Design of corneal cross-linking system: with real-time positioning of pupil position

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Abstract. This paper presents a design of a corneal cross-linking instrument with the function of tracking and locating the central position of the pupil in real time. According to the application requirements, based on the principle of uniform light of compound eye lens, the optical projection system of the corneal crosslinking instrument with the diameter of the treatment spot being 9mm and the uniformity being greater than 90% was designed. And put forward a kind of the pupil localization algorithm, the acquisition of the pupil image gray processing and calculate the histogram, according to the characters of histogram adaptively to take out the appropriate threshold binarization, again after the binarization of image contour tracking, get accurate boundary, the outline of the final vote based on the sliding arc length increment method to determine the pupil center and radius. Experimental results show that the corneal cross-linking system designed in this paper can not only accurately project the treatment of light spot, but also accurately track the central position of the pupil of the human eye.

1. Introduction

The keratoconus is a condition in which the cornea is conical in shape due to the non-inflammatory thinning of the corneal stroma. Thinning of the cornea causes the cornea to protrude forward, accompanied by irregular astigmatism and myopia of the eye, which leads to impaired vision and even blindness in severe cases. The uv-riboflavin corneal cross-linking therapy proposed by Spoerl et al [1-2], can well control the development of keratoconus in the early stage of keratoconus development. This method increases the mechanical strength of cornea by increasing the biomechanical and biochemical stability of corneal matrix tissue. In this method, riboflavin is added as a photosensitizer to the surface of the epithelialized cornea, and then the cornea is directly irradiated with ultraviolet light, and riboflavin is excited by ultraviolet light to generate free radicals, thereby forming new molecular crosslinks in the corneal stroma[3-4]. The matrix fibers are thicker in diameter and more ordered, and the mechanical strength of the cornea is increased, eventually stabilizing the cornea, so that the keratoconus stops developing.

At present, the imported commercial corneal cross-linking instrument has been clinically used in the market, but its expensive price has made many domestic small and medium-sized hospitals discouraged, and there is no relevant report on the development of domestic related instruments. The corneal cross-linking instrument currently used clinically has a problem of cumbersome operation in the treatment process. During the implementation of the cross-linking surgery, although the human eye will be anesthetized, occasionally, the human eye will move involuntarily, and at this time, the treating
doctor needs to move the robot arm to the treatment area in real time according to the position of the patient's eye. This process is not only cumbersome, but there are also cases where excessive exposure to non-therapeutic areas occurs[5].

Based on the above situation, this paper proposes a UV cross-linking system design that can track the position of the human eye in real time. Based on the principle of uniform eye lens homogenization, a projection optical system with a treatment spot diameter of 9 mm and a uniformity of more than 90% was designed. At the same time, a pupil tracking method for contour tracking was proposed.

2. How the System Works
The workflow of the cross-linking instrument system described in this paper is shown in Figure 1. The infrared image acquisition optical path collects the image of the human eye region. After image pre-processing and pupil positioning, the pupil center coordinates are calculated, and then the coordinated coordinate position is used to link motion. The control system causes the center of the treatment light path to coincide with the center of the pupil, allowing the crosslinking to proceed smoothly.

![Fig. 1 System overall work flow chart](image)

3. CXL Illumination Desings
The overall structure of the system is shown in Figure 2. It consists of two parts: the ultraviolet light projection path and the infrared imaging light path. These two parts are connected by a dichroic mirror that reflects ultraviolet light and transmits infrared light. Among them, the former is used to create an accurate treatment spot, and the latter is used to collect images of good quality required for subsequent image processing. The specific workflow can be divided into three steps: the infrared LED will illuminate the human eye area, and the image reflected by the human eye area is imaged on the camera.
through the infrared lens; The second step is to process the collected eye images and determine the location of the treatment center. The third step is to collimate the light with the central wavelength of 365nm from the UV LED and then enter the compound eye lens group and integral lens to achieve uniform light. After reflection by the dichroic mirror, the light spot is irradiated on the surface of the cornea evenly. During the treatment, the treatment spot is updated in real time along with the position of the cornea.

3.1 Treatment Parameters

The commonly used cross-linking protocol in clinical practice are: Dresden protocol and accelerated cross-linking protocol, the former one is to use 3mW/cm² light for 30 minutes, and the latter one uses the light of 10mW/cm² for 9 minutes, and the total dose of both methods was 5.4 J/cm².

The following optical system parameters can be determined by the Dresden protocol and the accelerated cross-linking method, as well as with reference to existing corneal cross-linkers:

1. Output spot diameter: 9±0.5mm;
2. Output optical power density: 0-10mW/cm²;
3. Illumination uniformity: ≥90%;
4. Working distance: 60±5mm;
5. Pupil positioning accuracy: ≥98%.

3.2 Optical Design

Compound eye array lens illumination is an improved homogenization method based on Kohler illumination[6]. The shape of the illumination can be determined by the shape of the compound eye microlens, and the illumination uniformity of the light source is also improved. Figure 3 is a structural schematic diagram of a compound eye illumination system. The light emitted by the ultraviolet LED source is first collimated into a wide beam by an aspherical lens, and the collimated wide beam is split into a plurality of sets of thin beams by a fly-eye lens, and each group of thin beams is integrated. After the lens, it is superimposed on the receiving surface. Since the uniformity of the beamlet is much better than the beam after collimation, the uniformity of the superimposed spot on the receiving surface is also improved[7].

![Fig.3 Compound eye optical system schematic](image_url)

According to the design parameters, the initial structural system parameters are input in the optical design software Tracepro, and the fly-eye lens array parameters as shown in Table 1 are obtained through software optimization. Figure 4 shows the optimized projection system diagram.

| Table 1. Compound eye lens array parameters |
|--------------------------------------------|
| Microlens diameter /mm | Microlens X direction number | Microlens Y direction number | Thickness/mm | Radius of curvature /mm | material |
|------------------------|-----------------------------|-----------------------------|--------------|------------------------|---------|
| 1.5                    | 7                           | 7                           | 29           | 10                     | N-Bk7   |
Fig. 4. Projection system diagram

In the tracepro software, the human cornea is set as the receiving surface, and 1 million rays of light are traced to obtain a corneal surface irradiance map of the human eye as shown in Fig 5. The spot size is a circle with a diameter of 9 mm, and the spot uniformity is calculated to be 92%, which meets the design requirements.

Fig. 5 Corneal surface irradiance map

4. Pupil Positioning Algorithm Design

In the process of surgical treatment, in order to achieve real-time tracking and positioning of the eyeball, the position of the pupil of the human eye must be accurately positioned first. The image collected by the infrared imaging system is shown in Fig 6.

Fig. 6 Corneal surface irradiance map

4.1 Pupil Image Binarization

Image binarization is one of the common methods in image analysis and processing. It refers to converting a grayscale image into a black and white image, that is, setting the gray value of all points
on the image from 0-255 to 0 and 1 fixed gray. The purpose of binarization is to divide the pupil image into two parts: the pupil and the background. The key is to find the appropriate threshold[8-9].

It can be seen from Figure 7 that the pupil portion of the pupil image has a lower gray value than the other portions, and the pupil image segmentation is first performed using binarization. The pupil portion is the position of the first peak in the histogram, as shown in Figure 8. In this paper, the peak value is obtained between the gray values 1-50, which is the pupil position, and then the peak value is obtained between the gray values 61-120, which is the background portion, and the trough between the two peaks, that is, the pupil position in the histogram. The first valley bottom appearing on the right side is used as a threshold to binarize the pupil image. The result of the binarization is shown in Figure 8.

4.2 Remove Noise

There is obvious lashes in the pupil image after boundary tracking binarization. The lashes are located above the pupil. As can be seen from Figure 8, all the noise areas are smaller than those of the pupil. At this point, we can determine the pupil contour by calculating the contour area method. If the pixel area of the contour area is less than a certain value, it is considered to be noise. In this paper, an image with a true pupil pixel value greater than 25000 and a pixel area less than 25000 will be considered as noise and removed.

4.3 Tracking Profile

Since the binary image has only 0 or 1 values, where 0 is the background and 1 is the target area, based on this feature, each of the unconnected edge segments in the binary image can be described by boundary tracking[10]. Get a series of sets of coordinates belonging to different edges. For a binary image R, it is first divided into a series of non-connected regions, namely R={R_1, R_2, ..., R_n}, and each region is subjected to boundary tracking. The specific steps are as follows:

1. Select the point where the top left position of the region R_i is 1 and record it as s_0 point. The variable s represents the current boundary point in the boundary tracking process. Select c_0 as the point to the left of s_0. Since s_0 is already at the far left of the area, the value of c_0 is 0 at this time, which is the background point. Starting with c_0, traverse the 8 neighborhoods of s_0 points clockwise, use variable c to save the current point in the traversal process, and let s_1 denote the first neighbor point encountered in the traversal sequence with a value of 1, c_1 a point immediately before s_1 with a value of 0 (background). Record the position of s_0 and s_1.

2. Reselect the current tracking point, let s_0=s, and c_1=c.

3. From the point c, traverse the eight neighborhoods n_1, n_2, n_3, n_4, n_5, n_6, n_7, n_8 of the s point in a clockwise direction. Find the first neighborhood point n_k with a value of 1.

4. Let the starting point s=n_k and traverse the starting point to c=n_(k-1).

5. If s_0=s and the next immediately adjacent boundary point is the originally recorded s_1, the algorithm ends, otherwise jumps to step 3.

Through the above method, the image is contour-tracked, and the obtained pupil contour map is as shown in Figure 9.
4.4 Pupil positioning

After the boundary is traced to obtain the edge of the pupil area, the center position and radius of the pupil need to be further positioned, and the shape feature of the pupil is approximately circular, so the problem translates into a problem of circular detection and positioning [11].

Ideally, after the pupil edge image is extracted, we can get a circle, then we can use the vertical bisector of the circle to cross the center of the circle, and determine the coordinates of the pupil center by the intersection of the two vertical bisectors as shown in Fig 10.

![Fig. 10 The intersection of the two vertical bisectors is the center of the circle](image)

The simultaneous equations E1 and E2 can solve the intersection coordinates of the two straight lines E1 and E2, which is the pupil center O(x, y).

\[
E_1: y = \frac{1}{2} (y_1 + y_2) + \frac{x_2-x_1}{y_1-y_2} \left[ x - \frac{1}{2} (x_1 + x_2) \right] \\
E_2: y = \frac{1}{2} (y_2 + y_3) + \frac{x_2-x_3}{y_2-y_3} \left[ x - \frac{1}{2} (x_2 + x_3) \right]
\]

The simultaneous equations E1 and E2 can solve the intersection coordinates of the two straight lines E1 and E2, which is the pupil center O(x, y).

\[
x = \frac{1}{2} \left[ (x_2^2 - x_1^2) \times (y_2 - y_3) - (x_1^2 - x_3^2) \times (y_2 - y_1) + (y_1 - y_2) \times (y_3 - y_2) \times \right. \\
\left. \frac{y_2-y_3}{y_3-y_2} \right]
\]

\[
y = \frac{1}{2} \left[ (x_2 - x_1) \times (x_3 - x_2)(x_1 - x_3) - (y_1^2 - y_2^2) \times (x_3 - x_2) + (y_2^2 - y_3^2) \times \right. \\
\left. \frac{x_2-x_1}{x_3-x_2} \right]
\]

\[
r = \frac{1}{2} \left( \sqrt{(x_1-x)^2 + (y_1-y)^2} + \sqrt{(x_2-x)^2 + (y_2-y)^2} \right)
\]

However, in many cases the contour of the pupil edge obtained after contour tracking is not a standard circle. It is very likely that the three points on the circle will be taken in the irregular area, resulting in the calculation of the center of the circle as a false center.

In order to solve the above problem, starting from point A on the edge, multiple chords are sequentially selected by increasing the sliding arc length until the length of the chord is less than the minimum value T_{\text{min}} (generally not less than 6 pixel values according to the size of the circle), Obtain a set of strings AB, BC, CD, DE, EF, FG. The string EF spans the incomplete circle, However, since D is taken in an irregular area, the vertical bisector obtained by the strings CD and DE is not the...
vertical bisector of the true circle. The simultaneous chord line equation calculates 5 center positions and radii respectively, and saves them in the array circles, but 3 of them do not match the actual ones. In order to get the correct round chord as much as possible, move the position of point A backward by \(1k\) of the total length of the edge, and repeat the previous calculation process to obtain the result shown in Fig 11. All the chords are taken at the correct position, Find 5 center positions and radii again and add them to the array circles, and 7 of the 10 center positions obtained are correct. Continue to move the position of point A backward by \(1k\) of the total length of the edge, and repeat the above process for a total of \(k\) times. Each possible center position in the array circles is taken out for voting. If the distance between the coordinates of the two centers is less than the threshold \(d\), the two points are considered to be the same point, and the voting may adopt a two-dimensional hash table method. The position of the center of the circle with the highest ticket is the true center position of the pupil[12]. The radius of the circle corresponding to the center of all the highest votes is averaged as the radius of the real pupil. The resulting image is shown in Fig 12.

![Fig.11 Multiple chord length growth method to determine the center of the circle](image1)

![Fig.12 Pupil center positioning](image2)

5. Experiment and Verification

According to the above design, the corneal cross-linking instrument is processed and assembled as shown in Fig 13, and the spot is irradiated on the paper of 9 mm diameter circle printed in advance, as shown in Fig 14, it can be seen that the spot is completely filled with a circle of 9 mm diameter.

![Fig.13 The UV illumination device prototype](image3)

![Fig.14 beam spots diameter](image4)
A CCD camera with a 1-inch target surface was selected to directly receive the projection spot, and a therapeutic illuminance of 10 mw/cm² was set on the device, and the acquired image is shown in Fig 15. According to the nine-point sampling method[13,14], the gray value of nine points is taken in Figure 15, and then according to the formula:

\[
\text{uniformity} = 1 + \frac{E_{\text{max}} - E_{\text{min}}}{E_{\text{average}}} \times 100\%
\]  

Among them, \(E_{\text{max}}\) is the maximum value of the gray value among the nine points, \(E_{\text{min}}\) is the minimum value of the gray value among the nine points, and \(E_{\text{average}}\) is the average value of the gray value of the nine points, and finally the spot uniformity is 90.2%.

During the experiment, 100 images of human eyes were taken by infrared imaging system, and the pupil tracking and positioning method described in this paper was processed to correct the error rate of less than 2%, which satisfies the parameter requirements.

6. Conclusion
The corneal cross-linking instrument can well prevent the development of keratoconus. For the needs of clinical corneal cross-linking instrument, this paper proposes a corneal cross-linking system design that can track the position of the pupil in real time. The system can output a diameter of 9mm. The uniformity reaches 90.2% of the treatment spot, and the energy adjustment range of the treatment spot is 0~10mw/cm², which satisfies the clinical use requirement. At the same time, based on contour tracking, a real-time tracking and localization algorithm for pupils is designed. The experimental results show that the design can meet the clinical needs well. The system has a high level of intelligence, which makes up for the shortage of domestic blanks and existing products of such products, and has great development prospects and market benefits.

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