

## New ultraviolet irradiation apparatus for Corneal cross-linking

**Krassimir Koev** <sup>\*1,2</sup> and **Latchezar Avramov** <sup>2</sup>

<sup>1</sup> Department of Ophthalmology, Medical University Sofia, 8 Bialo more, Sofia, Bulgaria

<sup>2</sup> Institute of Electronics, Bulgarian Academy of Sciences, 72 Tzarigradsko chause blvd., 1784 Sofia, Bulgaria

e-mail address: k00007@abv.bg

**Abstract.** We present a new ultraviolet irradiation apparatus for Corneal cross-linking optimized to perform faster. It is designed for treating keratoconus, ulcer, infectious keratitis and post LASIK ectasia. Using a plastic band around the patient's head, a matrix of UV- LEDs is located at a controlled distance from the cornea of the eye. The matrix-LEDs emits a total cut-off power of 40 mW at a wavelength of  $\lambda = 390 \pm 5 \text{ nm}$ . Using a widget, the matrix moves to the left or right eye. The duration of exposure is 2 minutes. The power density on the cornea of the eye is  $42,1 \text{ mW/cm}^2$  with an illuminated diameter on the corneal surface of  $d = 1.1 \text{ cm}$ . This corresponds to surface-density of the energy accumulated on the cornea of  $5.1 \text{ J/cm}^2$ . With the parameters described above, the ultimate effect can be achieved for a short time. The described apparatus is more convenient and features compactness, portability, functionality. Our new apparatus emits ultraviolet light of 390 nm wavelength in difference to the known from the literature apparatus using 360 nm. In this way we address the maximum absorption of ultraviolet light by collagen fibrils.

### 1. Introduction

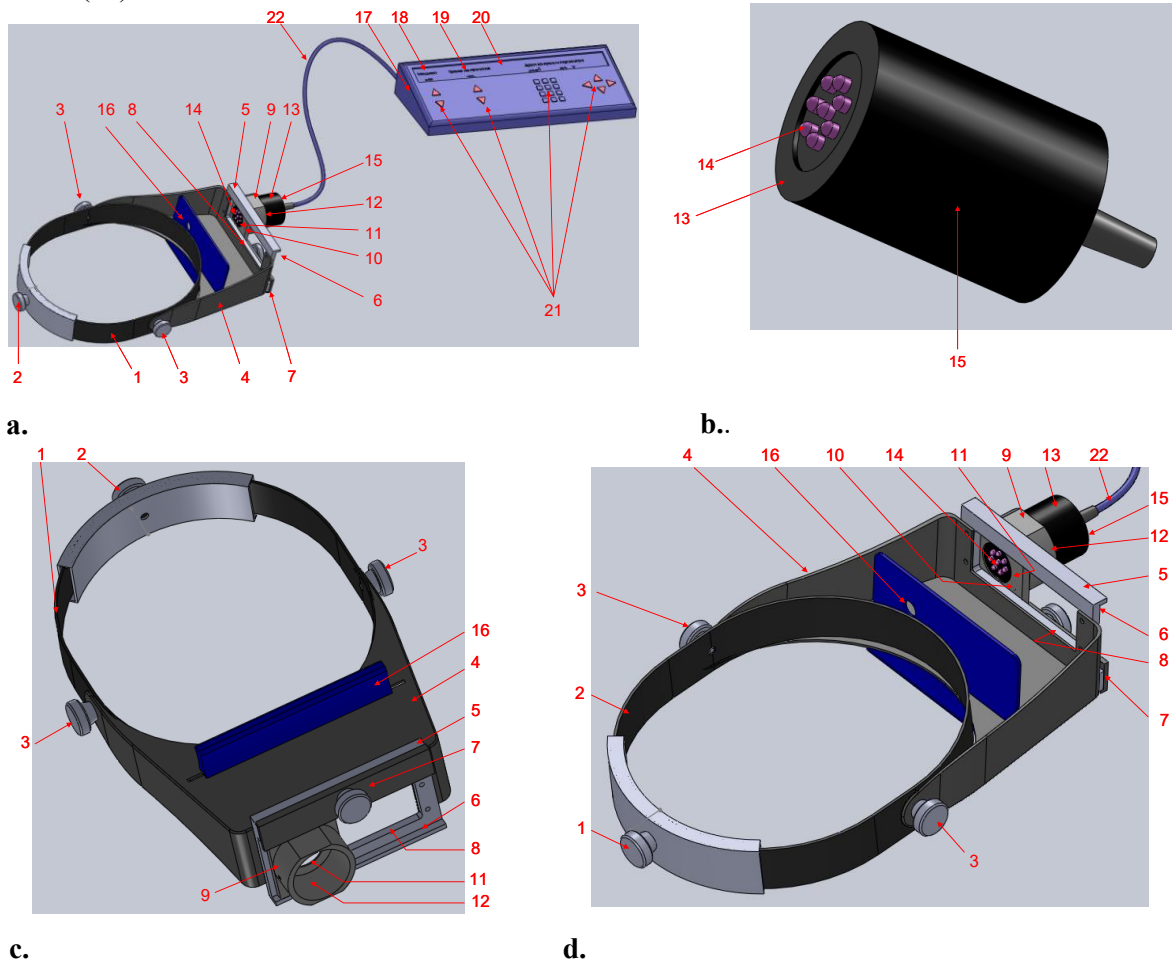
Corneal cross-linking (CXL) is nowadays the most widely used strategy for treatment of keratoconus [1,2]. CXL is a relatively non-invasive medical procedure designed to strengthen and stabilize the cornea and involves applying liquid riboflavin (vitamin B2) to the surface of the eye, followed by treatment of keratoconus, eye ulcer, infectious keratitis, post LASIK ectasia by a controlled application of 360 nm ultraviolet light [3,4]. Stationary ultraviolet irradiation devices have been used for corneal cross-linking with different exposure times of ultraviolet irradiation from 3 min to 30 minutes. Previously, a corneal cross-linking apparatus is described [5], in which a UV lamp irradiates the eye cornea for a period of 30 minutes, with a surface power density of  $3 \text{ mW/cm}^2$ . Other authors use corneal cross-linking apparatus [6] with UV corneal irradiation for 4 minutes at a power density of  $30 \text{ mW/cm}^2$ . The corneal cross-linking apparatus [7,8] uses a UV lamp irradiating the cornea of the eye for 10 minutes with a power density of  $10 \text{ mW/cm}^2$ . All these devices are stationary and of large size, which make their use difficult.

### 2. Objective

Development of a novel type of ultraviolet irradiation apparatus for corneal cross-linking for use in ophthalmology, in particular for treatment of keratoconus, eye ulcer, infectious keratitis, post LASIK ectasia.

### 3. Materials and methods

The ultraviolet irradiation apparatus for corneal cross-linking comprises a device consisting of a circular strap (1), the two ends of which are connected by means of a screwing mechanism (2) for clamping to the face of the patient (Figure 1). On its opposite side, the strap (1) is movably attached to a hood (4) by means of screws (3). A mechanical adapter (5) is attached to the hood (4). The mechanical adapter (5) consists of a guide (6) at one end of which there is a screw press (7). On the flat surface of the mechanical guide (6) there is a rectangular opening (8). In the guide (6) there is a slide (9). It is a detail with a flat rectangular surface (10) with a circular opening (11) and a cylindrical socket (12).



**Figure 1.** Description of the apparatus components for UV irradiation of the eye's cornea.

The ultraviolet light source (13) is composed of ultraviolet LEDs (14) (one or several, LED UV3TZ-390-30). They are mounted in a cylindrical housing (15) with diameter corresponding to the inner diameter of socket (12). A diaphragm (16) is located at a distance away from the source of ultraviolet light (13).

The ultraviolet radiation apparatus for corneal cross-linking also includes an electronic module (17) electrically connected to the source of ultraviolet light (13). The electronic module (17) comprises a power control unit (18), providing 20 mA current to each individual LED. It also comprises an irradiation time control unit (19) (radiation exposure time on the cornea of the eye), as well as a display (20) and buttons (21) for monitoring and setting the parameters of the electronic module (17). The electronic module (17) is connected to the source of ultraviolet light (13) by means of cable (22).

To guarantee the reliability of the apparatus, the output power of the ultraviolet radiation is controlled by an external power meter (Power meter, Coherent, Model: PM USB UV/VIS).

#### 4. Results and discussion

The ultraviolet irradiation apparatus for corneal cross-linking is operating as follows:

A solution of riboflavin (vitamin B2) is dropped onto the eye cornea continuously for about 30 minutes. Then, the irradiation with ultraviolet light is applied.

The diaphragm (16) controls the diameter of the illuminated spot on the cornea of the eye. By means of the carriage (9), the ultraviolet light source (13) is shifted to the left or right eye to irradiate each eye's cornea.

The matrix-LEDs emits a total cut-off power of 40 mW at a wavelength of  $\lambda = 390 \pm 5$  nm. Using a widget, the matrix is moved to the left or right eye. Figure 2 represent a photo of the module attachable to the patient's head.



**Figure 2.** Photo of the prototype of the apparatus - component that allows functional attachment of the UV light source to the head of the patient.

The duration of exposure is 2 minutes. The power density on the cornea of the eye is  $42.1 \text{ mW/cm}^2$  with an illuminated diameter on the corneal surface of  $d = 1.1$  cm. This corresponds to energy surface density of  $5.1 \text{ J/cm}^2$ , accumulated on the cornea.

Corneal collagen cross-linking is a minimally invasive procedure that stiffens the anterior corneal stroma by creating strong covalent bonds between collagen fibrils. Corneal collagen cross-linking with irradiated riboflavin was first introduced in the late 90s by Sporn [9]. It leads to the formation of strong covalent bonds between stromal collagen fibrils leading to a long-lasting increase in the biomechanical rigidity of the cornea.

The so far used standard Dresden cross-linking protocol was carried out in most studies [10] and consisted of the following:

- (1) Eight to 9 mm central epithelial debridement (Epi-Off technique) with a blunt metal spatula or a soft brush.
- (2) Photosensitization with an isotonic 0.1% Riboflavin mixed with 20% dextran solution, usually for 30 minutes before irradiation and then every 2 to 5 minutes during irradiation to maintain saturation of the cornea.
- (3) Uniform ultraviolet A irradiation at  $3 \text{ mW/cm}^2$  for 30 minutes, accounting for a surface dose of  $5.4 \text{ J/cm}^2$ .
- (4) Trans-epithelial cross-linking (Epi-ON technique).

After the completion of the 15 minute riboflavin application procedure, accelerated CXL was performed by some authors [7] using 4 minutes of continuous UVA 365- $\mu\text{m}$  light (KXL System; Avedro, Inc., Waltham, MA) at an irradiance of  $30 \text{ mW/cm}^2$  ( $7.2 \text{ J/cm}^2$ ).

Similarly, a recent study by Mazzotta et al. [11] and our study found that accelerated CXL with a total dose of  $7.2 \text{ J/cm}^2$  did not cause any endothelial damage. This indicates that the increased intensity of the UV irradiance did not adversely affect the endothelial cell layer.

The new apparatus for UV irradiation, that we present has a number of advantages. The radiation time is reduced to only two minutes, compared to other cross-linking devices. The power density on the cornea of the eye is  $42.1 \text{ mW/cm}^2$ . Our apparatus emits ultraviolet light of 390 nm wavelength compared to the currently used wavelength of near 360 nm. The cornea is built mainly of collagen fibrils. The maximum absorption of ultraviolet light by collagen is near 390 nm. The Bunson–Roscoe [12] law describes the photo-response of a material to a certain energy dose. It concludes that all photochemical reaction processes depend only on the total absorbed energy that is determined by radiant intensity and exposure time. A recent ex vivo study evaluated the response of porcine eyes to irradiances between 3 and  $90 \text{ mW/cm}^2$  with illumination times between 30 seconds and 1 minute [13,14,15]. These studies showed that irradiation levels up to  $45 \text{ mW/cm}^2$  produced significantly stiffer corneas, whereas levels of  $50 \text{ mW/cm}^2$  and above did not show significantly greater stiffness.

In the new apparatus we propose a new technical solution to rapidly re-direct the radiation from the left- to the right-eye, by means of a slide. A novel technical solution is the fixation of the apparatus to the head of the patient, that differs as an approach from the rest of similar apparatus, that are not mobile. This provides the opportunity to avoid the movement of the eye out of the UV-radiation beam.

## 5. Conclusion

With the parameters described above, an optimal effect can be achieved for a short time. The described apparatus for UV irradiation is more convenient and features compactness, portability, functionality. The presented above new apparatus emits ultraviolet light of 390 nm wavelength in difference to the known from the literature apparatus using 360 nm. In this way we address the maximum absorption of ultraviolet light by collagen fibrils. The new apparatus for UV irradiation provides the method with mechanical stability.

## 6. References

- [1] Wittig-Silva C, Chan E, Islam F M, Wu T, Whiting M and Snibson G R 2014 *Ophthalmology* **121** 812-21
- [2] Soeters N, Wisse R P L, Godefrooij D A, Imhof S M and Tahzib N G 2015 *Am. J. Ophthalm.* **159** 821–28
- [3] Marino G K, Torricelli A AM and Giacomini N 2015 *J. Refract. Surg.* **31** 380–4
- [4] Hafezi F, Tabibian D and Rychos O 2015 *J. Ophthalm. Vis. Res.* **10** 77
- [5] Fadlallah A, Dirani A, El Rami H and Cherfane G 2013 *J.Refr. Surg.* **29** 84-90
- [6] Shetty R, Nagaraja H, Jayadev C, Pahuja N K, Kummelil M K and Nuijts R M 2014 *BioMed Res. Intern.* Article ID 894095
- [7] Ozgurhan B, Kara N, Cankaya K I, Kurt T and Demirok A 2014 *J. Refr. Surg.*, **30**, 843–9
- [8] El Rami, Chelala E. Dirani A. and Fadlallah A 2015 *BioMed Res. Intern.* Article ID 257927
- [9] Sporl, M H, Kasper M and Seiler T 1997 *Der Ophthalmologe: Zeitschrift der Deutschen Ophthalmologischen Gesellschaft* **94** 902–6
- [10] Seiler T and Hafezi F 2006 *Cornea* **25**, 1057–9
- [11] Mazzotta C, Traversi C, Paradiso A L, Latronico M E and Rechichi M 2014 *J. Ophthalm.* Article ID 604731
- [12] Bunsen R W and Roscoe H E 1862 *Proc. of the Royal Society London* **12** 306–12
- [13] Peyman A, Nouralishahi A, Hafezi F, Kling S and Peyman M 2016 *J. Refr. Surg.* **32**, 206–208
- [14] Konstantopoulos A and Mehta J S 2015 *Eye Contact Lenses* **41**, 65–71
- [15] Eissa S A and Yassin A 2018 *Int. Ophthalm.* doi: 10.1007/s10792-018-0898-y

## Acknowledgments

The authors are thankful to Dimitar Slavov for helping with the design and preparation of the mechanics and with the UV light sources.