Published in final edited form as:

Conf Proc IEEE Eng Med Biol Soc. 2018 July ; 2018: 1–5. doi:10.1109/EMBC.2018.8513304.

Evaluation of a Force-Sensing Handheld Robot for Assisted Retinal Vein Cannulation*

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Abstract

Approximately 16.4 million people are affected by retinal vein occlusion (RVO) resulting from hyper-coagulability, low blood flow or thrombosis in the central or the branched retinal veins. Most common current treatments for RVO aim to limit the damage. In recent years, an experimental procedure, retinal vein cannulation (RVC) has been studied in animal models as well as human eye models. RVC is a procedure for targeted delivery of a therapeutic agent into the occluded retinal vein for dissolving the thrombi. Although effective treatment has been demonstrated via RVC, performing this procedure manually still remains at the limits of human skills. RVC requires to precisely insert a thin cannula into a delicate thin retinal vein, and to maintain it inside the vein throughout the infusion. The needle-vein interaction forces are too small to sense even by an expert surgeon. In this work, we present an evaluation study of a handheld robotic assistant with a force-sensing microneedle for RVC. The system actively cancels hand tremor, detects venous puncture based on detected tool-tissue forces, and stabilizes the needle after venous puncture for reduced trauma and prolonged infusion. Experiments are performed cannulating the vasculature in fertilized chicken eggs. Results show 100% success in venous puncture detection and significantly reduced cannula position drift via the stabilization aid of the robotic system.

I. Introduction

Retinal vein occlusion (RVO) is one of the most common retinovascular diseases, affecting approximately 16.4 million people worldwide [1] and has a prevalence of 1.8% and 0.5% for central and branch retinal veins, respectively [2]. RVO typically occurs when there is

*Research supported in part by the National Institutes of Health under 2R01 EB000526–07, and 1R01 EB023943–01, and in part by Johns Hopkins University internal funds.

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thickening of the crossing artery, low flow, hyper-coagulability, or thrombosis in the central or the branched retinal veins of the eye. This results in the affected retinal vein becoming dilated, tortuous and hemorrhaging into the retinal tissue. Patients with RVO are reported to experience blurred or distorted vision, and in severe cases blindness results [3]. The available treatments for RVO including photocoagulation, hemodilution, radial optic neurotomy, vitrectomy and intra-vitreous injections currently are focused on limiting the damage induced by the occlusion, rather than directly resolving the occlusion [4]. Retinal vein cannulation (RVC) is an experimental surgical procedure proposed to treat RVO by direct therapeutic agent delivery methods to the site of occlusion. The procedure involves three main steps: (1) accurately bringing a sharp tipped cannula onto the occluded retinal vein, (2) puncturing through the vein wall and precisely halting the cannula tip at the right depth, and (3) maintaining the cannula inside the vein for several minutes, during which time the therapeutic agent presently tissue plasminogen activator (t-PA) or ocriplasmin is delivered to dissolve the obstructing thrombus. This is a very demanding and risky procedure because of the small size and fragility of retinal veins especially if the occlusion is at a branch retinal vein (typically $\varnothing < 200 \mu\text{m}$) rather than the central vein [5].

Retinal vein cannulation using microfabricated needle in porcine eyes showed technical feasibility, and this was further supported by successful clinical demonstrations on human retinal veins [6]. Challenges of RVC procedure such as need for precise needle placement inspired development of robotic assistants aiding in removing hand tremor [7] and non-perceivable needle-vein interaction forces lead to development of micro-force-sensing surgical instruments for providing force feedback [8], [9]. Willekens *et al.* presented robot-assisted retinal vein cannulation in an in vivo porcine retinal vein occlusion model [10]; however, the robotic system hindered surgeon's perception of interaction forces due to the heavy weight and inertia. A handheld robotic assistant could potentially address the limitations of a bulky robotic system. Riviere *et al.* developed a 6-DOF handheld active tremor canceling microsurgical tool called Micron [11]. Though Micron addressed complexities of using a bulky robotic assistant and eliminating force perception, it has smaller workspace and lacks capability to provide scaled force feedback, which could be unfavorable for safer vitreoretinal surgery. Lee *et al.* presented hand-held force sensing tool for measuring the tip forces and proportionally creating magnified force between the tool handle and a brace attached to the operator's hand [12].

Despite the aforementioned progress in improving the available instruments and realizing effective RVC, the procedure still remains at the limit of human performance. Impeding reason for this are: tremulous tool tip motion, non-perceivable retinal vein puncture forces, and injection of agents (t-PA or balanced saline solution) at the correct depth. Tests on the chorioallantoic membrane (CAM) model [13] have confirmed that most RVC forces lie below the human perception threshold, yet there is still a sharp force drop upon venous puncture, as observed in a conventional venipuncture [14]. Therefore, continual monitoring of these very fine tool-tissue interactions via a very sensitive force sensor has the potential to inform the operator of the moment of venous puncture during RVC. Combining a force-sensing cannulation tool with a robotic assistant could be a powerful potential solution to overcome the challenges in RVC. Precisely identifying the moment of venous puncture and

fixating the cannula to attain an extended period of intravenous cannula stability during delivery of the drug are each important to success.

Previously our team developed a robotic assistive system combining a force-sensing microneedle with a handheld micromanipulator [15]. The system was shown to reduce the undesired movement of the cannula after the venous puncture during tests in an artificial phantom by multiple users with varying level of skill, including an expert vitreoretinal surgeon [16]. This work takes our experimental evaluation effort one step forward via tests on live tissue and varying sizes of veins. We assess the performance of our puncture detection method and motion stabilization aid after the venous puncture despite the mechanical behavior and size variation among the target veins. In the following sections, we will first present the components of our system and its working principle. This will be followed by cannulation experiments using CAM of fertilized chicken eggs. The paper concludes with a discussion of the results.

II. System Components

A. Force-Sensing Microneedle

Monitoring tool-tissue interaction forces in RVC requires force sensing with a very fine resolution (sub-mN) and high accuracy (sub-mN) [14]. In addition, the sensor needs to be integrated within a very small diameter (sub-mm) to be able to fit through the sclerotomy and take measurements directly at the tool tip without being influenced by the reaction forces at the insertion port. Based on fiber-Bragg grating strain sensors, our team previously developed several force-sensing instruments for vitreoretinal surgery. Among these tools is a motorized force-sensing microneedle, which has a tool shaft diameter of under 0.9 mm and the motorized mechanism deploys out a pre-bent micro-needle ($\varnothing$ 70 μ m) [16]. Along the tool shaft embedded are 3 FBGs, which provide sensing of forces at the micro-needles tip with a resolution of 0.25 mN and within an accuracy of 0.3 mN along the needle axis. The force measurement was shown to be immune to ambient temperature changes with the compensation method implemented based on the common mode of the FBGs. As shown in Fig. 1a, the motorized tool is a compact modular unit that can be easily used on a robotic system as an end effector.

B. Handheld Micromanipulator: Micron

Handheld robotic devices are ungrounded and used in a very similar way to conventional manual tools. They are often relatively compact, low-cost, and easily integrated into a clinical workflow. Riviere *et al.* have developed a 3-DOF handheld active tremor canceling microsurgical tool called Micron [11]. Its optical tracking system, Apparatus to Sense Accuracy of Position (ASAP), measures the tool movement with 4 μ m resolution and up to 2 kHz sampling rate. Its control system distinguishes between desired and undesired user motions, and then actively cancels the involuntary motions by actuation of the tool tip within a workspace of approximately a $1 \times 1 \times 0.5$ mm volume centered on the handle position. Micron offers the surgeon a very intuitive interface to enhance manipulation precision, but it also preserves a 1:1 force feedback ratio and cannot provide scaled force feedback, which may seem to be a disadvantage in vitreoretinal surgery where forces are routinely below

what humans can feel. Nevertheless, it can be programmed to take assistive actions based on measured tool-tissue interaction forces, such as adjusting speed to maintain a safe level of force on the retina while peeling epiretinal membranes [17] or fixating cannula position after detecting venous puncture in RVC [16].

C. Venous Puncture Detection and Cannula Stabilization

Instant of venous puncture can be detected by continuously monitoring the tool-tissue interaction force, as the force drops rapidly upon puncture. But there is variability in the sharpness of the force drop depending on the user and the tissue properties. To robustly detect puncture despite user and tissue dependent variations, a more generalized method not only based on the force but also the monitored tool speed was developed [16]. The method was shown to work robustly on a consistent artificial phantom despite different user behavior. In this work, we aim to investigate the robustness of this method in the presence of variations in tissue properties as well. Until the puncture is detected, the handheld robotic system works in its default tremor canceling mode helping the operator precisely aim at the target vein. After the puncture is detected, the system works to actively compensate any motion, including both the high frequency tremor and low frequency drift of the user hand, to fixate the needle around the puncture point and maintain cannulation for a longer period with less tissue damage.

III. Experiments

In order to compare the performance with and without the motion stabilization aid after the venous puncture, we performed experiments using the vasculature of CAM of 12-day fertilized chicken eggs and the setup shown in Fig. 1d. 10 eggs were used in total to complete 20 cannulation attempts by a single non-surgeon operator with no prior cannulation experience but with extensive training on the robotic system. Each egg was used only twice since the CAM starts losing its tension and the veins start bleeding after this point. The experimental procedures described in this paper were approved by the Institutional Review Board.

Experiments were done altering between two operation modes of the robotic system in random order: pure tremor cancellation aid versus the active motion stabilization aid after the venous puncture. In both modes, after detecting the puncture based on the sensed forces by the needle and tracked tip position by the optical trackers, an auditory feedback was provided to the user to signal that the needle has entered the vein. After the event of puncture, using the first mode, only the tremulous movement of the cannula was actively compensated, which is the default mode of Micron system. In the second mode, the manipulator worked to fixate the cannula tip at the sensed puncture position by canceling out also the low frequency drift of the cannula.

Before the experiment, the egg shells were cracked on top of the egg and gently removed to gain access to the CAM surface. The internal shell membrane lying on the CAM was first wetted with water and then gently peeled off using micro-forceps to expose the CAM surface. Then, water was added atop the CAM to emulate the aqueous environment inside the eye after vitrectomy. During the experiments, to stabilize the floating CAM, the subject

used micro-forceps in left hand to grasp and tension the CAM toward one corner of the opening while holding the robotic cannulation system in the right hand. Veins of varying sizes were targeted during the experiment. Before cannulation, a microscopic image of the CAM was taken with a reference wire of known diameter (200 μm) lying on the CAM surface as shown in Fig. 1b. The sizes of the veins were computed in reference to the wire in the images.

The task in experiments was to cannulate the target vein on the CAM and maintain the needle inside the vein for 45 seconds after the event of puncture, which was sensed by the robotic system and fed to the operator as an auditory signal. Meanwhile the needle tip trajectory and tool-tissue interaction forces were recorded at 1 kHz. At the end of the 45 second period, air was injected to check if the needle tip is still inside the vein, double punctured it, or out of the CAM. If successfully maintained inside the vein, air could be seen spreading rapidly inside the veins (Fig. 1c). If the vein was double punctured, the injected air generated bubbles under the CAM. Finally, if the needle was completely out, bubbles were observed on the CAM surface. Apart from this check, the recorded trajectories were compared based on their average deviation from the point of puncture for each operation mode. Analyses were performed using one-way analysis of variance (ANOVA) followed by a t-test assuming unequal variance; statistical significance was defined as $p < 0.05$.

IV. Results and Discussion

A. Puncture Force and Detection Success versus Vein Size

Venous puncture was detected successfully in all cases regardless of the vein size. The rate of force drop upon puncture varied between -0.24 and -0.06 mN/s, and hence it is hard to conclude a puncture threshold only based on the force drop rate. However, as detailed in [16], using the dot product of tool tip velocity and the force drop rate, the event of puncture can be identified successfully without having to identify a threshold and despite variations in force characteristics due to tissue and/or user behavior. No statistically significant difference was identified between the assisted and non-assisted cases in terms of the level of puncture force ($p=0.49$) and the rate of force drop upon puncture ($p=0.25$), which shows that the two operational modes were experimented on similar platforms in terms of tissue mechanics. The puncture force varied between 3.6 mN and 8.5 mN for all the veins, with diameters ranging within 199 – 916 μm for the non-assisted trials while the forces ranged from 3.76 mN to 9.60 mN for vein sizes of 159 – 603 μm for the assisted trials. Our results did not reveal a direct correlation between the vein size and the puncture force (Fig. 2a), and between the vein size and the force drop rate (Fig. 2b). This can be attributed to the potential variation in the amount of stretch manually applied by the micro-forceps while trying to hold CAM fixed during cannulation since even slight discrepancies in the surface tension can significantly affect the magnitude of the puncture force and its rate of drop upon puncture. For the veins requiring larger puncture force, a sharper force drop was observed upon puncture as shown in Fig. 2c, yet even the sharpest drop is too fine to sense manually. In all trials, the user was provided with auditory feedback after the puncture was detected. The vein was double punctured in only 1/10 trials in each mode, where the injected air was observed under the CAM rather than inside the vein. Double punctures happened while

cannulating the smallest vein (under 200 μm in diameter) for both “only tremor canceling” and “motion stabilizing” modes, and trajectory analyses revealed that the failure was due to the bouncing back of the stretched tissue upon puncture even though the cannula insertion was stopped right after puncture, which shows that especially for cannulating smaller veins in mobile tissue fixating the cannula not in space, but relative to tissue is a required aid.

B. Cannula Motion versus the Hold Period

After the puncture was detected, based upon the recorded tool trajectory (Fig. 3), the distance of the needle tip from the detected point of puncture was analyzed for the first 15 seconds, first 30 seconds and the full trial period of 45 seconds. For the first 15 seconds, the mean deviation from the puncture point is slightly smaller in “stabilization aided” trials as compared to “only tremor canceling” cases ($200.24 \pm 80.87 \mu\text{m}$ vs. $329.80 \pm 101.98 \mu\text{m}$, $p=0.003$). As the hold period is increased, the deviation in the non-assisted cases rapidly rise as shown in Fig. 4, which mean more deformation of the vein and hence more trauma on the tissue. When the motion stabilization aid is activated after the puncture, the rate of increase in the motion of the cannula is smaller. For a 30 second injection period, with the active motion stabilization, the cannula is moved $231.00 \pm 65.35 \mu\text{m}$ away from the puncture point on the average as opposed to $442.54 \pm 74.90 \mu\text{m}$ with only tremor cancellation aid ($p=1.31 \cdot 10^{-6}$). For the full testing period of 45 seconds, the average cannula drift is reduced from $532.13 \pm 117.14 \mu\text{m}$ to $293.95 \pm 93.94 \mu\text{m}$ with the motion stabilization aid.

Overall, the largest deviations were recorded while cannulating smaller veins with only tremor cancellation, and most of the deviations were observed to be along the z-axis, i.e. perpendicular to the CAM surface. This can be attributed to the poor depth perception through the 2D microscope whereas the drift within the x/y plane can be better controlled via visual feedback. In 200 – 500 μm vein diameter range, 6 cannulations were performed for each mode. The non-assisted trials on these smaller veins revealed an average motion of $595.72 \pm 95.64 \mu\text{m}$ after the puncture. In one of the cases, while cannulating a 200 μm vein, the large deviations (658.52 μm) caused the needle to come out of the vein before the trial was completed. The trials with the motion stabilization aid for veins under 500 μm had significantly smaller cannula motion after the puncture ($299.94 \pm 105.87 \mu\text{m}$), and the cannula was maintained inside of the vessel throughout all 6 trials.

V. Conclusion

Retinal vein cannulation is a demanding procedure, and its feasibility is currently limited by the challenges in identifying the moment of venous puncture, achieving cannulation and maintaining cannulation during drug delivery. In this study, to address these problems we used a force-sensing microneedle in combination with a robotic handheld manipulator. This system helped the operator detect the instance of venous puncture, and actively canceled undesired movements of the operator to maintain cannulation for a prolonged infusion with less trauma on the vasculature. Our puncture detection method which makes use of both the tool tip force and position information together revealed a reliable prediction of the puncture for veins of varying size (200 – 900 μm). The developed automatic motion stabilization aid, which switches the robotic system from a sole tremor canceling mode to a full motion

cancellation, showed significant reduction in the cannula movement after the puncture, similar to our earlier evaluation on the artificial phantom.

In a real clinical scenario, the retinal veins of interest are typically under 200 μm in diameter, which has not been covered in this work. In addition, after the venous puncture, the cannula needs to be maintained fixed relative to the tissue rather than fixed in space. In our current work, the eggs were held fixed and the CAM was stabilized by stretching with micro-forceps, hence fixating the cannula in space was a sufficient aid. Nevertheless, to emulate the surgical conditions better, it is essential to allow for potential movements of the tissue and also have the system account for and take action against such motion. This can be addressed by using force information from the sensitized cannula to detect relative movements and stabilize the cannula relative to the vasculature. Alternatively, optical coherence tomography guidance can be used after integrating an additional imaging fiber on the sensitized cannula to track and fixate tool-tissue distance after the venous puncture, which are some of the potential future directions to pursue in this branch. In our future work, we aim to extend our evaluation study with more users including surgeons, from various levels of skill and using smaller veins that are more representative of the retinal vasculature.

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Figure 1.

(a) System components: The handheld robot, Micron, combined with a force-sensing microneedle. (b) The vasculature on CAM of 12-day chicken embryos were cannulated. To determine the exact size of the target veins, a reference wire was used. (c) The success of cannulation was checked by injecting air through the microneedle. Air flowing inside the vein shows that the cannula tip is successfully maintained inside the vein. (d) Experimental setup: Robotic system components, a fertilized chicken egg and the microscope.

Figure 2.

Results of the cannulation experiments on CAM: (a, b) No statistically significant difference was found between the two test modes in terms of the measured puncture force and the rate of drop upon puncture; (c) for trials with higher puncture force, the rate of force drop was also observed to be larger (fit trend shown in grey).

Figure 3.

Sample trajectories recorded during trials with only tremor cancellation vs. stabilization after puncture mode of the robotic system. The vein axis and the needle insertion are along the y-axis while z-axis is perpendicular to the CAM surface. Significantly reduced deviation from the point of puncture, especially along the z-axis, is observed with the stabilization aid.

Figure 4.

Comparison of cannula motion after the puncture using only tremor cancellation versus using the motion stabilization aid. As the hold period is increased, the average movement of the cannula from the point of puncture increases. The mean deviation is overall smaller and the increase with longer hold periods is slower with the motion stabilization aid.