Design and Evaluation of Retinal Models for Robotic Ophthalmic Procedures

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BRIEF. This study finds optimal protocols and recipes for the construction of inexpensive retinal models that mimic microvasculature and other local anatomy, on which robotic ophthalmic procedures can be performed.

ABSTRACT. This study investigates procedures for creating retinal models used for the refinement of robot-assisted surgery. We address separate models for two different types of retinal surgery—branch retinal vein occlusion (BRVO) and epiretinal membrane peeling. The first model is developed to test the feasibility of image-guided, micro-vascular retinal interventions. We investigated the optimal fabrication conditions for agar models of the retina while maximizing contrast for optical coherence tomography (OCT). Results showed that a recipe with roughly one part contrast agent for every part agar produced optimal visibility under an OCT probe. The second model is for testing robot-assisted epiretinal membrane peeling. The model mimics epiretinal membranes by using a newly reported method in the literature [7]. Coats of liquid skin bandage were used for fabrication of these membranes on agar plates. A robotic actuation mechanism for micro-tweezers used to peel epiretinal membranes was fabricated using Pro-Engineer and subsequently tested. Results showed that both the actuation mechanism and the membranes can be used effectively, though further refinement is possible. These models are expected to enhance the precision and effectiveness of robot-assisted retinal surgery.

INTRODUCTION.

Retinal surgery is an extremely precise procedure since the small anatomy can cause numerous complexities. For example, branch retinal vein occlusion (BRVO), the second most common vascular disorder of the retina, deals with the microvasculature of the eye. The disease causes clots to develop in retinal blood vessels, restricting blood flow and spawning problems including macular edema and vitreous hemorrhage [1]. However, since the afflicted blood vessels range in diameter from forty to one hundred-twenty micrometers, any intervention requires extreme precision [2].

This requirement is why robot-assisted surgery has recently been explored. Surgical robots have already revolutionized several surgical subspecialties, including: laparoscopic surgery, urology, gynecology, and orthopedics. The benefits of robot assistance are numerous—a handheld robot can remove tremor and scale down the motion of a surgeon's hand to make more precise incisions or excisions [3]. Many robotic safety measures are being explored such as hard stop boundaries, outside of which the robot will not move to protect adjacent anatomy [2]. Visual cues and force sensors can also be implemented to greatly aid the surgeon's dexterity.

In ophthalmics, however, only a few robots have been developed, including the Carnegie Mellon University Micron and the Johns Hopkins University Steady Hand [4]. As they continue to be prepared for surgical usage, it is clear that they must first be tested and refined on retinal models to ensure accuracy and repeatability. Currently, porcine eyes are often used for testing, but they are typically expensive and not easily replaceable. In order to solve this problem, cost-effective, simple, and replaceable models must be constructed.

This study focuses on the fabrication of such models for two retinal diseases—the aforementioned BRVO and epiretinal membranes (aka macular pucker or internal limiting membrane). In BRVO, robot-assisted surgical applications include cannulation—in essence, inserting a stent into a blood vessel to increase flow, similar to current cardiac procedures [2]. Furthermore, optical coherence tomography (OCT) imaging would be used for this procedure. Similar to B-scan ultrasonography, OCT uses reflected light instead of sound to produce cross-sectional images of the retina with a resolution of ten to seventeen microns [5]. An epiretinal membrane, on the other hand, is a layer of cell debris that accumulates above the retina [6]. As this layer is typically reflective, it can inhibit sight. Epiretinal membranes, only five micrometers thick, are very common, progressing naturally due to age or unnaturally because of complications following ophthalmic surgery.

Thus, the models must follow specific requirements. The BRVO model must include a vessel of comparable size to the retinal microvasculature, as well as possess a similar translucence for OCT compatibility. The epiretinal membrane model must be composed of a substance with comparable thickness to the membrane. Recent literature suggests that liquid skin bandage is a serviceable replacement, but further clarifications in those results are still necessary, including how it should be applied and on what surfaces [7]. This study seeks to answer those questions and finalize the protocols for the construction of these models.

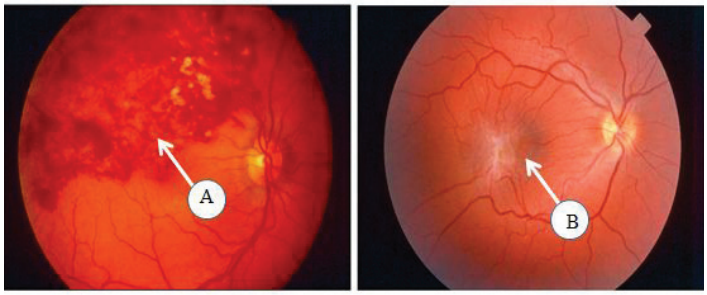


Figure 1. A. The image on the left is a retina with BRVO. The arrow points toward the clear hemorrhaging caused by this disease. **B.** The image on the right is a retina with an epiretinal membrane. The arrow points toward the membrane, which is clearly discolored. Photo credit: Bethesda Retina.

MATERIALS AND METHODS.

Fabrication of an OCT-compatible BRVO model.

In order for our model to be OCT-compatible, it had to be somewhat translucent so that the light would be partially reflected, similar to a retina. Thus, we decided to use an agar gel, as it is completely transparent, with a contrast agent. The agent we came up with was Coffee-mate® creamer, a cost-effective white powder.

We first prepared a transparent agar gel by using 4.8g of agar powder (CAS 9002-18-0) and 200mL of distilled water (24g/L). Creamer was also added, at a ratio of creamer to agar, in increments of .25, starting with .50 to 2.50 (thus, with a .50 ratio, there would be 2.4g of creamer to 4.8g of agar powder). After mixing the two in a beaker, we placed the beaker on a hot plate and set the curing temperature to 250°C. After the mixture boiled, we let it cool to 50°C and poured it into the Petri dish to let it solidify.

The Petri dish had been previously prepared with a wire in order to form the vessel. Two holes opposite one another had been drilled with a 550 micron drill bit into the sides of the dish. A 525 micron-wide wire was inserted through the holes to form a diameter of the Petri dish. The mixture was then carefully poured so that it would cover the wire by roughly half a millimeter (the average depth of retinal blood vessels) in the Petri dish. After the mixture solidified, the

wire was carefully pulled out to prevent it from breaking through the surface, leaving a hollow vessel behind.

After solidification, OCT and microscope images (45x) of each model were taken and compared to an OCT image of a retina.

Fabrication of an epiretinal membrane model.

Recent updates in the literature suggested that New-Skin® liquid skin bandage could effectively mimic the thickness of an epiretinal membrane. Liquid skin bandage does not have to be OCT-compatible, unlike the BRVO model, since epiretinal membranes are typically highly reflective and thus produce a noisy image. However, it remained unclear on which surfaces the liquid skin bandage would best be applied.

We thus decided to apply a coat of the bandage to an empty acrylic Petri dish, a rubber eye model, and an agar gel. After letting it dry, we attempted to peel the bandage off by hand. We quickly found that the bandage would attach itself to the acrylic and harden, whereas the bandage would be absorbed by the rubber and not be able to be pulled off. On the agar gel, however, the liquid skin bandage was able to be removed. Furthermore, visual confirmation showed that the thickness of the bandage was similar to the standard thickness of an epiretinal membrane, 5 micrometers.

Design of a robotic actuation mechanism.

In order to ensure that the liquid skin bandage served as an effective model of an epiretinal membrane, we had to confirm that it could be removed robotically. As such, we fabricated an actuation mechanism for a gripper often used in the removal of membranes through rapid prototyping. This mechanism and gripper would then be mounted on a parallel robot.

In order to do this, we used the software Pro/Engineer Wildfire 5.0 to make a three-dimensional design of the gripper on a computer. From this design, we realized that the way to manipulate the micro-tweezer was through the use of a small button located at its top, between the arms of the gripper. We thus came up with the idea to use a revolving cap, one side of which would be slightly elevated over the other side. Thus, as it revolved over the button, the button would press down and be released again. As this happened, the micro-tweezer would open and close.

The next step was to see if peeling would actually work. Thus, we used a three-dimensional printer to rapid prototype the design of our actuation mechanism and mount it onto the parallel robot. Computer code was then written so that the movements of the parallel robot would correlate with the movements of a joystick, and that the cap would revolve when the joystick was pressed. Finally, a Dragonfly camera was also set up above the parallel robot to record this process.

Two separate patches of liquid skin bandage were applied to the agar gel. One patch was removed by hand, while the other one was removed with robot assistance. After the Dragonfly camera recorded the peeling process for both, the procedures were analyzed in regards to three parts: grasping, lifting, and delamination.

RESULTS.

OCT-compatible BRVO model.

OCT and microscope (45x) images of each Petri dish were taken. They were then compared to an OCT image of a retina using two major criteria: the clarity of the blood vessel circumference and the contrast between the agar and the blood vessel. We reached the conclusion, along with an OCT technician, that the ratio of 1.00 most closely resembled the OCT image of the retina.

From the OCT image of the 1.00 ratio model, it is clear that there is significant contrast between the agar and the blood vessel and that the vessel circumference is also very clear. This model will greatly help surgeons and engineers practice robot-assisted cannulation prior to any operations on animal specimens or actual human eyes. While there is a difference between the model and the retinal OCT image, the OCT technician stated that it wasn't significant. In any case, a higher ratio model can be selected to limit vessel clarity for further practice.

Epiretinal membrane model and evaluation.

The liquid skin bandage, when applied on the Petri dish, was roughly 5 micrometers thick. This is the average thickness of an epiretinal membrane. It was also successfully removed by hand with the gripper, although the feasibility of robotic assistance still had to be confirmed.

The three major stages to peeling an epiretinal membrane are the grasping of the membrane, the lifting of the membrane, and delamination. Oftentimes, problems may occur during any of these three stages—for example, during the grasping procedure, surgeons may push the micro-tweezer too deep into the underlying anatomy and cause structural damage. During the lifting and delamination procedure, the micro-tweezer, if handled abruptly, could rip the epiretinal membrane and force the entire procedure to be repeated several times. Thus, removal of the liquid skin bandage by hand and with robot assistance were thus compared in each of those three steps to ensure feasibility.

DISCUSSION.

Protocols for creating the models.

As the focus of this experiment was to create a recipe for the fabrication of an OCT-compatible, BRVO model, it is as follows. First, prepare three Petri dishes by drilling two holes opposite one another and running a wire through the diameter for each dish. Next, measure out 4.8g of agar, 4.8g of creamer, and 200mL of distilled water. This quantity should be enough for three Petri dishes. Mix the agar and water in a beaker and place it on a hot plate set to 250°C. Stir the mixture as it boils. Once it boils, leave it on the hot plate for another minute and continue stirring. Remove the beaker and turn off the hot plate. Once the beaker cools to 60°C, pour in the creamer and stir until it has entirely dissolved. Finally, pour the mixture into the Petri dishes, carefully ensuring that its height does not exceed half of a millimeter above the wire. Let the mixture solidify into a gel and remove the wire, leaving behind a phantom vessel. The protocol for the creation of an epiretinal membrane model is much more basic; a thin coat of New-Skin liquid bandage must be applied to an agar model and spread evenly. This clarifies the previous procedures stated in Iyer *et al.*

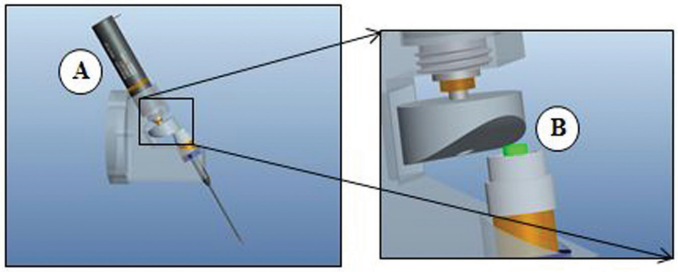


Figure 2. Gripper mounted onto a parallel robot in Pro/Engineer **A.** Parallel robot plate with battery to revolve the actuation mechanism **B.** Actuation mechanism.

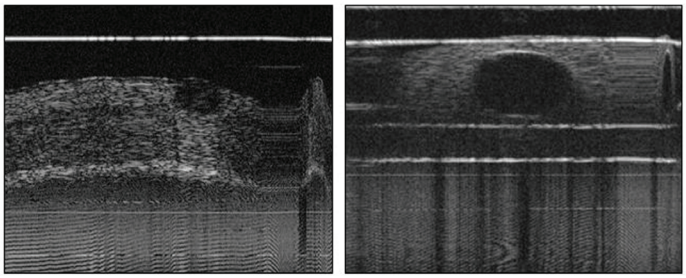


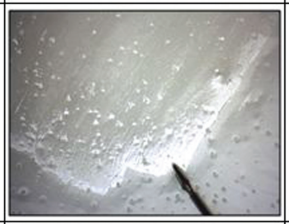
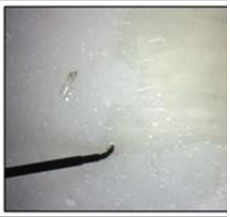
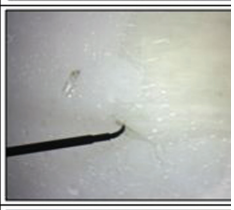
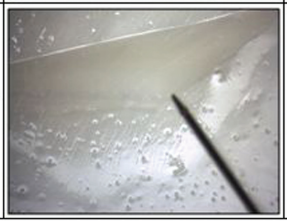
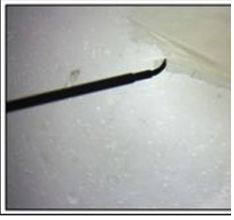
Figure 3. The image on the left is an OCT image of a real retina, whereas the image on the right is an OCT image of a 1.00 ratio agar model. The two have similar clarity in regards to blood vessel circumference and contrast between the agar and vessel.

Quality of the models.

It is clear that the 1.00 ratio agar model works well. It provides enough contrast between the agar and the blood vessel and also yields a clear vessel circumference. The procedure of inserting a wire, letting the agar solidify around it, and removing the wire also effectively creates a blood vessel.

For the epiretinal membrane model, it is also clear that liquid skin bandage effectively mimics the membrane when applied to an agar gel. However, experiments with this model were not entirely ideal. In regards to the robot actuation mechanism, the micro-tweezers often ripped through the membrane. The reason for this is likely due to the basic computer code used; at the time, the microtweezer could only completely close or completely open. It was thus likely that as it snapped shut, it would tear the membrane apart. If the mechanism or the code could be refined so that there is greater control over the open/close settings, the process should become more accurate and precise. In any case, the robot actuation mechanism did successfully remove the membrane, showing that such a procedure is, indeed, feasible.

Table 1. Comparison of epiretinal membrane removal. Both the hand-held and the robot-assisted removals were successful.

	By Hand	Robot-assisted
Grasping		
Lifting		
Delamination		

CONCLUSION AND FUTURE DIRECTION.

The BRVO model serves many benefits, beyond the fact that it can help determine if robot-assisted cannulation is feasible. For example, the ratios in the model and blood vessel diameters can be easily adjusted to create many unique models with different visibility levels. The easy availability of such models can also help mechanical engineers refine the robot to make it more precise during operation, without having to sacrifice valuable porcine eyes in the process.

While OCT imaging isn't always used during epiretinal membrane peeling, the usage of an agar model for the epiretinal membrane also adds many benefits. For example, OCT imaging is used during diagnosis of epiretinal membranes (its idiosyncratic fuzzy image actually helps to identify its presence) and after the surgery to confirm its complete removal. If the agar gel on which the liquid skin bandage is applied is OCT-compatible, this same idea could be applied. Furthermore, using an agar model can also help to identify physical damage to underlying anatomy; any ripped or damaged agar can be seen and measured.

The next step of the OCT-compatible BRVO model is to see if any innovative robot-assisted surgical techniques, namely cannulation, can be applied to the model. In order to do this, we suggest using a vessel poking wire to guide a stent into the phantom vessel. Once the appropriate angle of approach is found, the stent can be inserted with dye to see if it will move through the stent. Of course, the model does not perfectly mimic conditions in the retina, but the differences can be corrected for so that the transition from model to retina is seamless. For the epiretinal membrane model, the robotic actuation mechanism should be refined and made more dexterous, so that a better comparison between the robot and a handheld operation can be made.

The OCT-compatible BRVO model, epiretinal membrane model, and robotic actuation mechanism should serve as solid foundations for future improvements. All of the materials were cost-effective, a major objective in the construction of these models. While they can still be refined, the models and mechanism should enhance the precision and effectiveness of robot-assisted retinal surgery as well as better prepare surgeons for retinal interventions.

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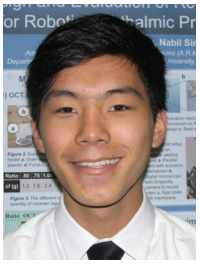

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