A Training System for Photodynamic Therapy using Modeling and Simulation

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Abstract

To become highly proficient at a given surgical procedure and to reduce risk to patients, physicians must gain experience through a number means. Some surgical procedures can be learned through practice on cadavers, animals, or physical models. Today computer models can provide the required realism to provide highly effective training. This paper presents a computer-based system that will be used for training ophthalmologists in the performance of two processes involving the application of laser to the retina: photodynamic therapy and panretinal photocaoagulation.

1. Introduction

"Health professional licensing bodies should implement periodic reexaminations and re-licensing of doctors, nurses, and other key providers, based on both competence and knowledge of safety practices." states the report "To Err is Human: Building a Safer Health System" [1] published by the National Academy of Sciences. As part of the effort to improve the expertise of doctors, several research centers have focused their efforts on the development of computer-based systems for modeling and simulation of emergency room techniques surgical procedures, and anesthetics [2]. In the field of ophthalmology, for instance, a number of researchers are applying modeling and simulation to eye surgery.

This paper reports on a project to create accurate simulations of the photodynamic therapy (PDT) and panretinal photocoagulation (PRP) to be used for clinical training. The simulations will be created in the Umbra simulation framework, a modeling and simulation tool created by Sandia National Laboratories and ORION International Technologies, Inc. [3].

The paper is organized as follows: Section 2 presents the medical background for the PRP and PDT procedures, section 3 gives a brief introduction to the Umbra framework, section 4 describes the elements of the computer simulation. Results and discussion are presented in section 5.

2. Medical background

In ophthalmology, two procedures involving the application of laser light to the retina are PRP and PDT. In the 20 years of laser treatment for symptoms associated with diabetic retinopathy, the benefits of these procedures have been established through numerous well-designed studies [4].

PRP is used in the treatment of diabetic retinopathy, which is the leading cause of blindness among adults of working age. The goal of photocoagulation is to stop the leakage from abnormal blood vessels in order to slow down vision loss. To achieve this, a laser beam is applied to the retina creating small burns in areas with abnormal blood vessels to help seal any leaks. The laser is applied to the retina through a contact lens into a dilated pupil. The contact lens reduces eye movement, but does not eliminate it entirely. In PRP, the abnormal neovascularization of proliferative diabetic retinopathy (PDR) are treated by applying the laser, sometimes over 1,000 times. This procedure requires a certain amount of planning and skill that is acquired partially through training, but especially through experience. The presented work will lead to a system that will allow realistic training to take place through computer simulation.

A process similar to PRP is used to treat diabetic macular edema. Again, the goal of the laser treatment is to stabilize vision by stopping damaged blood vessels from leaking fluid into the retina causing the edema. Both focal and grid laser treatments are used depending on the nature of the edema. The location of the leakage is detected in fluorescein angiograms (FA). Guided by the FA the ophthalmologist applies the focal treatment in a small number of discreet areas of the leakage. When the edema is diffused, a grid pattern of the laser is used, but avoids application near major vessels. Eye movement, though suppressed by the contact lens, can occur and present a challenge to the ophthalmologist.

PDT is a laser procedure used in treating choroidal neovascularization, a complication of age-related macular degeneration (AMD), another leading cause of blindness. PDT is a two-step process. In the first step, a patient receives an injection of a special dye called Visudyne (liposomal BPD-MA verteporfin) through a vein in the hand or arm. This dye is used for this treatment because of its unique properties. Specifically, this chemical circulates through the body and adheres to the walls of the abnormal blood vessels beneath the macula. At this point in the procedure, a laser is used to shine a light into the back of the eye. The energy produced by this laser is of a very low power and does not produce thermal effects and damage like PRP laser treatment. Instead, the light simply activates the chemical which is bound to the abnormal blood vessel wall. When the chemical is activated by the light beam, there is closure of the blood vessel. The result is stoppage of the fluid and blood which had been leaking beneath the retina. Over time, the body will absorb the blood and fluid, which results in stabilization or improvement in visual function. The blood vessel itself has not been completely destroyed, but rather is no longer leaking or actively growing.

3. The Umbra simulation framework

Umbra is a framework for modeling, simulation, and systems integration [3]. It allows users to quickly build models and simulations for intelligent system development, analysis, experimentation, and control while supporting trade-off analyses of complex robotic systems, device, and component concepts. Umbra also links heterogeneous collections of modeling tools such as 3D geometry and physics models of agents, devices, and their environments. Model components can be built with varying levels of fidelity and readily switched to allow models built with low fidelity for conceptual analysis to be gradually converted to high fidelity models for later phase detailed analysis. Within control environments, the models can be easily replaced with actual control elements.

Umbra is a universal connector that makes it possible to link any piece of software to any other piece. If a software module is an interface for a machine, it can build complexes of machines. Unlike other frameworks, Umbra is designed for agent-based simulation and integration. It provides a stage on which human and automated entities can interact. There is also a large “toolkit” of modules developed for Umbra, ranging from virtual reality presentation environments to cognitive science-based applications that mimic human behavior, including learning.

Umbra was developed by Sandia National Laboratory and ORION personnel, to meet the needs of a wide variety of applications, including medical, and is licensed to ORION for commercial applications.

4. Computer-based simulation for PRP and PDT

The simulation system developed in this research project will have two applications. 1) To show how the simulation system will aid the resident in acquiring the necessary skills to perform the surgery before attempting the procedure on a patient. 2) The second application is in the area of computer-assisted laser surgery. The power of computer/image-based tracking and enhanced visualization through overlaying of FA images onto a real-time view of the patient’s retina will aid immensely to the efficiency and accuracy of retinal laser therapy. One can easily envision a fully automated system for the application of the laser to surgeon defined locations or areas.

The simulation is composed of four building blocks: Pre-operation planning, multi-modality image registration, tracking the patient’s eye movement, and positioning the laser according to the pre-planned aim points. Figure 1 shows a block diagram of how these four blocks are placed in the overall simulation design.

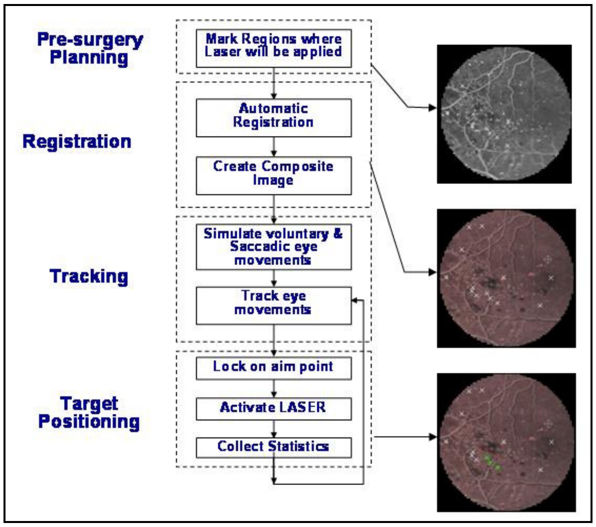

Figure 1. Block diagram of the computer-based simulation.

4.1. Operation pre-planning

Pre-planning will be done on the FA image (or sequence of images) placing markers over the spots or regions where the laser will be applied. This pre-planned image will serve two purposes. One, it will be graded against a 'ground truth' to see if he/she finds all the important pathology and plans to apply the laser where the 'expert' would. Two, it will be used to score the final outcome. Figure 1 shows a pre-planned image in Umbra; the color and FA images have been registered and overlaid, with "x" marks scattered through the spots where the laser is to be applied.

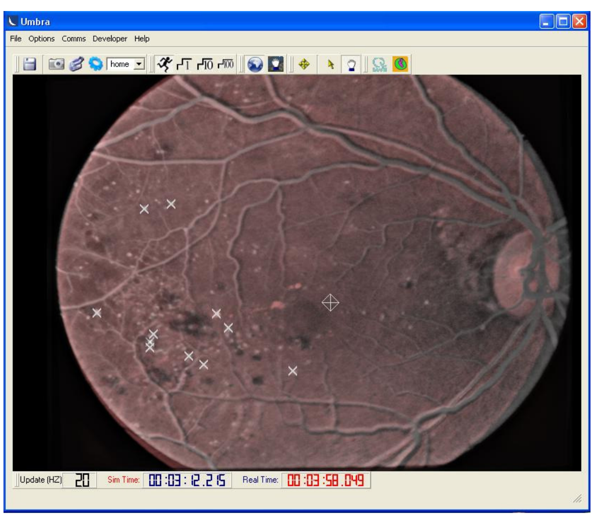

Figure 2. Image of pre-planned, targeted points, "X". Patient has MAs scattered through the retina. Is the "reticle" showing where the laser is currently aimed.

4.2. Image registration

The first step in building the simulation is to register the FA image and the color image. This is done offline before the start of the simulation and will allow the superposition of these two images on the screen. Techniques used for image registration were developed based on [5, 6].

4.3. Tracking

In practice, a contact lens is placed on the patient's eye to diminish the occurrence of micro-saccades. Even using the contact lens, the saccadic movement cannot be completely eliminated so the computer will simulate these movements. Also, the fact that there will be cooperative and non-cooperative patients will have to be taken into account, as this will change the frequency and amplitude of the eye movement.

Saccades are fast, usually conjugate, movements of the eyes. In humans the eyes reach peak velocities of up to 800 degrees per second in large saccades. Saccades serve to bring the retinal image of an object of interest to lie on the fovea. They might simply be thought of therefore, as a consequence of the need to exploit foveal vision. Saccadic eye movements are completed quickly. The duration of a 10 degrees saccade might typically be 45 ms. Saccades are also typically very accurate, bringing the eyes to within a fraction of a degree of the desired position. We have used saccadic models as proposed in [7] to simulate the movements that occur during the surgery. The voluntary movements can be simulated as slow, large random movements of the eye.

Even though the saccades are simulated by the software, in the future we will use sequences of images taken from the ophthalmologist camera and therefore we need to develop a tracking system to accurately keep the aim points in place after the saccadic and voluntary movements. To attain this objective we use block matching [8].

The blocks are defined by dividing the image into non-overlapping square parts. Each block from the current frame is matched into a block in the destination frame by shifting the current block over a predetermined neighborhood of pixels in the destination frame. At each shift, the sum of the distances between the gray values of the two blocks is computed. The shift which gives the smallest total distance is considered the best match. In the ideal case, two matching blocks have their corresponding pixels exactly equal.

Block matching is fast to compute and is used extensively for finding matching regions. Some of the most often used matching criteria based on pixel differencing are mean absolute distance (MAD), mean squared distance (MSD), and normalized cross-correlation (NCC). The saccade movements determine how fast the block matching algorithm has to be. If saccades are 50 ms apart, then the block matching has to be performed under that time constraint. The tracking update rate is limited by the video rate of the camera and image acquisition rate. Today, using the video output of 30 fps, we have 33 ms between updates to close the tracking loop on the simulation. Faster cameras exist and may be necessary to ensure more precise tracking capability.

4.4. Target positioning

The last step of the simulation consists of positioning the overlay targets for guiding the surgeon. The targets are previously defined in the FA image (in the pre-surgery preparation) and once the overlay is done they are incorporated in the image as guidelines. The targets need to move with the FA image, which is easy to do since the tracking step gives the coordinate changes for each frame.

Once the target is locked, the surgeon can activate the laser at the marked spots. A hit or miss indicator will show up on the screen and statistics for the accuracy will be measured in terms of distance from the target. The statistics collected will be used in the comparative study of the computer-based system.

Two types of training are available. The first mimics the way the surgery is performed now, where the surgeon has to look at the FA image in a separate screen and memorize the vessels patterns and the point (or points) where he will apply the laser. The second type of training involves the overlay of the FA over the color image with the aim points added in the overlay.

5. Results

A prototype simulation was developed in Umbra to demonstrate a realistic depiction of the PRP and PDT procedures. A color photograph of a patient with diabetic retinopathy was the starting point for simulating the ophthalmologist's view through the slit lamp being used to apply the laser treatment. On this patient's clinical examination, an area of retinal thickening was diagnosed temporally and inferior to the paramacular area by biomicroscopy. On fluorescein angiography, a clustering of significant microaneurysms (MAs) was seen in correspondence to the clinical retinal thickening.

The system models a situation where the ophthalmologist is "aided" by the software to perform the PRP. In this case, a slit lamp/laser system is simulated giving the ophthalmologist simultaneous views of the patient's retina and the FA image. The FA image is optically inserted into the field to simulate an arrangement where a beam splitter is used to overlay the FA onto the field of view of the ophthalmologist. This is currently represented as a transparent FA image presented onto the simulated live video on a computer monitor.

The video demonstration can be viewed at: http://www.orionint.com/Capabilities/Umbra.cfm. Still captures are presented in figures 3 and 4. In this simulation the ophthalmologist is given (or selects) points on the FA where the laser treatment will be applied (figure 3). The simulation registers the FA onto the color image of the patient's eye. In the simulation eye movement is set by the user with a certain amplitude and frequency of movement. The simulation tracks the eye movement and automatically re-registers the FA, so the ophthalmologist is always viewing the FA overlaid onto the color image and the fiducial markings used to identify the aim points of the laser are presented. As the ophthalmologist applies the treatment, the fiducials will change color from "white" (which show the planned locations) to "green" which show the locations already treated, or to "red" to indicate a location was "missed," as illustrated in Figure 4.

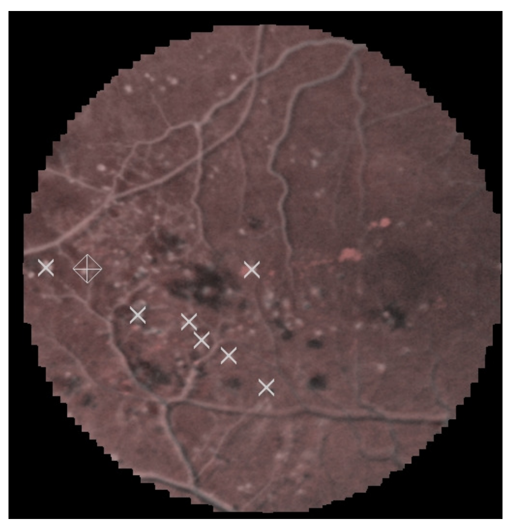

Figure 3. Overlay image where the "X" show the planned laser application.

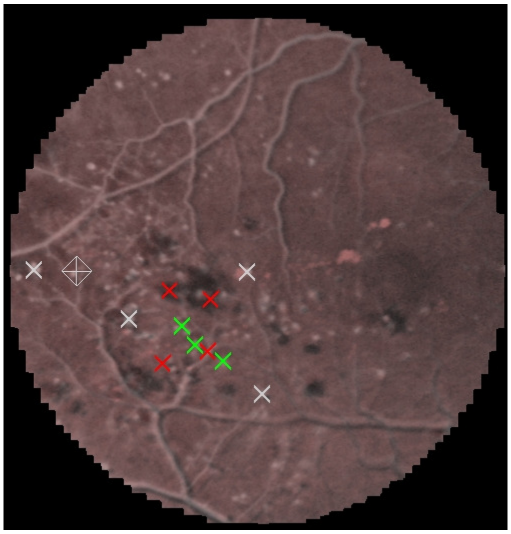

Figure 4. Overlay of the registered color and FA images with hit and miss markings. The green mark is a hit and the red mark is a miss. White marks are pre-planned spots where the laser has not yet been applied.

The system is currently under evaluation by doctors from the University of Iowa, Department of Ophthalmology. The next step in assessing the validity of the simulation is a statistical study involving two surgeons and two residents in training. The vision of this project is to integrate the software in an already existing ophthalmic device to increase the accuracy of the laser application procedure.

6. References

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