

## CORNEAL CROSS-LINKING THERAPEUTICS DELIVERY DEVICE

### RELATED APPLICATIONS

The present application claims the benefit of U.S. Provisional Application No. 63/463,738, filed May 3, 2023, and U.S. Provisional Application No. 63/538,641, filed September 15, 2023, the disclosures of which are incorporated by reference herein in their entireties.

### FIELD OF THE DISCLOSURE

The present disclosure relates to treating conditions of the cornea, and more specifically, to devices and methods for corneal cross-linking.

### BACKGROUND

Keratoconus is a disorder of the eye, which can result in thinning and/or weakening of the corneal structure such that the cornea progressively bulges into a conical shape. In many patients, this disorder can result in blurry vision, double vision, nearsightedness, irregular astigmatism, and light sensitivity, among other potential quality-of-life reductions. While the condition may initially be corrected with glasses or soft contact lenses, if the condition continues to progress specialized lenses may be required and, in a small number of people, permanent damage or scarring of the cornea can occur potentially requiring corneal transplantation. Considering these risks, corrective procedures such as corneal collagen cross-linking can be used to strengthen the cornea and potentially slow or stop further progression of the disease. Similarly, cross-linking can be performed to preserve the desired reshaping of corneal tissue produced by eye therapies, such as PRK, astigmatic-relaxing incisions, or the like.

Generally, corneal collagen cross-linking involves application of a cross-linking solution to the eye, such as riboflavin or other suitable solution, that is photo-activated by illumination with, for example, an ultraviolet light. The activated solution causes formation of new bonds across collagen strands in the stromal layer of the cornea, which restores much of the cornea's mechanical strength. In addition, the oxygen present in the collagen layers of the cornea is known to play a role in the crosslinking reaction. For example, it is generally known that the crosslinking reaction can be limited by the amount of oxygen present. For example, see U.S. Patent Nos. 8,574,277; 9,644,089; 9,907,698; and 10,010,449, which are incorporated herein by reference in their entirety. In addition, see U.S. Pub. No. 2014/249,509; and 2013/178,821, which are incorporated herein by reference in their entirety. In addition, see Hill et al., *Optimization of Oxygen Dynamics, UV-A Delivery, and Drug Formulation for Accelerated Epi-On Corneal Crosslinking*. Current eye research, 45(4), 450–458, 2020, incorporated herein by reference in its entirety.

The procedures for corneal collagen cross-linking, while beneficial, pose a series of challenges in terms of the effective delivery of oxygen and cross-linking solutions, such as riboflavin, to the corneal stroma. In "epi-on" procedures, where the corneal epithelium is kept intact, ensuring sufficient saturation of the cornea with riboflavin presents a substantial hurdle, as the epithelial layer acts as a lipophilic barrier. This intact epithelium also limits the oxygen access to the corneal stroma during the procedure, potentially compromising the cross-linking process, which relies heavily on the availability of oxygen. Conversely, "epi-off" procedures involve the removal of the corneal epithelium, facilitating better riboflavin penetration and oxygen access. However, this approach introduces its own complications, including an extended recovery time due to the need for the corneal epithelium to heal post-procedure, and the potential for additional complications that might arise from the healing process. These challenges underscore the need for an innovative solution that can enhance the effectiveness of corneal cross-linking procedures while mitigating the associated difficulties.

#### SUMMARY

According to embodiments of the present disclosure, a device for assisting in therapeutics delivery in corneal cross-linking procedures is disclosed. One or more embodiments addresses the drawbacks of prior art in the realm of corneal collagen cross-linking procedures, specifically in both "epi-off" and "epi-on" methods. Epi-off procedures, while a broadly adopted method, are accompanied by serious implications such as severe pain, discomfort, visual impairments, potential damage to the endothelium and intraocular structures, and increased risk of corneal infections. Furthermore, these procedures necessitate a recovery period of approximately 7-10 days, marked by potential complications such as corneal scarring and infection. These drawbacks make it an arduous, painful, and potentially risky process for patients.

Previous attempts have been made to advance "epi-on" procedures to mitigate these issues, with the aim of achieving a faster recovery and a better patient experience. However, the intact epithelium in epi-on procedures poses a significant challenge to the effective penetration of water-soluble riboflavin through the lipophilic barrier of the intact epithelium and into the corneal stroma, which is crucial for the success of the procedure as it is the corneal stroma that needs to be strengthened via crosslinking. Various approaches, like increasing the epithelial permeability or using iontophoresis, have been attempted but none have proved fully effective. As a result, epi-on procedures have been observed to be less effective in halting corneal ectasia progression when compared with epi-off procedures.

As such, various embodiments of the disclosure proposed herein address these challenges with a novel device for assisting in therapeutics delivery for corneal cross-linking. In one or more

embodiments, this device, featuring a body portion with a plurality of epithelial spikes, is designed to create a plurality of micro-perforations in the epithelial layer of the cornea. This circumvents the lipophilic barrier of the intact epithelium, facilitating better penetration and saturation of riboflavin into the corneal stroma. In such embodiments this increased riboflavin permeability will enhance the effectiveness of epi-on procedures, while rivaling the outcomes observed with epi-off procedures and reducing or potentially eliminating the recovery period seen in epi-off procedures by minimizing the physical effect on the epithelium.

In addition to the micro-perforation feature, this novel device is intended to work in tandem with other cross-linking devices. For example, various embodiments are intended to be used in tandem with the cross-linking device described in U.S. Patent Publication 2022/0117783, incorporated by reference herein, to maintain a constant and steady concentration of riboflavin above the epithelium. This combination should offer an improvement over the traditional and current method of intermittently dropping riboflavin onto the corneal surface. It also addresses the issue of excessive corneal dehydration and thinning associated with prolonged imbibition time. Together, these innovations aim to revolutionize epi-on procedures, offering a more effective and patient-friendly alternative to the current options in the field of corneal collagen cross-linking.

In one or more embodiments the device comprises a body portion having a top side and a bottom side. In various embodiments the bottom side includes a concave portion configured to be conformally placed on an epithelial layer of a cornea for uniformly distributing pressure across the epithelial layer when the device is in use. In one or more embodiments the device includes a plurality of epithelial spikes, each epithelial spike having a height of approximately 50 microns, wherein the plurality of epithelial spikes is positioned on the bottom side of the body portion, the plurality of epithelial spikes configured to create a plurality of micro-perforations in the epithelial layer of the cornea when pressure is applied to the top side of the body portion. The normal corneal epithelium is on average 50 microns thick. Thus, the spikes are designed to penetrate through the epithelial cell layer but not perforate or damage the underlying stromal tissue. In certain embodiments the device further includes a delivery system configured to deliver one or more riboflavin and oxygen through the plurality of micro-perforations created by the plurality of spikes into the corneal stroma.

The above summary is not intended to describe each illustrated embodiment or every implementation of the present disclosure.

#### BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

The drawings included in the present application are incorporated into, and form part of, the specification. They illustrate embodiments of the present disclosure and, along with the description,

explain the principles of the disclosure. The drawings are only illustrative of certain embodiments and do not limit the disclosure.

FIG. 1 depicts a perspective view of a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

5        FIG. 2 depicts a cross-sectional view of a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

FIG. 3 depicts a close-up partial cross-sectional view of a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

10       FIG. 4A-4B depicts stages of use of a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

FIG. 5 depicts a cross-sectional view of an eye and a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

FIG. 6 depicts a method of corneal crosslinking, according to one or more embodiments of the disclosure.

15       FIGS. 7A-7E depict spike patterns configured to change a shape of the cornea during a corneal cross-linking procedure, according to one or more embodiments of the disclosure.

FIG. 8A depicts a perspective view of a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

20       FIG. 8B depicts a cross-sectional view of the device of Fig. 8A, according to one or more embodiments of the disclosure.

FIG. 9 depicts a cross-sectional view of an eye and a device for assisting in corneal cross-linking, according to one or more embodiments of the disclosure.

FIG. 10A depicts a perspective view of a cross-linking device, according to one or more embodiments of the disclosure.

25       FIG. 10B depicts a cross-sectional plan view of a cross-linking device, according to one or more embodiments of the disclosure.

FIG. 10C depicts a perspective view of a cross-linking device in use, according to one or more embodiments of the disclosure.

30       FIG. 10D depicts a cross-sectional view of a cross-linking device in use, according to one or more embodiments of the disclosure.

FIG. 10E depicts a cross-sectional view of a cross-linking device in use in combination with a device for assisting in corneal cross-linking, according to one more embodiments of the disclosure.

FIG. 11 depicts a method of corneal cross-linking using the device in combination with a cross-linking device, according to one or more embodiments of the disclosure.

While the embodiments of the disclosure are amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail. It should be understood, however, that the intention is not to limit the disclosure to the embodiments described. On the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the disclosure.

#### DETAILED DESCRIPTION

Referring to FIGS. 1-3 and 5, a perspective view and cross-sectional views of a device 100 designed to assist in corneal cross-linking is presented, according to one or more embodiments of the disclosure. The device 100 incorporates a body portion 104, which, in some embodiments, takes on a lens-like shape with a top side 108 and a bottom side 110. The bottom side 110 features a concave portion 112, specifically designed to conform to the curvature of the cornea. Owing to the body's 104 lens-like shape, the device 100 can uniformly distribute pressure across the cornea or the epithelial layer during use, thereby enhancing its efficacy. While various figures herein portray the body portion 104 as having a lens-like shape, alternative embodiments may not necessarily adhere to this form. For instance, the top side 108 could be substantially flat or possess a different shape altogether. Nonetheless, in these embodiments, the bottom side 110 will maintain the concave portion 112, ensuring the device's 100 ability to conform comfortably to the cornea. In certain embodiments, the bottom side 110 of the device is flat. For example, in such embodiments the device would not include a concave portion but would still include epithelial spikes positioned on the bottom side 110.

In certain embodiments, the device 100 is designed with a multitude of epithelial spikes 114. These epithelial spikes 114 are strategically positioned on the concave portion 112 of the device 100, in various embodiments. Each spike 114 is designed as a micro-needle, with an approximate height of 50 microns, in several embodiments. However, the size of the epithelial spike 114 may vary in certain embodiments, with a potential height range of about 25 to 75 microns, for example. In various embodiments, the epithelial spikes 114 are designed to create multiple micro-perforations in the corneal epithelial layer once pressure is applied to the top side of the body portion 104. An operator may apply pressure, for example, by pressing upon the device with one's fingers. Suitable pressure will perforate the corneal epithelial layer without compressing the anterior chamber of the eye. In certain embodiments, the body portion 104 is crafted from an elastomer, which can be comprised of one or more materials such as silicone, latex, or rubber. The multitude of epithelial spikes 114 are typically constructed of silicone. However, in one or more embodiments the epithelial spikes 114 can be constructed from any suitable micro-needle material as known in the art. Moreover, the body portion 104 and the plurality of epithelial spikes 114 could be molded from a single piece of material, further

enhancing the device's robustness and durability. In certain embodiments, the body portion may be at least partially transparent, allowing for improved visualization during the procedure.

In certain embodiments, the device is designed to be compatible with or inclusive of a delivery system. This delivery system could be any appropriate cross-linking therapeutics delivery system recognized in the art. For instance, in some embodiments, the delivery system could be a fluid supply mechanism, incorporating a liquid reservoir and an oxygen supply. In such embodiments the delivery system could be connected to a separate cross-linking device that engages with the eye once the device 100 has created numerous micro-perforations in the corneal epithelium. Under such circumstances, the cross-linking device is generally designed to attach to the eye, and once connected, therapeutics like oxygen and/or riboflavin can be supplied to the eye via the fluid supply system.

In certain embodiments, the device 100 itself could be designed to deliver substances like riboflavin and oxygen through the multitude of micro-perforations created by the spikes, directly into the corneal stroma. For instance, in some configurations, the delivery system could be integrated within the body portion and could be designed to control the volume and delivery rate of riboflavin and oxygen to the corneal stroma, based on the multitude of epithelial spikes. Further, the delivery system could have a variety of configurations, including but not limited to the epithelial spikes being designed as solid microneedles, hollow microneedles, or dissolving microneedles. In various embodiments, the epithelial spikes 114 are uniformly distributed across the bottom side of the body portion, ensuring consistent and even delivery of therapeutics. In certain embodiments the delivery device could be configured as the cross-linking device described in described in U.S. Patent Publication 2022/0117783, incorporated by reference above, to maintain a constant and steady concentration of riboflavin above the epithelium.

FIG. 4A-5 illustrate stages of use for a device designed to assist in corneal cross-linking, according to various embodiments of the disclosure. In one or more embodiments, the device 100 is centered over and gently lowered onto the patient's eye 404. The body portion 104, specifically the concave section 112, is designed to conform to the shape and size of the cornea 408. The device 100 is engineered with a plurality of epithelial spikes 114 that, in various embodiments, are designed as a plurality of micro-needles. In such configurations, the height of the epithelial spikes is configured to approximately match the thickness of the corneal epithelium, enabling the epithelial spikes 114 to create numerous micro-perforations through the corneal epithelial layer once pressure is applied to the upper side of the body portion 104. This allows for the effective permeation of substances like riboflavin and/or oxygen into the corneal stroma. In certain embodiments, the epithelial spikes 114 are approximately 50 microns in size. However, the size of the epithelial spikes 114 may vary in some embodiments, with a potential height range of about 25 to 75 microns. For example, in certain

embodiments the epithelial spikes 114 may only perforate some of the depth of the epithelial layer while not totally extending all the way through. In certain embodiments, the body portion 104 is made from an elastomer, which can include one or more materials such as silicone, latex, or rubber. The epithelial spikes 114 are typically composed of silicone, but in certain embodiments, they can be made from any suitable micro-needle material known in the field. Moreover, the body portion 104 and the multitude of epithelial spikes 114 could be cast from a single piece of material, further enhancing the device's robustness and longevity. In specific embodiments, the body portion may be at least partially transparent, allowing for improved visualization during the procedure. In various embodiments, due to the device 100 being constructed from an elastomer or other flexible material, such as silicone, the device 100 can contract and conform to the eye in response to downward pressure applied to the device 100.

Referring to FIG. 6, a method 600 of cross-linking is depicted according to one or more embodiments of the disclosure. In one or more embodiments, the method 600 includes, at operation 604, positioning the device on an eye. In various embodiments, the device is the same or substantially similar as the device described and depicted above, including a body portion and a concave portion with a plurality of epithelial spikes. In various embodiments, the method 600 includes, at operation 608, applying pressure on the device to create a plurality of micro-perforations in the corneal epithelium. In various embodiments, the height of the epithelial spikes is configured to approximately match the thickness of the corneal epithelium, enabling the epithelial spikes to create numerous micro-perforations through the corneal epithelial layer once pressure is applied to the upper side of the body portion. In one or more embodiments, the method 600 includes, at operations 612-616, removing the device and proceeding to perform cross-linking procedure on the eye by positioning and using a cross-linking device such as that described in U.S. Patent Publication 2022/0117783, incorporated by reference herein, to maintain a constant and steady concentration of riboflavin above the epithelium. In various embodiments, the device may be left in place when providing therapeutics to the eye. For example, the cross-linking device may be placed over the device on the eye. In various embodiments, the cross-linking device may be used to apply pressure to the body portion of the device, either directly or indirectly. For example, gas or liquid delivered to a cross-linking device surrounding the body portion of the device may create sufficient pressure to create micro-perforations through the corneal epithelial layer. While various embodiments involve treating the corneal tissue using cross-linking agent it is intended that a method of treatment could include treating the cornea with any suitable medication. For example, in various embodiments a method could include treating the cornea with antibiotic/antifungal/antiamoebic drugs.

As discussed above, current corneal collagen cross-linking can be used to strengthen the cornea and potentially slow or stop further bulging. However, currently used techniques do not generally reshape the cornea in a predictable manner, and therefore offer little to no improvements or correction for vision altered by disease such as keratoconus. Generally, surgical techniques are employed when it is desired to reshape portions of the corneal stromal tissue to change how the eye is refracting light in order to improve vision. Various shapes and patterns are used during excimer ablation to achieve such effects. See, for example, MacRae, Scott, *Excimer ablation design and elliptical transition zones*, J Cataract Refract Surg, 25, 1191-1197, September 1999, incorporated herein by reference in its entirety.

As with all surgeries, reshaping the cornea through excimer ablation, incisions, or other techniques carries significant risks. There has been some success in adapting cross-linking procedures to reshape portions of the cornea by adjusting the UVA light delivered to the patient. For example, delivering the UVA light in specific patterns or varying intensities may cause collagen bonds created during cross-linking to impact refractive properties of an eye. See, for example, Juthani et al., *Corneal crosslinking in refractive corrections*, Transl Vis Sci Technol., 10(5):4, 1-10, 2021.

In specific embodiments, the spikes may be arranged into patterns, such that riboflavin is delivered to the eye in a corresponding pattern. Exemplary patterns are illustrated in Figs. 7A – 7E and discussed in detail below. These examples are not meant to be limiting, and other patterns are not beyond the scope of this disclosure. In Figs. 7A – 7E the pattern portion 702 of the figures shown in grey comprise epithelial spikes 114 as described in detail above, and the areas in white are where the concave portion 112 of the device 100 is devoid of spikes. By concentrating or restricting the riboflavin according to these patterns 702, only the corresponding areas of the eye will be substantially affected when UVA light is applied. As discussed above, UVA applied to the riboflavin creates new and stronger bonds between corneal stromal collagen fibers. The stronger bonds, in turn, pulls the tissue fibers closer together. This in turn flattens the curvature of the cornea in these regions. Limiting or otherwise concentrating this reaction to specific shapes, patterns, or the like alters the refractive curvature of the eye as the tissue is compressed together across the treated area where collagen fibers are now chemically linked and compressed closer together. The compressed tissue leads to localized corneal curvatures being altered (flattened). For example, referring to Fig. 7A, a device 100 with epithelial spikes 114 arranged in a generally solid circle pattern 702a in the center of the concave portion 112 of the device 100 may be used for myopic treatment. Spikes 114 arranged in a generally open circle pattern 702b about the center of the concave portion 112 of the device 100 may be used for hyperopic treatment. A device with opposing crescent shaped patterns 102c of spikes 114 on the concave surface 112 of the device 100 may be used for plus cylinder astigmatic treatment. A device

100 with a columnar region 702d of spikes 114 on the concave surface 112 of the device 100 may be used for minus cylinder treatment. The shapes or patterns shown and described are merely examples of treatment patterns and not meant to be limiting. Specific widths or orientations of the patterns may be adjusted to suit individual patients. Further, custom treatments may be implemented by arranging  
5 the spikes 114 in custom designed patterns 702e on a device 100 to correct particular defects for individual patients.

Referring to FIGS. 8A and 8B, a perspective view and cross-sectional views of a device 800 designed to assist in corneal cross-linking is presented, according to one or more embodiments of the disclosure. The device 800 incorporates a body portion 104, which, in some embodiments, takes on a  
10 lens-like shape with a top side 108 and a bottom side 110. The bottom side 110 features a concave portion 112, specifically designed to conform to the curvature of the cornea. As discussed above, the device 800 can uniformly distribute pressure across the cornea or the epithelial layer during use, thereby enhancing its efficacy. In these embodiments, the bottom side 810 will maintain the concave portion 812, ensuring the device's 800 ability to conform comfortably to the cornea. In certain  
15 embodiments, the bottom side 810 of the device is flat. Figs. 8A and 8B depict epithelial spikes 114 arranged in a columnar pattern 702d as depicted in Fig. 7D. As discussed above, this arrangement of epithelial spikes 114 in a column across the device 800 is suited for minus cylinder treatment. The depiction of the columnar pattern 702d on the device 800 is for illustrative purposes only. It should be understood that any of the patterns shown in Fig. 7A – 7E may be used with device 800, which includes  
20 a custom pattern configured to correspond to an individual patient's particular defects as determined by scanning or other examination or diagnostic techniques as known in the art. FIG. 9 illustrates a sectional view of the device 800 on a patient's eye 404. The body portion 104, specifically the concave section 112, is designed to conform to the shape and size of the cornea 408. As discussed above, the device 800 is engineered with a plurality of epithelial spikes 114 that, in various embodiments, are  
25 designed as a plurality of micro-needles of various potential heights to perforate the corneal epithelium, allowing for the effective permeation of substances like riboflavin and/or oxygen into the corneal stroma. As shown, the spikes are arranged in a generally columnar pattern 702d, which could be used, for example, for minus cylinder treatment during a cross linking procedure by directing substances to those particular areas on the eye.

Referring to FIGS. 10A and 10B cross-linking device 1000 is depicted according to one or more embodiments. In various embodiments, the device 1000 includes a main body 1004 that is defined by a sidewall 1008 that extends from a top portion 1012 of the device to a bottom portion 1016. Depicted in FIG. 10A, the device 1000 has a generally cylindrical or tubular shape with a side  
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portion 120 of the main body 1004 extending between the top portion 1012 to the bottom portion 1016 surrounding a central axis 1022.

5 In one or more embodiments, the top portion 1012 defines a top surface 1024 while the bottom portion 1016 defines a bottom edge 1026 and a primary aperture 1030 into an interior cavity 1034 of the device 1000 that is defined by the sidewall 1008. In one or more embodiments, the interior cavity 1034 includes at least two portions including an anterior chamber 1036 and an ocular chamber 1038 with a corneal gripping portion 1040 positioned between the chambers and defining a boundary therebetween. In one or more embodiments, the corneal gripping portion 1040 is a portion of the interior sidewall 1042 that is extended inwardly towards the central axis 1022 and defines an interior  
10 flange and/or ridge with an aperture positioned between the anterior chamber 1036 and ocular chamber 1038. In various embodiments the corneal gripping portion 1040 including one or more circumferential ridges 1041 that extend about the interior sidewall 1042. In certain embodiments, and described further below, the portion 1040 includes a vacuum recess 1043 configured to allow for a vacuum to be applied in the ocular chamber for attachment to a cornea while in use. In such embodiments, the circumferential  
15 ridges 1041 configure the gripping portion 1040 to selectively flex at portions of the interior sidewall between the ridges 1041 to create a gripping flexing movement that closely conforms the interior sidewall 1042 of the device 1000 to the cornea while in use.

As such, in one or more embodiments, and described further below the ocular chamber 1038 is shaped via the corneal gripping portion 1040 to have a curved or generally semi-spherical shape that  
20 is configured to conform to and fit to the shape of a patient's eye and/or cornea while in use.

In one or more embodiments, the anterior chamber 1036 has a volume that is defined by the placement of the corneal gripping portion 1040 along the length of the side portions 1020 and/or the diameter of the top surface 1024. For example, depicted in FIGS. 10A and 10B, the corneal gripping portion 1040 is placed, from the bottom edge 1026, approximately one third of the total vertical length of the side portions 1020. As a result, approximately two-thirds of the length of the side portions 1020  
25 function to define the volume of the anterior chamber while approximately one third of the length of the side portions function to define the volume of the ocular chamber 1038. Also depicted, top surface 1024 has a diameter that is greater than the diameter of the primary aperture 1030 defined by the bottom edge 1026. As such, a greater amount of volume is dedicated in the upper portion of the device  
30 1000.

In such embodiments, the anterior chamber 1036 will have a volume that is larger than the volume of the ocular chamber 1038. In some embodiments, the anterior chamber 1036 has a volume that is 5% to 50% larger than the volume of the ocular chamber 1038. However, in certain

embodiments the anterior chamber 1036 could have a volume that is 50% larger than the volume of the ocular chamber 1038.

5 In various embodiments, a multi-purpose fluid port 1046 is positioned on the side portion 1020 of sidewall 1008 and defines a pair of fluid pathways 1050, 1052 that connect a pair of exterior fluid ports 1053, 1054 to an anterior chamber port 1055, and an ocular chamber port 1056 respectively. In such embodiments, the fluid pathways 1050, 1052 define paths to allow for liquid, gasses, and other fluids to pass into and out of the interior of the device. As such, and as used herein the term “fluid” is intended to refer to both liquids and gasses.

10 In one or more embodiments, the multi-purpose fluid port 1046 includes two or more fluid pathways into the interior of the device. In such embodiments, the port 1046 allows for multiple fluid inputs or fluid draw functions to occur simultaneously while the device is being used. For example, described further below, the port 1046 allows for a vacuum to be applied to one fluid pathway while other fluids could be input or drawn from the device via the other fluid pathway.

15 In one or more embodiments, a pressure release port 1070 is additionally included in the side portion 1020 of the sidewall. In such embodiments, the port 1070 defines an additional fluid pathway into the anterior chamber 136 that can be selectively opened or closed via a plug 1074, valve, pressure valve, or other device. In one or more embodiments, the pressure release port 1070 allows for pressure equalization of the anterior chamber to prevent damage to the device and/or device pop-off while in use. For example, described further below, when the device is secured to a patient’s eye, the port 1070  
20 allows for use of a pump to introduce riboflavin or other fluids into the anterior chamber without over-pressurizing the anterior chamber. If over-pressurized the device could rupture or simply pop off the patient’s eye while in use. Similarly, the port 1070 allows a vacuum to be applied to the chamber to remove riboflavin from the anterior chamber while also preventing collapse of the sidewalls due to pressure of the applied vacuum.

25 In one or more embodiments, the device 1000 is constructed from one or more of polymer, elastomer, or the like. For example, in various embodiments the device 1000 is constructed from one or more of silicone, rubber, latex. In one or more embodiments, the device 1000 is constructed as a single piece. However, in some embodiments, the device 1000 could be constructed from multiple pieces that are assembled or otherwise fitted together.

30 In various embodiments, the material of the device 1000 is at least partially transparent. For example, in various embodiments the material is sufficiently transparent such that UV light can pass through the material of the device for activation of cross-linking solution within the anterior chamber 1036. For example, in various embodiments the top surface 1024 the device 1000 is constructed from

silicone, which has the desired property of allowing excellent transmission of UV light. Further, it additionally allows for clear viewing of a corneal surface by the surgeon while in use.

Referring to FIGS. 10C and 10D, perspective views and cross-sectional views of a cross-linking device 1000 are depicted while in use, according to one or more embodiments of the disclosure.

5 In one or more embodiments, the device is centered over and lowered onto a patient's eye 404. As described, the interior sidewall 1042 of the ocular chamber 1038 has a shape and size configured to conform to the cornea 408. In one or more embodiments, the corneal gripping portion 1040 defines a secondary aperture 1031 that is configured to allow passage of a portion 1007 of the cornea 408 into the anterior chamber 1036 such that the portion 1007 can be exposed to cross-linking solution and/or  
10 UV light source 1001 positioned above the device 1000.

As described, the ocular chamber port 1054 defines a fluid pathway 1052 into the ocular chamber 1038 of the device 1000. A such, when the device 1000 is positioned on the eye 404, the ocular chamber port 1054 can be attached to a vacuum source 1003 and suction can be applied via the fluid pathway 1052 to apply suction in the vacuum recess 1043 between the eye 404 and the interior  
15 wall 1042 of the ocular chamber 1038 thereby holding the device tightly to the cornea 408.

In various embodiments, because the device 1000 is constructed from elastomer or otherwise flexible material, such as silicone, the device 1000 will contract and conform against the eye in response to the force of the vacuum when applied between the eye 404 and the interior wall 1042. As a result, in various embodiments the corneal gripping portion 1040, circumferential ridges 1041, and  
20 interior sidewalls 1042 closely conform to the eye and the corneal gripping portion 1040 functions to seal off the anterior chamber 1036 and allow for insertion of liquids or other solutions into the anterior chamber 136 without leakage through the aperture 1031. As a result, cross-linking solutions can be more closely controlled for exposure onto only the exposed portion 404 of the cornea 408 while keeping the rest of the eye unexposed. In one or more embodiments, the circumferential ridges 1041  
25 configure the gripping portion 1040 to selectively flex at portions of the interior sidewall between the ridges 1041 to create a gripping flexing movement that closely conforms the interior sidewall 1042 of the device 1000 to the cornea while in use.

In one or more embodiments, the anterior chamber port 1053 defines a fluid pathway 1050 into the anterior cavity 1036. In one or more embodiments, a fluid supply system 1005 including  
30 a liquid reservoir 1009 and oxygen supply 1011 are connected to the port 1053 by one or more conduits 1013 so that, once the anterior chamber 1036 has been sealed off using the corneal gripping portion 1040 and the vacuum source 1003, fluid can be supplied into or out of the anterior chamber using the respective supplies 1009, 1011. In various embodiments, the liquid supply system 1005 may include elements such as pumps, valves, or other elements for controlling the fluid flow. For example, in one

or more embodiments, the liquid reservoir 1009 includes a cross-linking solution, such as riboflavin, that is first pumped or otherwise inputted through the port 1053. After saturation, the liquid can be suctioned out through the port 1053 and oxygen next pumped in through the same port 1053 via the oxygen supply 1011.

5 Referring to FIG. 11, a method 1100 of cross-linking using a cross-linking device is depicted according to one or more embodiments of the disclosure. In one or more embodiments, the method 1100 includes, at operation 1102, positioning a device on an eye with the cornea aligned with the concave portion. In various embodiments, the device is the same or substantially similar as device 100 described and depicted above, with epithelial spikes positioned against the cornea. In one or more  
10 embodiments, the method 1100 includes, at operation 1104, applying pressure on the device to create a plurality of micro-perforations in the cornea.

In one or more embodiments, the method 1100 includes, at operation 1106, positioning a cross-linking device on an eye. In various embodiments, the cross-linking device is the same or substantially similar as device 1000 described and depicted above, including at least two portions including an  
15 anterior chamber and an ocular chamber with a corneal gripping portion positioned between the chambers and defining a boundary therebetween. In one or more embodiments, the corneal gripping portion defines a secondary aperture that is configured to allow passage of a portion of the cornea into the anterior chamber. In such embodiments, the cornea of the eye is generally aligned with the aperture such that the portion of the cornea desired for cross-linking will pass through the aperture.

20 In various embodiments, the method 1100 includes, at operation 1108, applying a vacuum through a multi-purpose port of the device to secure the device to the eye and seal the anterior chamber. As described, because the device is constructed from elastomer or otherwise flexible material, such as silicone, the device will contract and conform against the eye in response to the force of the vacuum when applied between the eye and the interior wall in the ocular chamber. As a result, in various  
25 embodiments the corneal gripping portion and interior sidewalls closely conform to the eye and the corneal gripping portion functions to seal off the anterior chamber and allow for insertion of liquids or other solutions into the anterior chamber without leakage.

In one or more embodiments, the method 1100 includes, at operations 1110-1114, treating the corneal tissue in the anterior chamber with cross-linking agent applied through the multi-purpose port, removing cross-linking agent through the multi-purpose port, and providing a first amount of oxygen  
30 at the exposed portion of cornea through the multi-purpose port. As described, the anterior chamber port of the device defines a fluid pathway into the anterior cavity. In one or more embodiments, once the anterior chamber has been sealed off using the corneal gripping portion and the vacuum source, fluid can be supplied into or out of the anterior chamber using respective supplies.

In one or more embodiments, the method 1100 includes, at operation 1116, initiating cross-linking agent by activating the agent with a light source. In various embodiments, the light source is a UV light that initiates cross-linking activity by causing the applied cross-linking agent, such as riboflavin, to release reactive oxygen radicals in the corneal tissue. The agent acts as a sensitizer to  
5 convert O<sub>2</sub> into singlet oxygen, which causes cross-linking within the corneal tissue.

While in various embodiments the method 1100 involves treating the corneal tissue using cross-linking agent and activating the agent with a light source, it is intended that a method of treatment could include treating the cornea with any suitable medication and/or applying light to the cornea through the device. For example, in various embodiments a method could include treating the  
10 cornea with antibiotic/antifungal/antiamoebic drugs and using the device to insert the medication through the multi-purpose port such that the medication will remain in direct contact with the corneal tissue for as long as is desired. In addition, the chamber above the cornea containing the drug can be pressurized, pushing additional drug into the corneal tissue beyond simple diffusion rates based on drug concentration. The chamber allows even distribution across the entire cornea. This should allow  
15 drugs to reach much higher concentrations in the corneal stroma than eye drops can achieve. Oxygen gas can also be bubbled through the anti-infective liquid drug in the chamber, creating oxygen free radicals if desired. UVA light can also be delivered through the top of the chamber further killing infectious organisms.

The descriptions of the various embodiments of the present disclosure have been presented for  
20 purposes of illustration, but are not intended to be exhaustive or limited to the embodiments disclosed. Many modifications and variations will be apparent to those of ordinary skill in the art without departing from the scope and spirit of the described embodiments. The terminology used herein was chosen to explain the principles of the embodiments, the practical application or technical improvement over technologies found in the marketplace, or to enable others of ordinary skill in the  
25 art to understand the embodiments disclosed herein.

## CLAIMS

What is claimed is:

1. A device for assisting in corneal cross-linking, the device comprising:  
a body portion having a top side and a bottom side, wherein the bottom side includes a concave portion configured to be conformally placed on an epithelial layer of a cornea for uniformly distributing pressure across the epithelial layer when the device is in use;  
a plurality of epithelial spikes, each epithelial spike having a height of approximately 50 microns, wherein the plurality of epithelial spikes is positioned on the bottom side of the body portion, the plurality of epithelial spikes configured to create a plurality of micro-perforations in the epithelial layer of the cornea when pressure is applied to the top side of the body portion.
2. The device of claim 1, wherein the plurality of epithelial spikes is positioned on the concave portion.
3. The device of any of claims 1 or 2, wherein the body portion is constructed from an elastomer including one or more of silicone, latex, and rubber.
4. The device of any of the above claims, wherein the plurality of epithelial spikes is constructed of silicone.
5. The device of any of the above claims, wherein the plurality of epithelial spikes is evenly distributed across the bottom side of the body portion.
6. The device of any of the above claims, further comprising a delivery system, wherein the delivery system is configured to deliver one or more of riboflavin and oxygen through the plurality of micro-perforations created by the plurality of spikes into the corneal stroma.
7. The device of claim 6, wherein the delivery system is integrated with the body portion.
8. The device of any of claims 6 or 7, wherein the delivery system is configured to control the amount and rate of riboflavin and oxygen delivery to the corneal stroma based on the plurality of epithelial spikes.

9. The device of any of claims 6 - 8, wherein the delivery system includes the plurality of epithelial spikes being configured as solid microneedles.
10. The device of any of claims 6 - 8, wherein the delivery system includes the plurality of epithelial spikes being configured as hollow microneedles.
11. The device according to claims 6 - 8, wherein the delivery system includes the plurality of epithelial spikes being configured as dissolving microneedles.
12. The device of any of the above claims, wherein the body portion and the plurality of epithelial spikes are constructed from a single piece of material.
13. A device for assisting in corneal cross-linking, the device comprising:
  - a body portion having a top side and a bottom side, wherein the bottom side includes a concave portion configured to be conformally placed on an epithelial layer of a cornea;
  - a plurality of epithelial spikes, each epithelial spike having a height of approximately 50 microns, wherein each of the epithelial spikes is positioned in a pattern on the bottom side of the body portion such that plurality of epithelial spikes forms a pattern, the plurality of epithelial spikes configured to create a plurality of micro-perforations in the epithelial layer of the cornea when pressure is applied to the top side of the body portion.
14. The device of claim 13, wherein the pattern is configured to change a refraction of the cornea.
15. The device of any of claims 13 or 14, wherein the pattern is one of a circle, a circle with an open middle, a crescent shape, or a column.
16. The device of any of claims 13-15, wherein the pattern is associated with a defect in a shape of the cornea.
17. The device of any of claims 13-16, wherein the plurality of epithelial spikes is positioned on the concave portion.
18. The device of any of claims 13-17, wherein the body portion is constructed from an elastomer including one or more of silicone, latex, and rubber.

19. The device of any of claims 13-18, wherein the plurality of epithelial spikes is constructed of silicone.
20. The device of any of claims 13-19, wherein the plurality of epithelial spikes are configured as hollow microneedles.
21. The device any of claims 13-18, wherein the plurality of epithelial spikes are configured as dissolving microneedles.
22. The device any of claims 13-21, wherein the plurality of epithelial spikes is evenly distributed across the bottom side of the body portion.
23. The device of any of claims 13-22, wherein the body portion and the plurality of epithelial spikes are constructed from a single piece of material.
24. The device of claims 13-23, wherein the body portion is at least partially transparent.
25. A method of corneal cross-linking comprising:  
providing a device comprising;  
a body portion having a top side and a bottom side, wherein the bottom side includes a concave portion configured to be conformally placed on an epithelial layer of a cornea for uniformly distributing pressure across the epithelial layer when the device is in use; and  
a plurality of epithelial spikes, wherein the plurality of epithelial spikes is positioned in a pattern on the bottom side of the body portion, the pattern being associated with an aberration in a shape of the cornea; and  
applying pressure to the top side of the body portion to create a plurality of micro-perforations in the epithelial layer of the cornea using the plurality of epithelial spikes.
26. The method of claim 25, further comprising:  
delivering one or more of riboflavin and oxygen through the plurality of micro-perforations created by the plurality of spikes into the corneal stroma.

27. The method of claim 26, wherein delivering one or more of riboflavin and oxygen through the plurality of micro-perforations occurs using the plurality of epithelial spikes configured as solid microneedles.

28. The method of claim 26, wherein delivering one or more of riboflavin and oxygen through the plurality of micro-perforations occurs using the plurality of epithelial spikes configured as hollow microneedles.

29. The method of claim 26, wherein delivering one or more of riboflavin and oxygen through the plurality of micro-perforations occurs using the plurality of epithelial spikes configured as dissolving microneedles.

30. A system for corneal cross-linking, the system comprising:  
a device comprising:

a silicone body portion having a top side and a bottom side, wherein the bottom side includes a concave portion configured to be conformally placed on an epithelial layer of a cornea for uniformly distributing pressure across the epithelial layer when the device is in use;  
and

a plurality of epithelial spikes, each epithelial spike constructed from silicone, the plurality of epithelial spikes configured correct an aberration in a shape of the cornea to create a plurality of micro-perforations in a pre-determined pattern in the epithelial layer of the cornea when pressure is applied to the top side of the silicone body portion, wherein the plurality of epithelial spikes are configured as solid microneedles; and

a delivery system configured to deliver one or more riboflavin and oxygen through the plurality of micro-perforations created by the plurality of spikes into the corneal stroma.

31. The device according to claim 30, wherein the body portion of the device and the plurality of epithelial spikes are constructed from a single piece of material.

32. A method of corneal cross-linking configured to correct an aberration of a cornea comprising:  
providing a device comprising:  
a silicone body portion having a top side and a bottom side, wherein the bottom side includes a concave portion configured to be conformally placed on an epithelial layer of the cornea, the bottom side comprising a plurality of epithelial spikes in a shape corresponding to the aberration;  
applying pressure to the top side of the body portion to create a plurality of micro-perforations in the epithelial layer of the cornea, the plurality of micro-perforations corresponding to the shape of the plurality of epithelial spikes.
33. The method of claim 32 further comprising delivering one or more of riboflavin and oxygen through the plurality of micro-perforations created by the plurality of spikes into the corneal stroma.
34. The method of claim 33 further comprising directing UVA light at the corneal stroma.