TRANSEPITHELIAL CORNEAL CROSS-LINKING BY IONTOPHORESIS

FOR THE OPHTHALMOLOGIST
During irradiation to keep absorption through IONTOPHORESIS* (I - EPI-ON) Transepithelial CXL intervention procedure with UV-A irradiation. Adequate concentration and intrastromal distribution of this substance before proceeding valid method to overcome the lack of corneal permeability to riboflavin and obtain an of the epithelium.

B. Iontophoresis procedure

1. Connect the cable (fig. 5) to the I-ON CXL®
2. The iontophoresis procedure has been started and will last 5 minutes.
3. Connect the syringe by vacuum to the luer lock connector and check that the
4. Aspirate with the syringe (use your thumb to move the piston)
5. Make sure the generator is turned off before for the entire duration of the procedure
6. Rinse the eye with povidone iodide
7. The iontophoresis procedure has been started and will last 5 minutes.
8. TURN ON THE POWER GENERATOR, SELECT THE PULSE INTENSITY OF
9. The iontophoresis procedure has been started and will last 5 minutes.
10. Disconnect the power cable from the generator

Warnings

In the rare case that the generator does not activate at a 1 mA pulse intensity, proceed according to the following steps:

1. Press START to begin the procedure
2. The iontophoresis procedure has been started and will last 5 minutes.
3. Connect the cable (fig. 5) to the I-ON CXL®
4. The iontophoresis procedure has been started and will last 5 minutes.
5. Make sure the generator is turned off before for the entire duration of the procedure

Iontophoresis procedure

1. Before the surgery, proceed with:
   - 3B
   - 3A
   - 3
   - 2
   - 1

   Instillation of single-dose antibiotic from BLUsal® or BSS instillation
   - 20' before IONTO
   - 15' before IONTO
   - 5' before IONTO

   UV-A exposure
   - 30 minutes before "2% pilocarpine"
   - 5' before IONTO

   Instillation of single-dose topical anaesthetic
   - 20' before IONTO
   - 15' before IONTO

   Instillation of topical anaesthetic
   - 15' before IONTO

   Instillation of topical anaesthetic
   - 5' before IONTO

   Instillation of single-dose antibiotic from

   UV-A treatment
   - 30 minutes before "2% pilocarpine"

   Instillation of 2% pilocarpine 30" before UV-A treatment

   Protective patch
   - On the cornea to be treated (fig. 3B).

   Blepharostat
   - After applying the blepharostat (fig. 3A) position the

   Iontofor-CXL® applicator
   - If not, repeat steps 3 to 5.

   Aspirate with a needle supplied with RICROLIN®+

   Applicator for iontophoresis applicator (fig. 3C).

   Position
   - In the rare case that the generator does not activate at a 1 mA pulse intensity, proceed according to the following steps:

   Connect the cable (fig. 5) to the I-ON CXL®

   The iontophoresis procedure has been started and will last 5 minutes.

   Connect the syringe by vacuum to the luer lock connector and check that the

   Aspirate with the syringe (use your thumb to move the piston)

   Make sure the generator is turned off before for the entire duration of the procedure

   Disconnect the power cable from the generator
**INSTRUCTIONS**

**Elective indications**

- Keratoconus 1st- 2nd -3rd stage (Krumeich) evolutive
- Age > 10 years
- Clinical and instrumental progression (refractive, topographic, pachymetric, aberrometric) in the last 6-12 months
- Corneal thickness ≥ 350 μm at the thinnest point
- “Clear Cornea” (transparent cornea at biomicroscopy)

**Non-elective indications**

- Non-evolutive keratoconus in patients with poor compliance to optical correction
- Evolutive keratoconus in patients aged > 10 years with thickness between 350 and 390 μm at the thinnest point
- Corneal curvature < 60 D
- Vogt’s striae (also mild)
- Intolerance to corneal lenses
- Subjective worsening not instrumentally evident in patients intolerant to device-based optical correction and/or to contacts

**Contraindications**

- Corneal thickness (thinnest point) ≤ 350 μm
- Central corneal scarring
- Clinical-instrumental stability
- Reduced patient compliance
Transepithelial CXL intervention procedure with absorption through IONTOPHORESIS* (I - EPI-ON)

A. Preparation

In the days preceding surgery, proceed with:

- Instillation of single-dose antibiotic from 3 days before the intervention (1-2 drops 3 times a day)

Before the surgery, proceed with:

1. Instillation of 2% pilocarpine 1 drop 30 minutes before the surgery
2. Instillation of single-dose topical anaesthetic (1 drop 4 times every 5 minutes) from 20 minutes before the surgery
3. Cleaning of the area around the eye with povidone iodide
4. Irrigation of the ocular surface with antiseptic solution for ophthalmic use
5. Rinsing with saline solution

* Iontophoresis is defined as a non-invasive technique where a low-intensity electric current is applied to increase the penetration of ionised substances within a tissue without removal of the epithelium.

The cross-linking transepithelial procedure combined with iontophoresis is considered a valid method to overcome the lack of corneal permeability to riboflavin and obtain an adequate concentration and intrastromal distribution of this substance before proceeding with UV-A irradiation.
1. Apply the patch (positive electrode) to the forehead (fig. 1B), after having thoroughly cleaned it (fig. 1A).

2. Connect the white male plug of the cable to the return electrode (fig. 2A).

Connect the red female socket of the cable to the connector placed on the Iontofor-CXL® applicator (fig. 2B).

Connect the syringe by vacuum to the luer lock connector and check that the stop clamp is opened (fig. 2C).

3. After applying the blepharostat (fig. 3A) position the applicator for iontophoresis applicator (Iontofor-CXL*) on the cornea to be treated (fig. 3B).

The "T" position, in which the two tubes are arranged in the naso-temporal position and the cable connection faces the forehead, is recommended (fig. 3C).

Check the correct position of the applicator looking through the centre of the "well": cornea and applicator must be concentric to one another (fig. 3C).

4. Lightly press the applicator on the cornea, aspirate with the syringe (use your thumb to move the piston) equal to at least 2 ml (fig. 4) and close the stop clamp. Make sure that the applicator is secured to the cornea; if not, repeat steps 3 to 5.
During irradiation to keep 5

2C

In the days preceding surgery, proceed with:

A. Preparation with UV-A irradiation.

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valid method to overcome the lack of corneal permeability to ribo/f_lavin and obtain an

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of the epithelium.

is applied to increase the penetration of ionised substances within a tissue without removal

* Iontophoresis is de/f_ined as a non-invasive technique where a low-intensity electric current

B .Iontophoresis procedure

TRANSEPITHELIAL CORNEAL CROSS-LINKING

3 days before the intervention

Instillation of single-dose antibiotic from

from the vial (/f_ig. 6A-6B).

RICROLIN®+

6. Aspirate with a needle supplied with RICROLIN®+ from the vial (fig. 6A-6B).

7. Fill the applicator until the level of the solution rises above the grid (negative electrode) (fig. 7).

8. Turn on the power generator, select the pulse intensity of 1 mA and press START (fig. 8).

The iontophoresis procedure has been started and will last 5 minutes.

9. After completion of the iontophoresis procedure, insert a syringe into the yellow luer lock and aspirate RICROLIN®+ residue (fig 9A-9B).

10. Disconnect the power cable from the generator: the generator will automatically turn off after a few moments.

Open the stop clamp to stop the vacuum. Remove the applicator from the cornea and disconnect the power cables from the applicator and return electrode (fig. 10A-10B).
**TRANSEPITHELIAL CXL (EPI-ON) by IONTOPHORESIS**

**SURGERY STEP**

<table>
<thead>
<tr>
<th>Step</th>
<th>Timing</th>
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<tbody>
<tr>
<td><strong>Instillation of 2% pilocarpine</strong></td>
<td>30” before UV-A treatment</td>
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<tr>
<td><strong>Instillation of topical anaesthetic 4 times from 20’ before the intervention</strong></td>
<td></td>
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<tr>
<td>Instillation of topical anaesthetic</td>
<td>20’ before IONTO</td>
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<td>Instillation of topical anaesthetic</td>
<td>15’ before IONTO</td>
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<td>Instillation of topical anaesthetic</td>
<td>10’ before IONTO</td>
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<td>Instillation of topical anaesthetic</td>
<td>5’ before IONTO</td>
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<tr>
<td><strong>IONTOPHORESIS procedure</strong></td>
<td>5’</td>
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<tr>
<td><strong>UV-A exposure</strong></td>
<td>9’ continuous</td>
</tr>
<tr>
<td><strong>BLUsal® or BSS instillation</strong></td>
<td>During irradiation to keep the cornea moist</td>
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*“2% pilocarpine” 1 drop 30 minutes before UV-A treatment.*

**Warnings**

- For the iontophoresis procedure, see the illustrated description.

**For the iontophoresis procedure,**

1. Connect the white male plug of the cable to the connector placed on the Iontofor-CXL® applicator for iontophoresis applicator (Fig. 1).
2. Before the surgery, proceed with:
   - Instillation of single-dose topical anaesthetic (1 drop 4 times every 3 minutes) from 20 minutes before the surgery.
   - Iontophoresis.
3. Iontophoresis is defined as a non-invasive technique where a low-intensity electric current is applied to increase the penetration of ionised substances within a tissue without removal.
4. **B. Iontophoresis procedure**
   - 5’ IONTOPHORESIS procedure
   - UV-A exposure: 10 mW/cm² 9 continuous minutes
5. Make sure the generator is turned off before disconnecting the power cables from the applicator and returning the electrode (Fig. 10A-10B).
6. Open the stop clamp to stop the vacuum. Remove the applicator from the cornea and turn off after a few moments. The generator will automatically disconnect the power cables from the applicator and return the electrode (Fig. 10A-10B).
7. Fill the applicator until the level of the solution rises above 7.5 cm from the vial (Fig. 8).
8. After completion of the iontophoresis procedure, insert a syringe into the yellow luer lock and aspirate RICROLIN®+ residue (Fig 9A-9B).
9. Rinsing with saline solution.

**BY IONTOPHORESIS**

**CORNEAL CROSS-LINKING**

**TRANSEPITHELIAL**

**Clinical-instrumental stability**

**Central corneal scarring**

**Contraindications**

- Intolerance to corneal lenses
- Vogt’s striae (also mild)
- Keratoconus 1st- 2nd -3rd stage (Krumeich) evolutive
- Evolutive keratoconus in patients aged > 10 years with thickness between 350 and 390 /uni03BCm at the thinnest point
- Non-evolutive keratoconus in patients with poor compliance to device-based optical correction and/or to contacts
- Non-elective indications
- “Clear Cornea” (transparent cornea at biomicroscopy)
- Age > 10 years
- Keratoconus 1st- 2nd -3rd stage (Krumeich) evolutive

**Warnings**

- During irradiation to keep the cornea moist.
- “2% pilocarpine” 1 drop 30 minutes before UV-A treatment.
- Reduction of patient compliance.
In the days preceding surgery, proceed with:

A. Preparation

with UV-A irradiation.

The cross-linking transepithelial procedure combined with iontophoresis is considered a non-invasive technique where a low-intensity electric current is applied to increase the penetration of ionised substances within a tissue without removal of any substance.

B. Iontophoresis procedure

Aspirate with a needle supplied with RICROLIN®+ from the vial (Fig. 6A-6B).

Connect the cables to the I-ON CXL® generator.

Connect the red female socket to the I-ON CXL® applicator for iontophoresis (Fig. 5). Make sure the generator is turned off before connecting the cables of the electrodes to the generator itself.

5. Make sure that the grid of the electrode is always covered with riboflavin.

6. Fill the applicator until the level of the solution rises above 7.5 ml (Fig. 4).

7. The iontophoresis procedure has been started and will last 5 minutes.

8. Turn on the power generator, select the pulse intensity of 1 mA and press START button once again, the procedure will automatically start at 1 mA after a few seconds (approximately 30), press the PAUSE button and select 1 mA initially select 0.5 mA.

In the rare case that the generator does not activate at a 1 mA pulse intensity, proceed as follows:

9. If not, repeat steps 3 to 5.

10. Disconnect the power cable from the generator before the surgery.

11. Open the stop clamp to stop the vacuum. Remove the applicator from the cornea and turn off after a few moments.

12. Instillation of single-dose topical anaesthetic 1 drop 4 times every 5 minutes from 20 minutes before the surgery.

13. Instillation of 2% pilocarpine 1 drop 30 minutes before.

14. Clean the area around the eye with povidone iodide.

15. Irrigation of the ocular surface with antiseptic solution for 15’ before IONTO.

16. Instillation of single-dose topical anaesthetic 1 drop 4 times every 5 minutes before IONTO.

17. Aspirate with a needle supplied with RICROLIN®+ residue (Fig 9A-9B).

In the rare case that the procedure cannot be completed:

18. If not, repeat steps 3 to 5.

Subjective worsening not instrumentally evident in patients intolerant to optical correction.

Contraindications

- Non-evolutive keratoconus in patients with poor compliance to "Clear Cornea" (transparent cornea at biomicroscopy) thinnest point
- Age > 10 years
- Central corneal scarring
- Vogt's striae (also mild)
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Central corneal scarring

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