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Design and control of a visual servomechanism for automating corneal cross-linking treatment in keratoconus patients

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Abstract: A novel mechatronic system designed for automated corneal cross-linking (CCL) treatment in keratoconus patients is introduced. Keratoconus is a serious illness that if not treated may cause serious distortion of vision. Currently, the CCL operation, which is the most promising treatment of this disease, is performed manually. The automated system developed is the first of its kind to automate the treatment with visual feedback, and it aims to increase the efficiency in treatment and to eliminate any potential side effects and risks of the treatment. To track the eye of the patient, the system consists of a camera, an image processing algorithm developed on OpenCV sharp, a planar servomechanism system consisting of various mechanical and electronic components, and a PIC microcontroller that contains digital PID controllers. The proposed system and the algorithms are designed and simulated in Matlab, and then the system is manufactured and various experiments with an eye pattern and animal eyes are performed. The results are shown and discussed.

Key words: Keratoconus treatment, eye tracking, system identification, digital PID design, corneal cross-linking

1. Introduction

Keratoconus is a noninflammatory cone-like ectasia of the cornea; it is usually bilateral and progresses over time. Keratoconus can cause substantial distortion of vision, as well as vision with multiple images, streaking, and sensitivity to light. The deterioration in vision can affect the patient's ability to drive a car or read. Its reported frequency is approximately 1 in 2000 in the general population [1].

If not treated, this illness can cause serious distortion of vision. Treatment options range from contact lenses to penetrating keratoplasty (corneal transplantation). In early stages of keratoconus hard and soft lenses can be used. Surgical methods, such as photorefractive surgery (excimer lasers), intracorneal ring (ICR) surgery [2–7], and penetrating keratoplasty are other treatment options for keratoconus patients. It is reported that penetrating keratoplasty is needed in 20% of keratoconus patients [8,9]. However, all of these treatment options are only able to correct refractive errors (improves vision), and cannot stop the progression of keratoconus [10]. Another treatment option is the corneal cross-linking (CCL) operation, which is a parasurgical technique. The goal of the treatment is to halt progressive and irregular changes in corneal shape known as ectasia. It was developed in Germany in 2000 [10]. In CCL, UV light and a photosensitizer are used to strengthen chemical bonds in the cornea. Thus, the CCL operation is a unique and the most important treatment of keratoconus.

CCL provides a potential means for stiffening the cornea by means of photosensitizing radiation. In vivo

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experiments have revealed that a combination of UV radiation and riboflavin is the most effective and least harmful procedure for inducing collagen cross-linking in the human cornea [10].

The CCL operation is conducted under sterile conditions in an operating theatre. The treatment involves two 30-min sessions. At the beginning of surgery topical anesthetic eye drops are applied and the doctor abrades the epithelium on the cornea. During the first 30 min, riboflavin (B2 vitamin) is applied to the cornea in every 3 min [11]. In the second session, in addition to the riboflavin solution, an optical system that consists of 7 ultraviolet A (UVA) diodes applies UVA irradiation to the cornea. Irradiance is performed for 30 min using a dose of 3 mW/cm^2 (corresponds to a surface dose of 5.4 J/cm^2 from a working distance of 6 cm [11]). Application of riboflavin and UVA irradiation showed important results in keratoconus patients. The rigidity of treated corneas is significantly increased in 70% of the patients [11]. No complications or adverse event are observed. In addition, no decrease in endothelial cell density or cataract formation is observed. Therefore, the CCL operation proved to be an efficient solution for keratoconus patients [11].

Application of UVA irradiation has a significant effect on the success of the treatment. In many studies [11–14], it is mentioned that "95% of UVA irradiation will be observed within the cornea". Therefore, the deficiency of the current treatment occurs in the application of the UVA irradiation source. In the regular CCL treatment the UVA irradiation source is stable. During the treatment the patient should look directly into the UVA irradiation source for 30 min (Figure 1). However, patients lose their concentration because of the long operation time, or external light or sound sources and these disturbances can make patients move their eyes. These movements decrease the effect of UVA irradiation and decrease the success of the treatment. Moreover, the UVA irradiation is dangerous for healthy cells in the sclera (white part of the eye). In surgery, these movements should be carefully compensated for by the operator, manually. The computer controlled system proposed in this paper aims to eliminate any unwanted irradiation application by tracking the patients' eyes and moving the UVA irradiation source to compensate for any error.



Figure 1. Manual treatment of keratoconus.

In order to automate the treatment, an eye-tracking algorithm has been developed using the OpenCVSharp library [15,16]. The algorithm identifies the position of the eye with a camera and in the case of an eye movement a mechanical system driven by two DC motors moves the UVA irradiance source to the desired position. Thus, the system prevents damage to the eye. Moreover, the system improves the quality of the treatment and reduces the workload of the operator.

2. Eye detection and tracking

A successful automated treatment system depends on fast and accurate eye detection and tracking. Eye gaze trackers (EGTs) are devices that can estimate the direction of the gaze of a person [17]. This information can be used in ophthalmology, neurology, psychology, and related areas, or as an input device for computer interfaces to be used by people with disabilities [17–19]. Eye gaze detection is also used for improving safety of drivers to prevent accidents due to sleeping [20–22]. Some techniques for eye gaze tracking require equipment to be put in physical contact with the user, such as contact lenses, electrodes, and head mounted devices. Nonintrusive techniques are mostly vision-based [23]. Vision-based eye gaze tracking techniques rely on some characteristics of the eye (such as pupils) that can be detected by a camera. Although the pupils are harder to detect and track, these techniques have better accuracy since they are not covered by the eyelids. In order to enhance the contrast between the pupil and the iris, many eye trackers use an infrared light source.

There are various techniques to determine and track eye gaze using vision that do not require calibration, and a few enable some degree of free head motion. A comparison of the speed, accuracy, and level of allowed head motion of some recent methods is presented in [23]. Some of these algorithms use complex computations and involve time lags, making them unsuitable for real-time control. In these studies, algorithms commonly try to determine where the eye looks. The real time position of the eye is not the main interest in these algorithms, and the position of the camera is fixed. In our study, instead of gaze direction of the eye, its position with respect to the camera should be determined. Unlike previous studies, the head motion in our task is almost zero, since the patient rests on his/her back. Moreover, the camera is not fixed; it will move via an automated system that has the UVA source directly plugged in. The camera is not stationary, and it behaves as an eye-in-hand visual servoing system. The visual-servo control uses the features on the image plane and the servo controls them to the goal position [24]. In visual servoing typically point-based features are used, which are the centers of some features or the coordinates of the edges. Various studies have been performed on eye-in-hand systems in which a camera is placed on the end-effector of a manipulator to guide it to the desired location [25–29]. This approach has clear benefits in our study. The difference between the required position of the eye and its current position can be used as an error signal, and the desired motion of the camera can be directly derived from the image plane information.

Alternatively a system with mirrors could also be used. When the algorithm detects an eye movement, motors can drive a mirror and focus the beam in the correct position. However, due to the limited lifetime and the gradually decreasing reflection properties of mirrors, and due to the complex calibration procedures, we decided not to use mirrors.

Fast eye movement detection and enabling rapid and accurate corrections are unique goals of this system. Luckily due to the nature of the treatment, the system needs to track only a single eye. The algorithm should be adaptive and accurate in tracking. In this study, an eye detection algorithm was developed by image processing techniques of OpenCV library. C # is preferred for the user interface, and in order for the OpenCV library to work, OpenCvSharp wrapper is used.

The proposed image processing algorithm, presented in Figure 2, uses multiple filters to avoid any distortions caused by light, shadows, or other environmental conditions. Firstly, frames are captured by a camera. Afterwards a background subtraction is applied to the frame to determine areas of interest. This subtracted image is then applied with a "Gaussian Blur" (Gaussian smoothing) by a Gaussian function to reduce image noise. Gaussian filter is used to remove noise, and to preserve high frequency edges. The next step is the color conversion from RGB to gray. After the color conversion, a threshold is applied to the frame

to obtain a binary image. In experiments, both the adaptive and binary threshold techniques were tried. The adaptive threshold is more beneficial when there are uneven lighting conditions, and when there is a need to segment a lighter foreground object from its background, it is performed by analyzing each pixel with respect to its local neighborhood. In our experiments, the performance of the binary threshold was more satisfactory, due to the nature of the controlled lighting conditions, and therefore the adaptive threshold was excluded from the system. Finally, a "flood-fill" filter is added to the algorithm. The flood fill is a useful function to mark or isolate portions of the image for further analysis. A seed point is selected from the frame; all similar neighboring points are colored with uniform color. The result of the flood fill operation will be a single contiguous region.

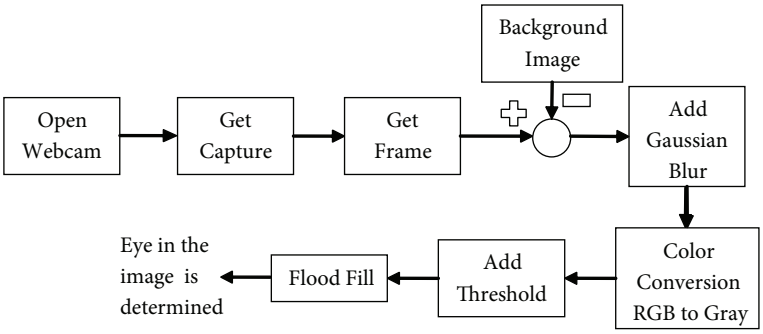


Figure 2. Flow diagram of image processing algorithm.

The final processed frame is the detected eye. The final result can be seen in Figure 3 in the third frame. A minimum enclosing circle is drawn around the detected contours. The developed image processing algorithm is able to detect the eye movements of the patient accurately and rapidly (at 30 fps) using a standard notebook computer. The notebook computer is selected due to ease of transportation to field treatments. The eye position error, which is the position difference between the eye center on the image and the desired eye location, is then sent to the controller by the serial connection.

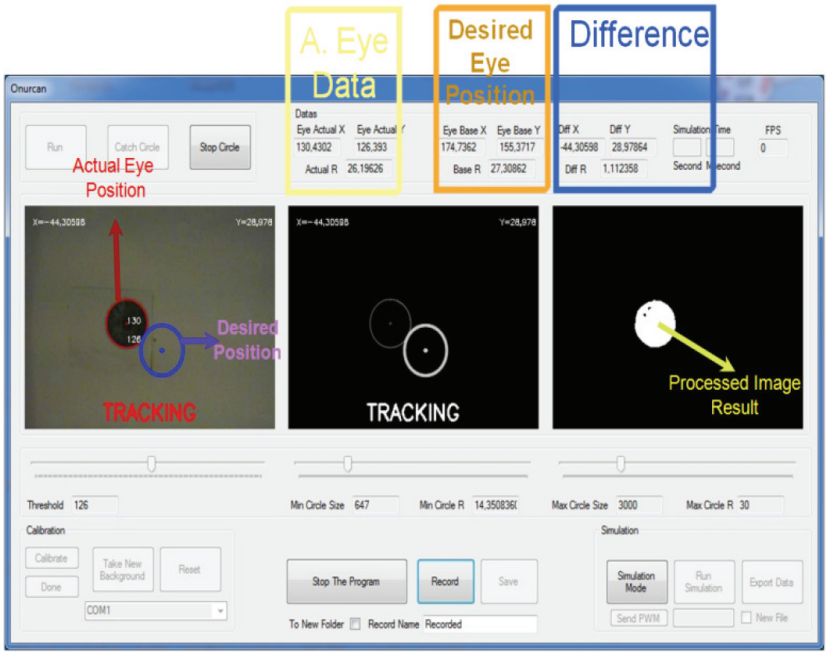


Figure 3. Developed eye tracking application and the graphical user interface.

A graphical user interface has been developed so that the operator can easily change some properties of the algorithm, such as the threshold value, min–max sizes of the detection circle, and enabling or disabling any filter. The eye detection algorithm is the most important factor for stability of the system, where calibration has unique importance. Since the vertical distance of the camera with respect to the patient's eye can be different for each treatment, a calibration procedure is necessary for the vision system to perform accurately. This calibration procedure is performed initially before each treatment. The operator can also calibrate the system using the information module of the graphical user interface with a standard eye pattern.

3. The electromechanical system design

A device designed for treatment of human patients has to be fast enough to track the eye and compensate for any errors, but also (since the treatment is applied to a patient who is awake) the system should not disturb or scare the patient. Designing a fast and stable system that considers the patient's condition is a challenge.

The purpose of the proposed electromechanical system is compensation for patients' eye movements. Figure 4 presents the flowchart of the system, which consists of a mechanical and an electronic subsystem.

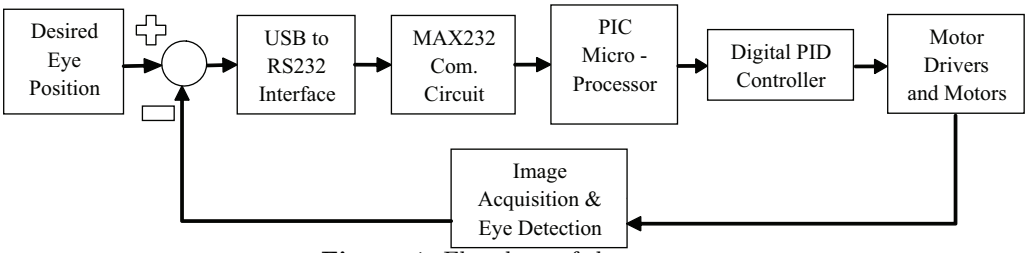


Figure 4. Flowchart of the system.

3.1. Mechanical system

The system is required to follow the patient's eye movements. The developed system is modeled similar to the manual system, where the patient lays face-up on a bed and the laser is facing down towards the patient. The UVA irradiation source can easily be plugged into the prototype.

The mechanical system (Figure 5) has two motors and the platform. Each motor is connected to a lead screw. The rotations of screws are transferred to linear motion, and the linear motions of the platform give the ability to compensate for errors in the x and y axes.

Mechanically the platform can move up to 25 cm in each axis. While the overall size of the eye to track is approximately 12 mm, laboratory pre-evaluations showed that the highest error that system is going to face is expected to be approximately 10–15 mm. On the other hand, regular movements during the treatment to compensate for patients' eye movements are approximately 1–5 mm. The rotational movements of motors are advantageous in these sensitive correction motions. The mechanical system is driven by two 750 RPM DC motors. With the careful selection of the pitch value of the mechanical screw, each revolution of the motor shaft corresponds to 1 mm linear movement along any axis. Desired motion data, calculated from PID controllers, are transferred to pulse width modulation (PWM) pulses to drive the motors.

3.2. Electronic system

The purpose of the electronic system is the collection of the visual data (eye location) from the PC with a serial interface, implementation of the controllers on a PIC microprocessor with PID controllers, and driving the motors on the mechanical system with PWM signals. To use the electronic system safely in the field and to

make it compact and movable, a hardware box is designed (Figure 6). Designed printed circuit boards (PCBs) are easy to improve. The electronic circuits are produced as independent modules so that each module can be easily replaced. These modules have their own proper voltage regulators and the fuse circuit protects modules for any voltage/current oscillations.

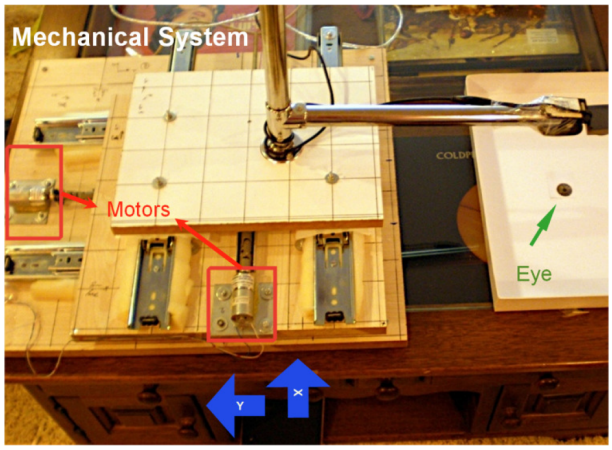


Figure 5. Mechanical system with two DC motors (each for one axis).

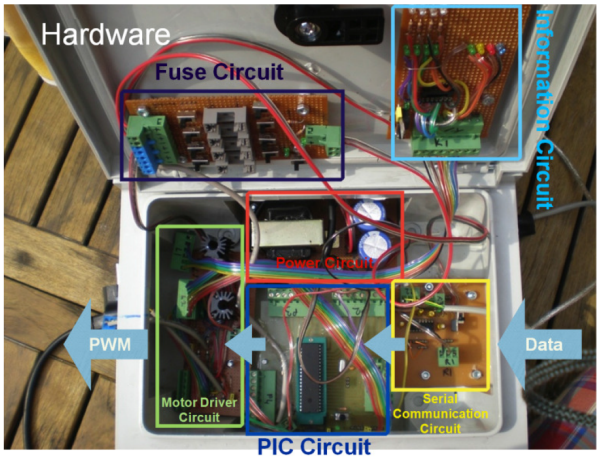


Figure 6. Developed electronic system.

Considering Figure 6, the electronic system takes the error data from the serial communication circuit (yellow). This circuit has a MAX232 integrated circuit to reduce communication errors and to protect the PIC for any voltage/current irregularities. A communication protocol is also implemented for identification of the correctly transferred data.

The data are then passed to the PIC circuit (turquoise). The PIC microcontroller is responsible for the application of the digital PID algorithm and for the transfer of the calculated control outputs to the motor driver circuit. The motor driver circuit drives the motors by PWM signals. It also eliminates the need for a personal computer for the control tasks. The fuse circuit (purple) checks the system condition and protects the other circuits from short circuit by using specific fuses. The power circuit takes 220 V data and converts it to 25 DC V. The information circuit (blue) provides status data about the condition of the circuit and motors.

3.3. PID controller

A proportional-integral-derivative (PID) controller is a generic controller widely used in industrial control systems. The control system in this study uses the center coordinates of the patients eye, and control two motors to compensate the error along the x and y axes. The motions along the x and y axes are independent. Therefore, the system can be treated as two independent single input single output (SISO) systems for control, and a PID controller can be developed and tuned for each SISO system. In this study, after considering many digital PID algorithms [30-33], a discrete PID controller is preferred and implemented in Matlab.

3.4. User interface

Although the system is intended for automatic operation, a graphical user interface (GUI) has been developed. The GUI (Figure 3), which was written in C# language, gives many abilities to the surgeon and the design engineer for operation and simulation.

The GUI involves calibration, information, and simulation modules. In the calibration module, the user can define PID gains and image processing properties (such as setting adaptive-linear threshold, selecting filters, defining size of detection circle, selecting COM port, and taking new background for subtraction). The information module gives real-time data about the condition of the system. The simulation module gives the ability to simulate the system and PID controller performance. The simulation module can export the simulation data to a file. Moreover, the system can be directed with keyboard input to compensate for error manually with a specified PWM value. Additionally, all simulation and operation processes can be recorded and exported.

4. Simulations

In this study, Proteus ISIS software and various toolboxes of Matlab were used to design the system through simulations.

For electronic system design and testing, Proteus ISIS software was used. All elements were embedded in the simulation software, and the PIC code and the electronic components were tested. After the successful simulation of the electronic circuits on this software these elements were used to make PCBs. Additionally the system was tested on a bread board for successful operation.

When the electronic system's simulations and manufacturing of the PCB were complete, the components were assembled on the mechanical and electronic subsystems. The system was ready to be analyzed to obtain its characteristics with the system identification toolbox on Matlab [34–36]. Especially when there is a need for precise control, the system in question can be subjected to identification analysis. With the analysis, unknown parameters due to mechanical or electrical subsystems can be estimated, or a suitable transfer function that represents the system's behavior can be obtained. In this study, the system identification toolbox is used to estimate the system's transfer function, which will then be used to develop the necessary controllers. In system identification, firstly the system is driven by random inputs and then the corresponding outputs are measured (Figure 7). Many approaches were tested and the results clearly showed that the *AutoRegresive model with eXternal input* (ARX) model is the best to estimate the real system. The system identification toolbox is used to obtain the best na, nb, and nk values (zeros, poles, delays). In this estimation, it is seen that the developed transfer function model fits the real physical system in 86.7% on motions along the x and y axes (Figures 8 and 9). This means that the real physical system (involving mechanical and electronic components) is modeled accurately, and the transfer function obtained describes the system behavior accurately.

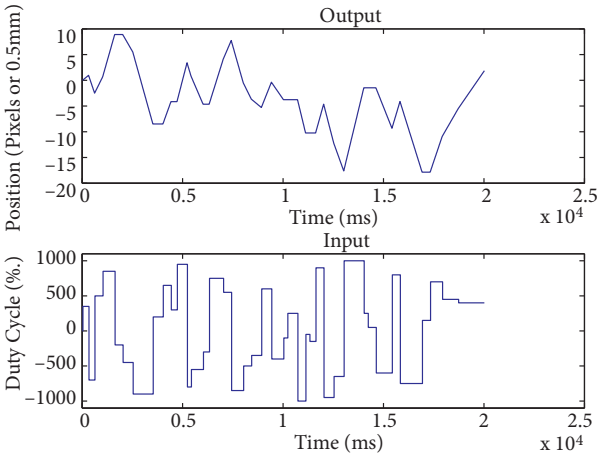


Figure 7. Input/output characteristic of the real system.

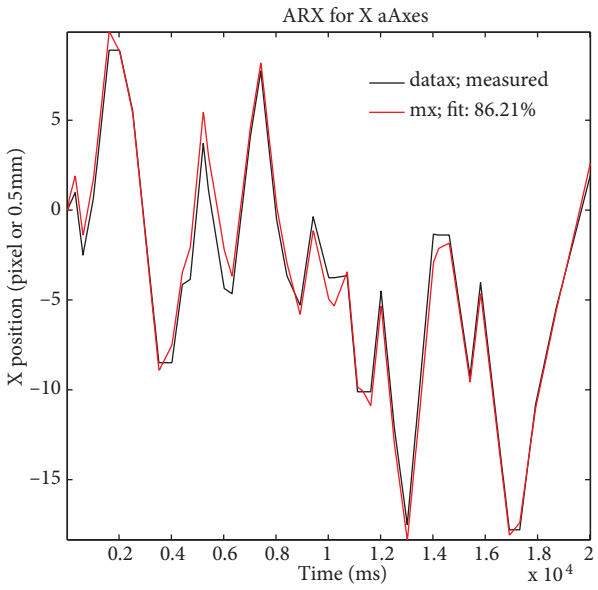


Figure 8. Fitting results of RSys and ESys (real and estimated system) for x-axis.

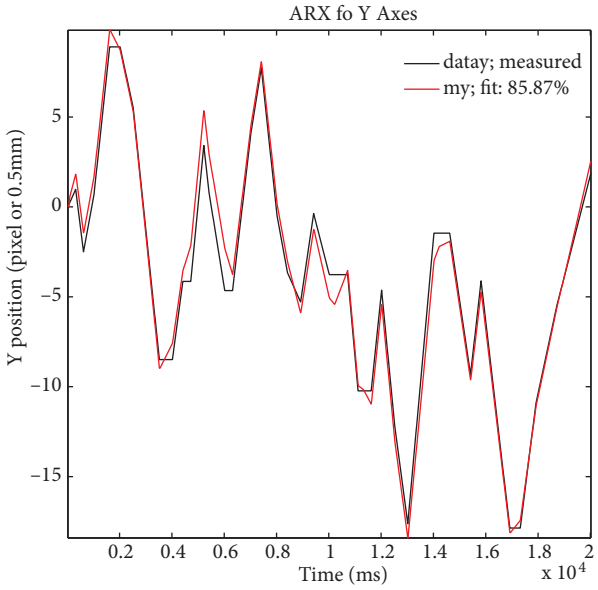


Figure 9. Fitting results of RSys and ESys (real and estimated system) for y-axis.

Matlab SISO toolbox is a useful tool for designing controllers. The obtained transfer functions are transferred to the Matlab SISO tool to obtain appropriate PID controller coefficients for the two SISO controllers (one for each axis). These controller coefficients will be implemented in the PIC controller to control the motors based on feedback from the camera. First, a compensator is designed for controlling the system. Both systems (x and y axes) have a pole at 1, which means systems are at the stability limit. With root locus techniques it can be seen that with a proportional gain the system can be easily stabilized. The controller should make the system stable, and the system's behavior should have small settling time and the response's overshoot should be limited. With root locus techniques, a system with minimum settling time and overshoot lower than 10% is designed. Figures 10 and 11 show the simulation results with the PID controller for 10 pixels or 5 mm error.

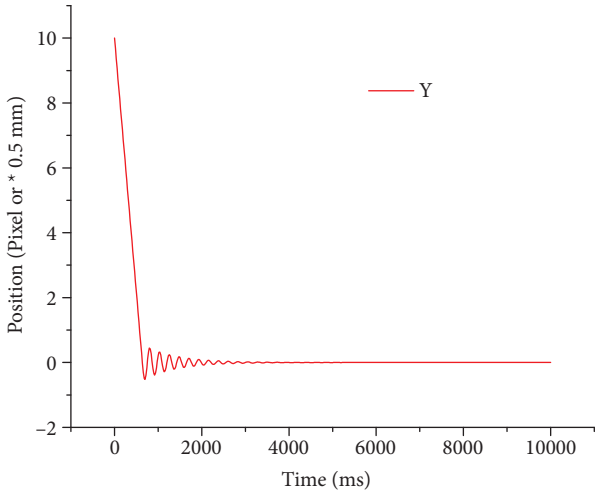


Figure 10. Matlab simulation results with PID controller for y-axis.

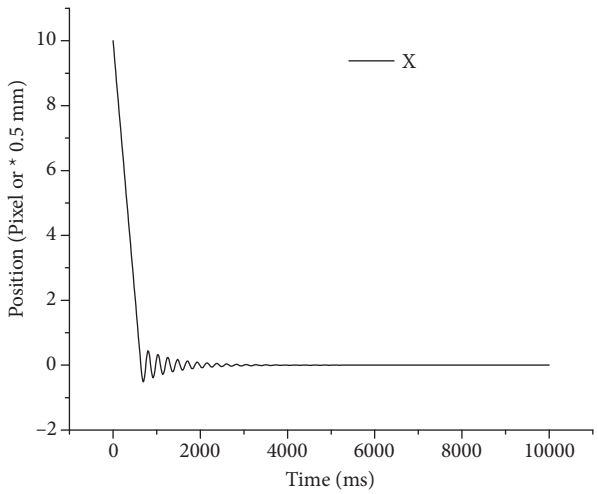


Figure 11. Matlab simulation results with PID controller for x-axis.

It is observed from simulations the x and y axes have small differences. The PID gains that satisfy the design requirements were obtained with 5% overshoot. Suitable PID gains are determined to be 180 for K_p, 50 for K_i, and 1 for K_d, which will be used in the PIC controller during the experiments.

5. Experiments

The developed system cannot be directly tested on human eyes without proper approval and certification for clinical study. The initial field tests during the certification will involve experiments performed on animal eyes, such as pigs and rabbits. In this study, we performed two experiments to show the performance and usability of the system in the field: one of them with an eye pattern and the other with an animal eye.

The first experiment is performed with an eye pattern. This pattern is moved as if it is simulating the eye movements of a patient during treatment. The performance of the system observed by the second camera and the image plane errors are presented in Figure 12. In this experiment the system detected and tracked the eye figure accurately.

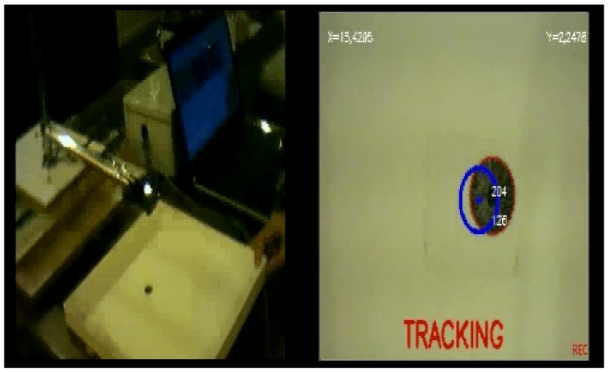


Figure 12. The tracking experiment.

Figure 13 shows the characteristics of the system for small errors. It can be seen that the system compensates for the error within less than a second. These compensation results meet the treatment criteria.

Since the system will be subjected to noise in real world conditions, the next simulation involved providing the system with different disturbances. As shown in Figure 14, the control system was able to keep the error considerably small.

In all figures, about 1 pixel oscillation is observed. These small oscillations occur due to the limited resolution of the mechanical system and as well as the control system. These small oscillations do not affect the performance of the system and can be omitted. This undesired response can be removed by limiting the movement of the system for very small errors by applying a dead-band in the control system.

In conclusion, the experimental results are satisfactory in the 0–5 mm error range, which is within the desired working distance. For higher distances, simulation and experimental results are slightly different. However, the experimental results gave better characteristics than the expected simulation results.

The second experiment involves the use of an animal eye. The use of a real eye is a more realistic test of the vision system than the printed eye pattern in Figure 15. In the experiment the effects of UVA irradiation and riboflavin could be clearly observed. Firstly, the animal eye is prepared, and the epithelium is abraded. Secondly, the eye is placed under UVA irradiation. The figure also shows the laser system used for the treatment. The main difficulty in the experiment was the effect of the UVA irradiation. When irradiation was applied to

the cornea with riboflavin a second circle appeared. The background subtraction was able to eliminate this effect. In the final processed frame the eye can clearly be detected and tracked successfully (Figures 16 and 17). The mechanical response of the system in this experiment is identical to that of the previous experiment.

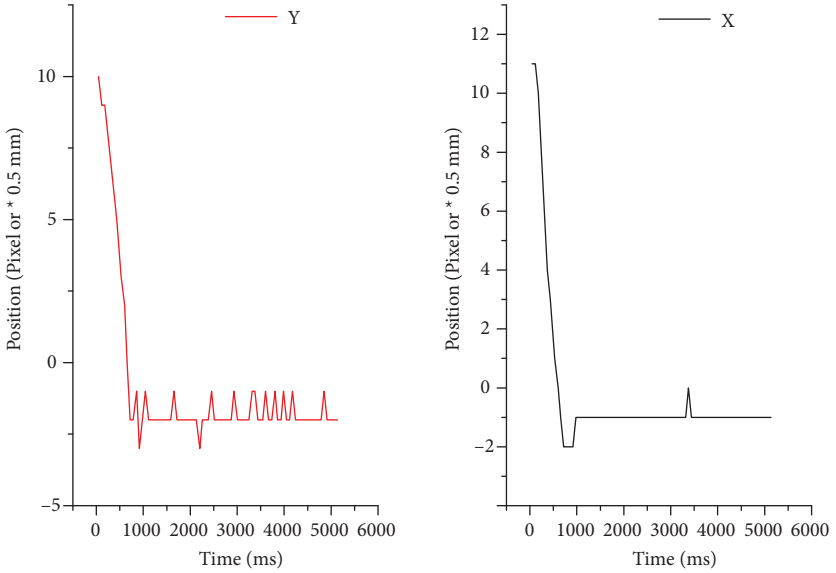


Figure 13. Correction experiment for 5 mm for x-axis and y-axis, respectively.

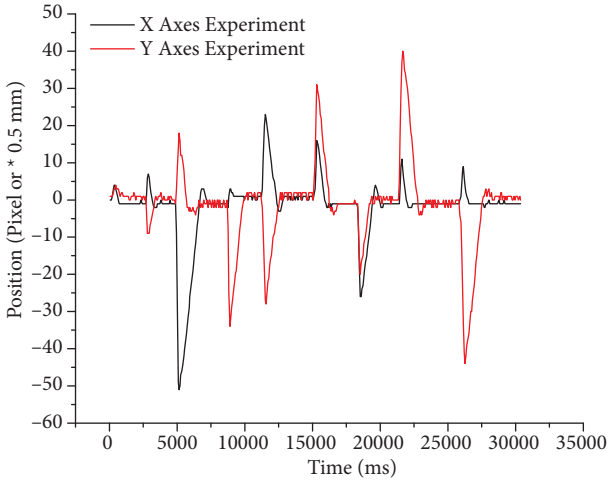


Figure 14. Response of the system to different disturbances.

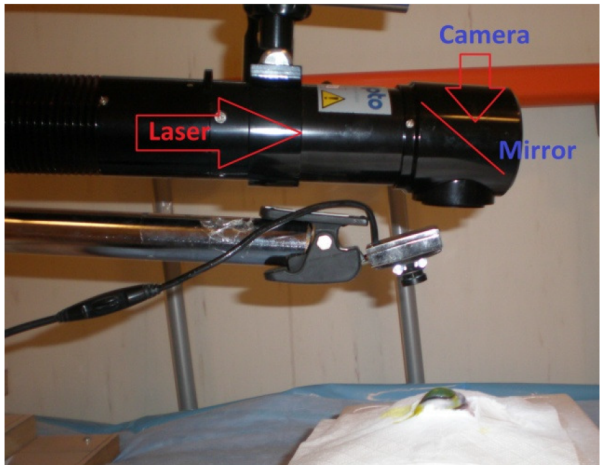


Figure 15. Field experiment setup.

Both experiments showed that the prototype system is working properly. A video of the experiment of the developed system is available at: http://www.youtube.com/watch?v=Fi2iATgvs2o.

6. Conclusion

Treating keratoconus using the CCL operation is performed manually under the supervision of a doctor. A novel automatic system proposed in this paper automates this operation using visual feedback. With this system, efficiency in treatment can be increased, and any potential side effects and risks of the treatment can be minimized.



Figure 16. Processed frame under UVA irradiation.



Figure 17. Field experiment eye detection.

The developed prototype of the system is complete and working efficiently. Moreover, based on opinions of our medical advisors, obtained response characteristics satisfy the demands of the CCL treatment. As far as we know, this is the only automated CCL treatment system available in the literature; because of this, no performance comparison could be performed.

As a future work, we plan to improve the system with other sensors. With the addition of encoders, additional and more accurate information to control position data can be obtained. Furthermore, this will provide a better control ability to the system. Moreover, we plan to implement an IR camera in the system. The pupil (black part of the eye) can easily be separated under IR LED illumination and the IR cameras would give clearer visual data for the image processing algorithm to work with. In order to eliminate the calibration step for each patient, a sensor will be used to estimate the correct distance to the patient's eye. Alternatively, the size of the detected eye could as well be used within the vision algorithm to perform self-calibration. One other planned addition to the system is a single-board vision computer to eliminate the dependence on a PC in the field.

Due to the nature of the treatment, the system needs to track only a single eye. For those patients requiring treatment for both eyes, an alternative system can be developed. A system that can track two eyes at the same time and compensate for movements would be a nice improvement.

The real success of the prototype can only be seen by a comparable clinical study, where the treatment with the proposed automated system will be compared to that of the classical manual treatment in a medical setting. This will be the topic of further research, and has significant importance in refractive surgery. The developed automated vision-based system will also give a chance to future medical clinical studies to improve their results by eliminating human errors involved.

Acknowledgment

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