Cryopreserved Amniotic Membrane for Treatment of Corneal Conditions

Presenter: Marc Bloomenstein, OD, FAAO
Objectives

• Review of Amniotic Membrane and CryoTek Preservation Process

• Review Prokera For Use With Corneal Involved Dry Eye and Extended Pathology

• Questions
Bio-Tissue’s Industry-Leading Technology
Normal Adult Wound Healing

Our body does not achieve optimal healing on its own…

- **Residual Haze**
- **Prolonged Inflammation**
- **Scar Formation**
Scarless Fetal Wound Healing

*Speed & Quality of Healing Count!*

Giant neck mass resection at 26 weeks *in-utero*

HC-HA/PTX3, found naturally in amniotic membrane, is the critical biologic component responsible for scarless fetal wound healing.

3 months

*Courtesy of fetal surgeon, Michael Harrison, M.D. (UCSF)*
The Ocular Surface Landscape
HC-HA/PTX3 Improves the Quality of the Stem Cell Niche Environment

Normal Adult Healing
Stem Cell
Regenerative Healing with HC-HA/PTX3
Bio-Tissue’s proprietary CryoTek cryopreservation process is the ONLY technology available to eye care specialists that:

1. Provides an allograft that is equivalent to fresh tissue, maintaining the natural structure and biology of the membrane.
2. Retains meaningful quantities of HC-HA/PTX3 to activate regenerative healing
3. Retains the original tensile strength of AM, facilitating ease of handling during surgery
Where Does the Tissue Come From?

Tissue Safety & Quality Assurance

- Full Term Birth Via Elective C-Section Delivery
- Comprehensive Donor Eligibility Screening
- Track Record: 0 Reported Adverse Events
Chemical Burn

Patient Presents 8 Days after Chemical Burn

Complete Epithelium Damage

PROKERA® is placed on first day of treatment

Day 3

Day 5

Day 7

Day 10

Day 12

Day 15

Day 17

Complete Scarless Healing
Diabetic Foot Ulcer

**Diagnosis & Patient History**
Patient suffering from a chronic diabetic wound open for 5 years; failed serial debridement, wound vats, and allografts. Now the patient has formed a contralateral ulcer.

**NEOX® Treatment & Outcome**
Patient brought to the OR for sharp debridement and first NEOX® application. Second and third NEOX® applications placed in the first 4 weeks with both wounds nearly healed to date (10 weeks).

- Debridement
- Umbilical Cord #3
- 1.0 cm width x 2.0 cm length x 5 mm depth
- 4 WEEKS After Cryopreserved Umbilical Cord #1 & #2
- 10 WEEKS
Prokera®
Facilitates Healing of the Ocular Surface
• PROKERA® is the only amniotic tissue that is recognized by the FDA for wound healing. With early intervention, PROKERA® modulates inflammation and minimizes scarring therefore preventing sight threatening complications.

• PROKERA® can be used in your clinic for a wide number of ocular surface diseases with severity ranging from mild, moderate, to severe.

• PROKERA® has a unique CPT code 65778 placement on AMT without sutures that reimburses a national average of $1,440.21.
Corneal nerves play a significant role in the maintenance of corneal sensation and ocular surface health.


Benítez et al. (2004) An in vivo confocal masked study on corneal epithelium and subbasal nerves in patients with dry eye. IOVS
Purpose

To evaluate the efficacy of self-retained cryopreserved amniotic membrane (CAM) in promoting corneal nerve regeneration and improving corneal sensitivity in dry eye disease (DED)

Methodology

- This is a prospective randomized clinical trial done on 20 subjects

- Inclusion criteria included subjects 21 years and older who had moderate to severe DED, grades 2–4, as defined by the Report of the International Dry Eye Work Shop (DEWS)

- Changes in signs and symptoms, corneal sensitivity, topography, and in vivo confocal microscopy (IVCM) were evaluated at baseline, 1 month, and 3 months.
Clinical Evaluation

All subjects underwent complete ophthalmic evaluations, which included the following tests:

- Pain Score: measured subjectively using the **Visual Analog Scale (VAS)**. Range: 0 (none) to 10 (the worst).
- SPEED Questionnaire Scoring.
- Corneal Topography: measured using Nidek OPD Scan ARK 10000.
- Corneal Sensitivity: measured using the contact nylon thread Luneau 12/100mm Cochet-Bonnet Esthesiometer.
- Detection of MMP-9: measured using InflammaDry Detector.
- Central corneal in-vivo confocal microscopy: Laser IV CM assessments were performed on the central cornea using HRT III/RCM.
- Grading of DEWS score.
Key Outcomes

**Rapid Reduction of Symptoms, Pain, and Corneal Staining**

![Graph showing Corneal Staining Grading](image)

![Graph showing Pain Scoring](image)

![Graph showing SPEED Questionnaire Scoring](image)

Before Prokera

After Prokera

Key Outcomes

PROKERA® PROMOTING A LASTING EFFECT BY INCREASING CORNEAL NERVE DENSITY

Conclusions

- CAM in PKS exerts a direct positive impact on the corneal nerve regeneration. This notion is supported by the finding that nerve growth factor (NGF) known to play an important role in nerve regeneration and epithelial healing is abundantly present.

- Conventional topical anti-inflammatory therapies such as cyclosporine, corticosteroids, or nonsteroidal anti-inflammatory drugs not only can suppress inflammation but also compromise corneal nerves and subsequently delay corneal wound healing.

For example:

- Cyclosporine eye drops reduce cytokine expression in the cornea and retards regenerative sprouting from transected corneal stromal nerve trunks in an animal model.

- Additionally, corticosteroids decreased the levels of tear NGF in patients with DED.
A total of 97 eyes of 84 patients; 12 (14%) male, 69 (82%) female and 3 (4%) unknown was included in this study.

The average duration of PKS placement was 5.4 ± 2.8 days.

Upon removal the AM was intact (28%), partially dissolved (20%), totally dissolved (42%) or not stated (10%).

After removal, 74 patients (88%) demonstrated an improved ocular surface along with notable reduction of the severity of dry eye symptoms.

The overall DEWS score was significantly reduced from 3.25 ± 0.6 at the baseline to 1.44 ± 0.6 at 1 week (p<0.001), 1.45 ± 0.6 at 1 month (p<0.001), and 1.47 ± 0.6 at 3 months (p<0.001).
In 10 eyes, they found pain severity improved by 72.5% and corneal nerve density improved 36.6% after 6.1 days.
New Study: Efficacy of self-retained cryopreserved amniotic membrane for treatment of neuropathic corneal pain

- During follow up of 9.3 days, only 2 patients reported recurrence of pain.
- The study concluded that PKS/PKC provides an effective treatment approach to achieve sustained pain control in patients with NCP. This paper is the first report demonstrating positive clinical and IVCM-based results of self-retained cryopreserved amniotic membrane placement in the acute treatment of neuropathic corneal pain.
Dehydrated AM Loses:
HMW HA, HC and PTX3


**HMW Hyaluronic Acid**

- HMW HA Not Present
- HC Not Present
- PTX3 Not Present

**Heavy Chain**

**Pentraxin 3**
### The Unique Advantages of Cryopreserved Amniotic Membrane

<table>
<thead>
<tr>
<th>THE PROKERA ADVANTAGE</th>
<th>PROKERA</th>
<th>DEHYDRATED</th>
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<tr>
<td><strong>CLINICALLY PROVEN</strong></td>
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<td>300+ Publications</td>
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<td>Associated with Corneal Nerve Regeneration</td>
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<td>Accelerates Healing of the Ocular Surface in DED</td>
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<td>Indicated for Active Infections in the Acute Phase</td>
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<td><strong>SUPERIOR TECHNOLOGY</strong></td>
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<td>Maintains Biologic &amp; Structural Integrity</td>
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<td>Contains HC-HA/PTX3</td>
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<td>Maintains Extracellular Matrix</td>
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<td><strong>MEETING THE HIGHEST REGULATORY &amp; QUALITY STANDARDS</strong></td>
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<td>Wound Covering</td>
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<td>Anti-Angiogenesis</td>
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<td>Minimizes Pain</td>
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<td>Hydrated</td>
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<td>Easy to Insert</td>
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<td>Full Limbal Coverage</td>
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<td><strong>PARTNERING WITH YOU FOR SUCCESS</strong></td>
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*Source: Biotissue*
Prokera®
Achieving Clinical Success with PROKERA®
Why Offer PROKERA® as a Dry Eye Therapy?

Your Current Toolbox

<table>
<thead>
<tr>
<th>Target</th>
<th>Therapy</th>
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<tr>
<td>Lids</td>
<td>Warm Compresses, Lid Hygiene, Cliradex®</td>
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<td>Tear Supplementation</td>
<td>Drops (i.e. Systane)</td>
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<td>Inflammation</td>
<td>Steroids, Cyclosporine &amp; Lifitigrast, NSAIDS, Cliradex®</td>
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<tr>
<td>Diet</td>
<td>Vitamins (i.e. Fatty Omega Acids)</td>
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<td>Cornea</td>
<td>PROKERA®</td>
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There has not been an effective therapy for treating the cornea when managing DRY EYE until now: PROKERA
Most Commonly Treated Corneal Pathologies

- Superficial Punctate Keratitis
- Filamentary Keratitis
- Recurrent Corneal Erosion
- Corneal Ulcers
- Neurotrophic Keratitis
- Exposure Keratitis
- Sjogren’s Syndrome
Most Commonly Treated Corneal Pathologies

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Superficial Punctate Keratitis

SPK before

1 W after PKS
Implementation

Recommended Protocol

 ✓ Has some staining 25%
 ✓ Has some inflammation
 ✓ May have symptoms and pain
 ✓ 1-2 first line therapies have failed
 ✓ Has some fluctuating vision
 ✓ Is on or being considered for Restasis or Xiidra
Managing Patient Expectations

Setting patient expectations is key to compliance. Share with your patients the following key tips during PROKERA wear:

• Do not rub your eye
• Do not submerge your face in water
• Close lids tightly while showering
• On the first day of insertion, go home and rest your eyes
• Look with your nose: try not to move eye
• Call patient later that day
Tegaderm/Tapesorrhaphy
Lower Lid Tightening for Entropion

Lower Lid Tightening for Ectropion
81 y/o F has long history of severe dry eye and exposure keratopathy (OD>OS) due to incomplete blinking and lagophthalmos because of blepharoplasty. She did not respond to drops, Restasis®, and punctal plugs. PROKERA® SLIM was inserted OD for one week.

After removal of PROKERA®, the patient was extremely satisfied, the eye was quiet and with a crystal clear cornea. The membrane was intact but cloudy upon removal.
Questions?