Table 7: Mean Percent Change Difference in Endothelial Cell Counts

<table>
<thead>
<tr>
<th>Population</th>
<th>Mean Percent Change</th>
<th>Lower 95% Confidence Limit</th>
<th>Upper 95% Confidence Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT: All Randomized Subjects</td>
<td>1.05 (SE 0.80)</td>
<td>-0.53</td>
<td>2.64</td>
</tr>
<tr>
<td>Safety: All Paired-Eye Subjects</td>
<td>1.11 (SD 1.19)</td>
<td>-0.52</td>
<td>2.74</td>
</tr>
</tbody>
</table>

- Percent Change=Postop ECC Minus Preop ECC/Preop ECC with Difference= Feronmed OVD Percent Change Minus Control OVD

Table 8: Change in ECC from Baseline to 3 Months (Safety Population-Paired Eye Subjects)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>Fermented</td>
<td>206</td>
<td>2552.96</td>
<td>361.65</td>
</tr>
<tr>
<td>Control</td>
<td>206</td>
<td>2543.75</td>
<td>355.64</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>206</td>
<td>9.21</td>
<td>131.54</td>
<td></td>
</tr>
<tr>
<td>3 Months</td>
<td>Fermented</td>
<td>206</td>
<td>2410.82</td>
<td>420.16</td>
</tr>
<tr>
<td>Central</td>
<td>206</td>
<td>2377.14</td>
<td>433.53</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>206</td>
<td>33.68</td>
<td>313.36</td>
<td></td>
</tr>
<tr>
<td>Percent Change</td>
<td>Fermented</td>
<td>206</td>
<td>-5.55</td>
<td>9.99</td>
</tr>
</tbody>
</table>

1. The difference between OVD groups at preoperative visit was not statistically significant (p-value=0.3162)
2. Percent Change=(Postop ECC Minus Preop ECC)/Preop ECC)
3. [Healon PRO OVD](https://www.healon.com) is a sterile, nonpyrogenic, viscoelastic preparation supplied in disposable glass syringes, delivering 0.85 mL or 0.55 mL sodium hyaluronate (10 mg/mL) dissolved in physiological sodium chloride phosphate buffer (pH 6.8 – 7.6). Each mL of Healon PRO OVD contains 10 mg of sodium hyaluronate.

The Healon PRO OVD syringes are terminally sterilized and aseptically packaged.

A sterile single-use 27 G cannula is enclosed in the 0.55 mL and 0.85 mL boxes.

Refrigerated Healon PRO OVD should be allowed to attain room temperature (approximately 30 minutes) prior to use.

For intraocular use.

Store at 2 to 8°C (36 to 46°F).

Protect from freezing.

Protect from light.

Definition of symbols on cannula, syringe-, blister label and carton.

- **Caution, see instructions for use**
- **See instructions for use**
- **Do not reuse**
- **Protect from light**
- **Do not use if the packaging has been opened or damaged**
- **Protect from freezing**
- **Temperature limitation**
- **Temperature limitation**
- **Sterilized using steam**
- **Sterilized using irradiation**
- **Manufacturer**
- **Batch code**
- **Use by (YYYY/MM/DD; year month-day)**

**References**


**Instructions**

1. **Sterile opening technique**
   - Tear off the paper covering.

2. **Assembly**
   - Press the plunger completely into the holder so that the needle perforates the membrane.

3. **Remove the plastic rod.**

4. **Screw the plastic rod into the plunger.**
   - Connect the cannula.

5. **Check for proper function.**
   - System is now ready.

For single use only

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Sodium Hyaluronate

**Product Information**

**Description**

The Healon® PRO Ophthalmic Viscosurgical Device (OVD) is a sterile, nonpyrogenic, viscoelastic preparation of a highly purified, high molecular weight fraction of sodium hyaluronate. The sodium hyaluronate used in the Healon® PRO OVD contains (10 mg/ml of sodium hyaluronate dissolved in physiological sodium chloride phosphate buffer pH 4.8 – 7.4). This high molecular weight polymer is made up of repeating disaccharide units of sodium glucuronic acid and sodium glucosamine linked by 1-3 and 1-4 glycosidic bonds.

**Characteristics**

Sodium hyaluronate is a physiological substance that is widely distributed in the extracellular matrix of connective tissues throughout the body. For example, it is present in the vitreous and aqueous humor of the eye, the synovial fluid, the skin and the umbilical cord. Sodium hyaluronate polymerizes from high to lower molecular weights and is not chemically different from either other.

The Healon® PRO OVD uses a specific fraction of sodium hyaluronate developed as an ophthalmic viscosurgical device and a series of stringent procedures. It is specific in:

1. It has a high molecular weight.
2. It is reported to be nonantigenic.
3. It has a high molecular weight.
4. It has a high viscosity.

Furthermore, the 1% solution of the Healon® PRO OVD is transparent, is reported to remain in the anterior chamber for less than 6 days and protects corneal endothelium and other.

**Uses**

The Healon® PRO OVD is indicated for use in a surgical air interface (intracameral, extracameral), iris manipulation, correction of power, filtration surgery and removal of foreign objects.

**Contraindications**

The Healon® PRO OVD is contraindicated for use in the presence of an active eye infection in the instillation of the Healon® PRO OVD serves to maintain a deep anterior chamber during surgery, allowing for efficient manipulation with less trauma to the corneal endothelium and other surrounding tissues.

Furthermore, its viscosity helps to push the back the viscose and form prevention of a postoperative flat chamber.

In posterior segment surgery the Healon® PRO OVD serves as a surgical aid to poorly separate, transparent, narrow and hold tissues. The Healon® PRO OVD creates a clear field of view thereby facilitating into and post-operative inspection of the retina and photoreceptors.

**Contraindications**

As there are no known contraindications to the use of the Healon® PRO OVD when used as recommended.

**Precautions**

These normally associated with the surgical procedure being performed.

Overfilling the anterior or posterior segment of the eye with the Healon® PRO OVD may cause increased intraocular pressure, glaucoma, or other anterior chamber.

Postoperative intraocular pressure may also be elevated as a result of presencing glucose, preservative outdated due to operative procedures and therapeutic reasons, including systemic antiseptic agents, absence of internalization to form cortical structures, and by blood flow in the anterior vitreous chamber in the anterior segment.

Since the exact role of this factor is difficult to predict in each individual case, the following precautions should be considered:

- Don’t overtrop the eyes with the Healon® PRO OVD (caution in glaucoma surgery - see Application Advisory).
- In posterior segment procedures in aphakic diabetic patients special care should be associated to avoid using large doses of the Healon® PRO OVD.
- Remove any Healon® PRO OVD by irrigation and/or aspiration at the close of surgery (see Application Advisory).
- Contend react the intraocular pressure, especially during the intramural postoperative period.
- Postoperative inflammation with no adverse effect associated with the potential problem.

Cereals should be kept at avoiding provoking or bubbles behind the Healon® PRO OVD.

Because of reports of occasional release of minute rubber particles, presumably formed by degradation of the Healon® PRO OVD, x-ray examination should not be used after the break down has been damaged.

**Adverse reactions**

The Healon® PRO OVD is extremely well tolerated after injection into human eyes.

A transient rise of intraocular pressure (IOP) spikes exists with the use of the OVD, which potentially is observed with saline solution. Therefore, it is recommended that the Healon® PRO OVD be removed from the eye by gently irrigating and removing with sterile irrigation solution to reduce the risk of early post-operative IOP spikes.

Do not use the scleral stromal patch has been damaged.

**Applications**

1. Cataract surgery - IOL implantation

To remove surgical complications, on their own, or in combination with other surgical complications.

2. Glaucoma filtration surgery

A sufficient amount of the Healon® PRO OVD is slowly and carefully introduced through a corneal incision to reconstitute the anterior chamber.

Further injection of the Healon® PRO OVD can be continued allowing it to extrude into the subcapsular/cortical fiber zone and through the weakened anterior fiber slit.

3. Corneal transplant

Current complications exclude any increase in intraocular pressure by a large amount of the Healon® PRO OVD.

4. Retinal detachment

The Healon® PRO OVD may be also used as surgical instruments and the IOP prior to insertion.

5. Additional Healon® PRO OVD can be injected during surgery to replace any Healon® PRO OVD lost during surgery (see Application Advisory).

6. Glaucoma filtration surgery

In conjunction with performing of the trabeculectomy, the Healon® PRO OVD is injected slowly and carefully introduced into the anterior chamber.

Further injection of the Healon® PRO OVD can be continued allowing it to extrude into the subcapsular/cortical fiber zone and through the weakened anterior fiber slit.

Current complications exclude any increase in intraocular pressure by a large amount of the Healon® PRO OVD.

7. The Healon® PRO OVD has also been used as the anterior chamber of the eye during prior to preparation to extracapsular lensectomy of the corneal stromal cell of the graft.

**Restorative surgery**

The Healon® PRO OVD is slowly introduced into the vitreous cavity. By directing the injection, the Healon® PRO OVD can be used as a viscoelastic preparation (e.g. opacified membranes) away from the retina for cell release and release of traction.

The Healon® PRO OVD serves to maintain a deep anterior chamber during surgery, allowing for efficient manipulation with less trauma to the corneal endothelium and other surrounding tissues.

8. The Healon® PRO OVD has also been used in the anterior chamber of the eye during prior to preparation to extracapsular lensectomy of the corneal stromal cell of the graft.

**Clinical Trial Of The Fermented Healon® OVD (2016-2017)**

A clinical trial was conducted in the United States in 2016-2017 that was designed to evaluate safety and effectiveness of the fermented Healon® OVD compared to the animal-derived Healon® OVD. A total of 211 bi-weekly visits were randomized, 146 visited clinically investigated with the fermented Healon® OVD used in eye and the remaining 65 visits were randomized with 3 subjects treated in either one or both eyes across 8 states in the US. A total of 212 eye visits were randomized to the fermented Healon5® OVD (fermented group) or to the animal-derived Healon5® OVD (control group). Of the treated subjects, 208 were bilaterally treated with the fermented OVD in one eye and the control OVD in the fellow eye, and five subjects were unilateral treated.

The results of the study were revealed the non-inferiority of the fermented Healon® OVD compared to the animal-derived Healon® OVD as its end study endpoints were achieved and results compared between groups.

**Intracorneal Pressure**

The primary safety endpoint of the cumulative rate of intraocular pressure (IOP) spikes ≥30 mmHg (compared to control) was statistically non-inferior to the cumulative rate in the control group as shown in Table 7. The rate of IOP spikes ≥30 mmHg in the control group was 1.7% (95% CI 1.1-2.4). The rate of IOP spikes ≥30 mmHg in the fermented group was 0.3% (95% CI 0.0-1.1).

**Inflammation**

The distributions of the grades of inflammation for epithelial edema, stromal edema, cells, plasma, neutrophils, polymorphonuclear, and fibrin were ordered over time between OVD groups. The cumulative rates of inflammation are presented in Table 6. The most frequently reported types of inflammation were cells and fibrin. The frequency of inflammation declined in both OVD groups with the greatest frequency of inflammation occurring in early postoperative period (hours 1 and 2).