency, and flexibility depending on the indication of use. We designed a study to test the utility of a PEG polymerizable adherent synthetic hydrogel ocular bandage (Ocular Therapeutix, Inc, Bedford, Massachusetts) to seal sutureless 23-G vitrectomy incisions as well as to test its integrity for sealing 20-G vitrectomy incisions that have traditionally been closed with sutures.

## METHODS

Eight fresh, intact, human whole globes were obtained from the Michigan Eye Bank. Each eye was analyzed for the absence of conjunctiva. The experimental setup consisted of a 16-G needle (BD 305197; BD, Franklin Lakes, New Jersey) inserted into the side of each globe and secured with cyanoacrylate glue (910FS; Permabond, LLC, Pottstown, Pennsylvania) to prevent leakage. This was attached to a 3-way connector that communicated with a pressure gauge (ITX-20; Comark Corp, Medfield, Massachusetts) and a peristaltic pump (mini-pump ITX-10; VWR International, LLC, Radnor, Pennsylvania). Normal saline was used to vary the pressure in the globe (**Figure 1** and **Figure 2**). After the globes were secured in a styrofoam head mount, physiological intraocular eye pressures (IOPs) were verified.

All surgical procedures were performed by an experienced vitreoretinal surgeon (S.M.H.). In group A, a total of 4 eyes underwent creation of 23-G vitrectomy beveled incisions (trocar and cannula system of Alcon, Inc, Fort Worth, Texas) along with incision manipulation with a 23-G vitreous cutter for a duration of 5 minutes. Incisions were made in 2 of the quadrants, fashioned 4 mm posterior to the limbus. After removal of the vitreous cutter and cannula, the IOP was slowly elevated and the IOP at which the incisions leaked was recorded by observing for fluid leak with a Weck-Cel Sponge (Medtronic, Inc, Jacksonville, Florida) under the operating microscope. The IOP was confirmed using a handheld IOP-measuring device

(Tono-Pen; Mentor Ophthalmics, Norwell, Massachusetts). The incision was then sealed using cyanoacrylate glue and was confirmed to be watertight using a Weck-Cel sponge before proceeding to the next incision. The first 2 incisions served as controls in each eye (n=8 total). The third and fourth incisions were similarly created and manipulated in the other 2 quadrants, and the hydrogel ocular bandage was applied. These served as the experimental group (n=8 total). Using a sponge-tipped applicator, a small amount (<5  $\mu$ L) of liquid precursor was transferred to the incision. Within 2 minutes of application, the hydrogel-treated incisions were similarly pressure tested. If no leak was noted up to 140 mm Hg, pressure testing was stopped and that pressure was used in calculations as the leak pressure. The order of treatment (control or hydrogel treated first) was alternated between eyes.

In group B, 20-G vitrectomy straight incisions were constructed with an MVR blade (EG-5560; Eagle Labs, Rancho Cucamonga, California) in 4 eyes. Eight incisions were closed with a 7-0 polyglycolic acid suture (PolySyn; Angiotech Pharmaceuticals, Inc, Vancouver, British Columbia, Canada), while 8 incisions were sealed with hydrogel *without* an underlying closure suture. Each of the incisions was subjected to the same pressure testing as described for group A.

The statistical significance of differences in incision leak pressure was determined using a 2-tailed heteroscedastic *t* test (Excel 2007; Microsoft Corp, Redmond, Washington).  $P < .05$  was considered to be statistically significant.

## RESULTS

### GROUP A

Group A included sixteen 23-G MIVS incisions from 4 eyes. Sclerotomy sites sealed with hydrogel were compared with bare (ie, without hydrogel) sclerotomy sites. All 8 bare incisions leaked with increasing IOP. The mean (SE) IOP at which the bare incisions leaked was 39.5 (5.2) mm Hg (**Table**). One hydrogel-treated 23-G incision leaked at 74.2 mm Hg, while the remaining 7 incisions sustained pressures of up to 140 mm Hg without leakage for a mean (SE) leak pressure of 131.8 (8.2) mm Hg ( $P < .001$ ).

### GROUP B

Group B included sixteen 20-G sclerotomy incisions from 4 eyes. Sclerotomy sites closed with sutures were com-

**Table. Data From 23- and 20-Gauge Incisions<sup>a</sup>**

Incision	Treatment	Leak Pressure, mm Hg	Incision	Treatment	Leak Pressure, mm Hg
<b>Group A, 23-Gauge Incision</b>					
1A	Incision only	46.0	1C	Incision + gel	140.0
1B	Incision only	51.0	1D	Incision + gel	74.2
2C	Incision only	40.0	2A	Incision + gel	140.0
2D	Incision only	67.0	2B	Incision + gel	140.0
3A	Incision only	24.0	3C	Incision + gel	140.0
3B	Incision only	29.0	3D	Incision + gel	140.0
4C	Incision only	28.7	4A	Incision + gel	140.0
4D	Incision only	30.0	4B	Incision + gel	140.0
Mean (SE)		39.5 (5.2) <sup>b</sup>			131.8 (8.2) <sup>b</sup>
<b>Group B, 20-Gauge Incision</b>					
5A	Incision + suture	110.0	5C	Incision + gel	140.0
5B	Incision + suture	140.0	5D	Incision + gel	140.0
6C	Incision + suture	140.0	6A	Incision + gel	140.0
6D	Incision + suture	140.0	6B	Incision + gel	140.0
7A	Incision + suture	140.0	7C	Incision + gel	140.0
7B	Incision + suture	140.0	7D	Incision + gel	140.0
8C	Incision + suture	140.0	8A	Incision + gel	140.0
8D	Incision + suture	140.0	8B	Incision + gel	140.0
Mean (SE)		136.3 (3.8) <sup>c</sup>			140.0 (0.0) <sup>c</sup>

<sup>a</sup>If no leak was detected at 140 mm Hg, testing was stopped and that value was recorded as the leak pressure.

<sup>b</sup>Two-tailed *t* test, *P* < .001.

<sup>c</sup>Two-tailed *t* test, *P* = .35.

pared with sclerotomy sites sealed with hydrogel. On elevation of IOP, 1 sutured incision leaked at 110 mm Hg, while the remaining 7 sutured incisions withstood 140 mm Hg without leaking. The mean (SE) leak pressure was 136.3 (3.8) mm Hg. In comparison, all 8 hydrogel-sealed incisions withstood 140-mm Hg pressure without leaking (mean [SE], 140.0 [0.0] mm Hg) (*P* = .35).

#### COMMENT

The hydrogel sealant demonstrated a secure, watertight sealing effect for sutureless 23-G vitrectomy incisions as well as 20-G vitrectomy incisions. In the setting of this *in vitro* experiment, equivalence to sutured wound closures was observed. Our laboratory experiment showed that the hydrogel seal was sufficiently strong and maintained ocular integrity at IOPs beyond those experienced by the globe during eyelid blinking, eye rubbing, coughing, or eyelid squeezing.<sup>12</sup>

The hydrogel sealant is formed by a reaction of ester-functionalized PEG and trilycine. Polyethylene glycol is one of the most widely used polymers in the pharmaceutical industry in both solid and liquid forms owing to its water solubility and inert nature, and it is frequently used as a component in topical drug formulations. Many ophthalmic products including lubricant eye drops, ophthalmic corticosteroids, ocular decongestants, and artificial tears also contain PEG. The hydrogel consists of about 95% water, with the solids consisting of PEG cross-linked with trilycine. The link between each PEG and trilycine molecule contains a hydrolyzable segment. Thus, in the months following implantation, the hydrogel gradually weakens and then liquefies, releasing the individual PEG and trilycine molecules. This gel degradation process is solely dependent on the pres-

ence of water and is not affected by enzymes. Trilycine is a synthesis product of L-lysine, which plays an important role in the formation of collagen and is a naturally occurring essential amino acid. The PEG and trilycine molecules are rapidly absorbed and cleared from the body via renal filtration.

Using a foam-tipped applicator, a small drop of precursor is applied to the incision, where the liquid polymerizes (solidifies) within 30 seconds without producing heat. This hydrogel also contains a blue colorant (FD&C blue 1) that acts as a visualization agent to assist the surgeon in determining hydrogel thickness and the location of the application. The blue colorant diffuses from the gel within hours of application, leaving an optically clear, transparent, smooth, adherent, lubricious bandage over the incision. Because the components are not derived from animal or human products, there is no potential for viral transmission. Similar PEG-based *in situ*-forming hydrogels are approved as medical devices for use as dura mater sealants, lung sealants, and abdominopelvic adhesion barriers.<sup>13</sup> These compounds have been engineered to form adherent hydrogel coatings of varying absorption, consistency, and flexibility depending on the indication for use.

The hydrogel has been shown to be noncytotoxic, nonirritating to the ocular surface, and nonsensitizing and demonstrates no acute systemic toxic effects. Following application, the hydrogel bandage adheres to the incision and then sloughs off as the underlying tissue heals. A separate study in a different set of eyes has tested the ability of the hydrogel bandage to prevent the entry of ocular surface fluid into sutureless incisions. The eyes in this study underwent histological processing. On microscopic examination, the hydrogel bandage was seen as a hematoxylin-stained covering over the ocular surface.<sup>14</sup>

Sutureless vitrectomy incisions have been shown to allow ocular surface fluid ingress.<sup>15,16</sup> The absence of immediate postoperative closure as well as the architecture of the wound may predispose to postoperative endophthalmitis as well as early postoperative hypotony.<sup>17</sup> More recently, injection of subconjunctival antibiotics at all incision sites in sutureless vitrectomy procedures has been proposed as there may be vitreous prolapse at these locations.<sup>18</sup> However, a potential concern is the entry of high antibiotic concentrations into the vitreous cavity, which could be toxic to the retina, especially in the air- or gas-filled eye. Furthermore, it has been observed that gas fill after certain retinal procedures may be less than expected after MIVS as gas may leak out of a poorly constructed MIVS port. A sealant applied over these ports would ensure a secure seal, thereby possibly decreasing rates of endophthalmitis or hypotony and rendering sutures unnecessary. In our experience, the hydrogel is found to be elastic and conforms to the contour of the globe where it is applied. This feature may enhance patient comfort.

This laboratory experiment suggests that the hydrogel bandage may allow a secure and strong closure of sutureless 23-G vitrectomy incisions. Furthermore, future research may show that the hydrogel functions as a novel substitute for sutures in standard 20-G vitrectomy incisions. This technology is a significant step toward making sutureless incisions safer as it may prevent incision leakage as well as the entry of microorganisms into the eye.

**Submitted for Publication:** December 29, 2009; final revision received May 13, 2010; accepted May 31, 2010.

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**Author Contributions:** Dr Singh had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Financial Disclosure:** Dr Hariprasad has been a consultant for Alcon, Allergan, Genentech, Baxter, OD-OS, Ocular Therapeutix, Optos, and Bayer and has participated in speaker's bureaus for Alcon, Allergan, and Genentech.

**Funding/Support:** Ocular Therapeutix provided samples of synthetic hydrogel ocular bandage to conduct this study.

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