HAND-HELD ROBOTIC DEVICE FOR VENIPUNCTURE PROCEDURES

By

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ABSTRACT OF THE THESIS

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Venipuncture, obtaining venous access for clinical intervention, is an essential first step in patient healthcare. Consequently, it is the most prevalent medical procedure and leading cause of injury to patients, with difficulties in obtaining venous access costing the US healthcare over $4 billion annually. Venipuncture success rates rely heavily on clinician experience and patient physiology, in which non-visible, non-palpable, or rolling/deforming veins create challenges for clinicians placing a needle. Previously in our lab, a benchtop image-guided robotic device was developed to introduce a needle for venous access. However, its large size, lack of mobility, and high costs makes it difficult for clinical translation and emergency care use. The work proposed here is to develop a cost-effective, hand-held, robotic venipuncture device that is capable of performing safe, quick, and efficient blood draws and catheter placements in patients with difficult venous access. The main objectives of the proposed work are to: prototype a hand-held, compact device for precise needle placement, develop a novel ultrasound and force-feedback system for automated venipuncture, and clinically validate the device against traditional venipuncture in a human study. The results of this work will provide a device that can improve first-stick accuracy, reduce average venipuncture procedure times, and reduce injuries and complications associated with failed venipunctures.

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Specific Aims

Aim 1: Develop a miniaturized, hand-held venipuncture device capable of precise needle placement and catheter advancement.

Motivation: The previous benchtop devices large size makes it difficult to implement in other clinical scenarios, such as emergency care. The goal of this aim will be to develop a venipuncture device for hand-held portable use, as well as development an additional sub-system for catheter placement capabilities.

Objective 1: Miniaturize previous bench-top venipuncture device into a compact, hand-held form.

Objective 2: Develop catheter insertion sub-system for the hand-held device.

Objective 3: Perform human pilot study to evaluate needle placement capabilities and obtain in-human data.

Aim 2: Combined ultrasound and force feedback system for automating venipunctures.

Motivation: A large challenge for the device is determining when the needle tip has reached the vessel center, especially during cases of high vessel rolling and deformation. Furthermore, the device lacks capabilities to segment and track suitable vessels for cannulation during the procedure. These challenges can be addressed by utilizing novel machine learning algorithms for an ultrasound and puncture detection system to automate the vein localization and insertion step in venipuncture.

Objective 1: Vessel segmentation and classification from temporal ultrasound image sequences.

Objective 2: Combined framework for simultaneous vessel tracking and puncture prediction.

Objective 3: Train and evaluate the puncture detection and vessel segmentation framework.

Aim 3: In-human comparison study comparing the efficacy of a hand-held venipuncture device to manual venipuncture.

Motivation: Comparing against manual venipuncture is essential to prove improvement over traditional approaches. First-stick accuracy and time-to-completion of the device will be compared against manual venipuncture in a focused patient group with a history/likelihood of difficult venous access (DVA).

Objective 1: Compare hand-held device against manual venipuncture for obtaining venous access.

Completion of these aims will result in a clinically validated, hand-held venipuncture device that improves both first-stick accuracy and procedure time for blood draw procedures in difficult venous access patients compared to the manual approach. We aim to improve patient care and clinical workflow through automated venipuncture, ultimately reducing facility costs from complications of difficult venous access.

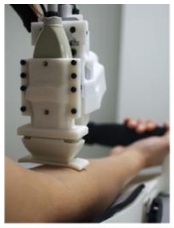
Background and Significance

Obtaining peripheral venous access in patients is one of the most essential and common first steps taken in any clinical intervention, whether it be blood sampling for diagnosis or catheter placement for intravenous intervention. Traditionally, this procedure is accomplished manually where a clinician visually identifies a suitable vein for cannulation and then manually inserts a needle into the vein lumen center. Unfortunately, the level of experience, training, and coordination of performing venipunctures varies greatly between healthcare personnel. Venipuncture is the most commonly performed clinical procedure worldwide, with over 1.4 billion venipuncture procedures performed each year. It is also the leading cause of injury to both patients [1] [2] and clinicians [3] [4] [5] [6] in healthcare facilities. The challenges of obtaining intravenous access are exacerbated in patients with difficult venous access (DVA), where failure rates are reported at 27% for patients without visible veins, 40% for patients without palpable veins, and 60% for patients who were emaciated [7] [8]. Failure rates are also noticeably high in pediatric care, with a failure rate as high as 47% and averaging >3 needle stick attempts to gain peripheral venous access in DVA situations [9]. Repeated failures to start an intravenous line have been shown to significantly increase the chance of tissue damage and blood borne disease transmission, and may necessitate alternative rescue pathways for obtaining venous access of much greater cost and risk [10] [11]. Additionally, difficulties in obtaining venous access can cause even simple procedures such as IV catheter placements to become lengthy, ranging anywhere from 15 minutes to two hours and requiring additional personnel and rescue-paths to achieve [12]. In total, difficulties in obtaining venous access affect not only patients and clinicians, but also the healthcare system as a whole, with costs estimated to exceed $4 billion per year in the U.S. alone. [13] [14] [15] [16].

Challenges associated with venipuncture have pushed for the development of technologies to assist clinicians in finding and identifying suitable veins for cannulation. Imaging technologies that use near-infrared (NIR) light, such as the *VeinViewer,* have been commercially developed to aid clinicians by highlighting non-visible veins in a patient's forearm [17]. However, these NIR imaging technologies only provide a limited accuracy of the vein location on the forearm, and do not provide any vein depth information to the clinician. Additionally, the penetration depth of the NIR is limited to around 4mm in tissue, making it unsuitable for obese populations [18] [19]. Overall, research findings are unclear regarding the efficacy of NIR imaging systems to assist in venipuncture procedures [20]. Several studies observe no significant difference in first-stick success rates when compared to manual procedures when using NIR image assistive devices, indicating that the actual insertion of the needle may prove to be the limiting factor in failed venipunctures, not the identification of a suitable vein [21] [20] [22]. Another medical device used to assist clinicians in difficult venous access is ultrasound (US). Ultrasound imaging can be used for real-time needle imaging, providing clinicians with visual feedback of the needle during insertion into the vein lumen [23]. However, the problem with the current use of US imaging for assisting venipunctures is its high learning curve, noisy images, and time-consuming set-up, making it cumbersome and impractical for common, high volume venipunctures such as routine blood draws [24] [25]. In addition to vein visualization, there are many commercial devices that demonstrate the benefit of robotically-guided needle insertions for a broad range of applications [26] [27] [28], including orthopedic [29], endoscopy [30], prostatectomy [31] [32], and brachytherapy [33]. However, while these robotically guided devices have been shown to improve the treatment time, accuracy, and overall outcome of their respective surgery [34] [35] [36], no existing system has been commercially developed for venous access.

Over the past decade, other research groups, including ourselves, have attempted to solve this problem of venous access through robotically-assisted venipuncture. One such group, known as Veebot (2013), developed a robotic venipuncture device that utilizes a large, multi-degree-of-freedom (DOF) robotic arm and ultrasound imaging probe to guide the needle tip to the vessel center [37]. However, this device is very large, must be transported on a cart, and because of its large size and number of motors, is very expensive. The accuracy and efficiency of the device is unknown, as no publications or clinical trials have been reported since its's public release (2013). More recently, another research group from the Singapore University of Technology and Design has begun work to develop a smaller venipuncture device to assist clinicians in performing peripheral intravenous catheter (PIVC) placements [38]. Their device features a hand-held design with compact motors for needle actuation and an electrical impedance sensor fitted to the needle to detect vessel punctures from changes in impedance as a result of the needle coming into contact with blood. They report an average catherization success of 88% using their device on phantom, practice arms. While their device does solve the problem of both size and cost, it does not actually identify or image suitable veins for cannulation, a major challenge for venous access in a large demographic of patients (obese, dark skin pigment). Ultimately, the device cannot find hidden vessels on the forearm, but instead assumes the vessel is easily visible and trackable. Additionally, the device requires the user and patient to remain completely still during insertion to assure the needle reaches its target. Overall, while this hand-held device is compact and low-cost, it lacks imaging tools necessary to identify suitable vessels for cannulation in patients with difficult venous access.

Previously in our lab, a benchtop robotic device was created to automate the venipuncture process and increase first-stick accuracy and safety (**Figure 1b)**, and has been shown to work effectively at drawing blood on phantom arm models [39]. This device utilized a NIR imaging system to scan suitable veins for cannulation, a US probe to provide real-time needle steering during insertion, and a 9 degree-of-freedom (DOF) robotic system to place the needle manipulator and perform the needle insertion [40]. While it demonstrated high first-stick success rates in phantom studies, its large size, lack of mobility, and high cost make it difficult to implement in a number of clinical scenarios [41] [42] (**Figure 1)**. Venipunctures, whether blood draws or PIVC placements, require the clinician to obtain venous access from the patient quickly, safely, and unencumbered. A hand-held device, capable of assuring first-stick accuracy in any difficult situation, would have a wide use of applications in the medical field, especially in emergency settings (**Figure 1a)**. Furthermore, by limiting the number of DOF (motors) as well as frame size, a hand-held device would prove to be more cost-effective for obtaining venous access, thereby further facilitating clinical translation into the healthcare work flow.

a)  b) 

Hospital / clinic	Hospital / clinic
Clinical Laboratory	Clinical Laboratory
First-responder	X
Pediatrics	X
Bed-ridden patients	X
Emergency Care	X
In-surgery use	X
Military	X
Portable	Benchtop

Figure 1: Areas of application for a Portable and Benchtop Venipuncture Device. a) Hand-held (2-DOF) device, b) Benchtop (9-DOF) device.

HYPOTHESIS and IMPACT: *The major goal for the proposed research is to develop an easy-to-use hand-held device that can aid clinicians in performing blood draws and intravenous catheter insertions by assuring a successful first-stick.* The underlying

hypothesis is that robotically and image-guided venipuncture can address the major challenges associated with difficult venous access (DVA); the localization of veins for cannulation, and the actual needle insertion itself. A hand-held robotic venipuncture device has the potential to impact a number of areas in vascular access, including: 1) infant, elderly, and high BMI patients; 2) general hospital and medical facility phlebotomy; 3) first-responder and emergency medicine care; 4) military and trauma applications; and 5) chronic disease patients (dialysis, multiple infusions).

Summary

The goal here is to develop a hand-held device that can quickly, efficiently, and safely obtain venous access in difficult settings, thereby improving patient outcomes while simultaneously reducing burden to both healthcare facilities and personnel. This major goal is broken into three aims, which include 1) development of the hand-held venipuncture device, 2) development of an ultrasound imaging and puncture detection system, and lastly 3) an in-human comparison study of the hand-held device versus manual venipuncture. Completion of these specific aims will result in the completion of a simple to operate, hand-held device for safely obtaining venous access in both normal and DVA patients. The work proposed here will also establish the groundwork for future robotically-assisted devices for other related venipuncture procedures, such as anesthesiology administration, dialysis, and arterial line placements. Our hypothesis is that a robotic venipuncture device has the potential to improve patient care and optimize clinical workflow for difficult venous access patients compared to manual venous access. Some of the benefits of a robotic and image guided approach include: 1) automated vein identification in non-visible and non-palpable veins, 2) precise and quick needle placement

for difficult needle placements, and 3) reducing burden to clinicians and decreasing procedure time through automation of the venipuncture procedure.

Research Plan

Aim 1: Develop a miniaturized, hand-held venipuncture device capable of precise needle placement and catheter advancement.

The previous benchtop device's large size makes it difficult to implement in a number of clinical scenarios, such as emergency care or in ambulatory settings. The goal of this aim will be designing and developing a hand-held, robotic device capable of precise needle placement for blood drawing and catheter insertion procedures. The objective will involve miniaturizing and redesigning the previous larger benchtop venipuncture device into a hand-held, compact form for portable, efficient, and safe venipunctures. To facilitate clinical translation of such a device, the design requirements of the device are listed in **Table 1.** The final result of this aim will be a hand-held venipuncture device capable of precise needle placement (RMS error <0.5) and IV catheter placements.

User Needs	Design Specs
High-first stick accuracy	> 95% first-stick accuracy
Compatible for Difficult Venous Access patients	- US imaging depths 0-20mm - Precise needle control for rolling veins - High precision (<.5mm accuracy)
Pediatrics Use	- Vein diameters >1mm
Portable	- Hand-held design - Light weight (<2lbs)
Quick procedure time	Procedure time <1 minute
Patient and Clinician safe	Automated needle handling and contactless needle loading.
Cost-effective	- Reduced number of DOF - ~ $2,000.00

Table 1: User needs and design specs for the hand-held, venipuncture device.

<u>Objective 1.1:</u> Miniaturize previous bench-top venipuncture device into a compact, hand-held form. The previous benchtop device created in our lab, as seen in **Figure 1b**,

can be further reduced in size and numbers of DOF [40]. Firstly, the device features a 9-DOF robotic system, three of which are responsible for controlling the large motions of the manipulator component (gantry system). The needle manipulator, which is responsible for aligning and inserting the needle with the target vessel, makes up the remaining six DOF. It is responsible for assuring the needle trajectory is parallel with that of the target vessel. In transitioning to a hand-held device, a large reduction in DOF can be made. Firstly, the large gantry system (3-DOF) can be removed entirely, as the device will be manipulated by the user and brought over the intended insertion area. An additional 4-DOF can be removed, which are responsible for aligning and adjusting the needle trajectory with the imaged vessel, as well as making insertion angle adjustments between 0-40 degrees. Finally, we are left with two essential DOF that are responsible for the actual needle insertion itself, and for adjusting needle height to reach varying vein depths.

An initial prototype of the hand-held device (**Figure 2)** has been developed and evaluated. It features an out-of-plane 2D US probe for imaging subcutaneous veins up to 30mm in depth, a high precision 2-DOF manipulator for needle actuation and alignment, and a force sensor along the needle axis to record forces during insertion. The 2-DOF robotic manipulator accomplishes the task of aligning the needle trajectory with the target vessel in the Z-axis (Z-axis-DOF) and

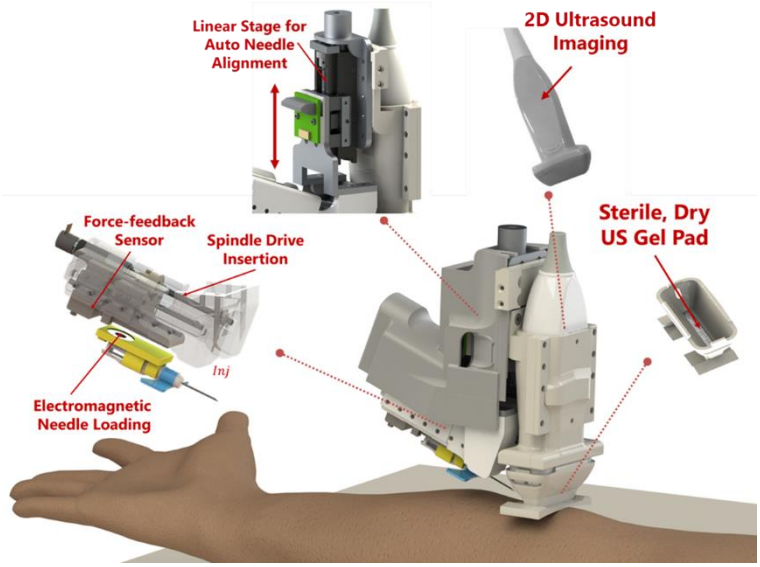


Figure 2: Venibot: Hand-held robotic venipuncture device. Features (left-to-right): 1) Needle injector (Injection-axis) with electromagnetic needle loading and force sensing; 2) Linear stage (Z-axis) for needle trajectory alignments with subcutaneous vessel; 3) 2D ultrasound imaging probe for vessel localization; 4) US dry gel clip for acoustic coupling between transducer and forearm.

autonomously injecting the needle towards the vessel center (Injection-DOF). An electromagnet is designed into the needle clip housing and is used to magnetically load and unload needles for safe and quick exchanges. Device frame components and housing are composed of ABS plastic and were fabricated using an extrusion 3D printer. Parts requiring higher precision were fabricated using a stereolithography (SLA) Form Labs 3D printer. In total, the entire device weighs 1.2 lbs.

The hand-held device is manually controlled by an operator, in which the user places the device over the intended insertion site to begin the procedure (major device operations during operation can be seen in **Figure 5** below). The device uses an attached 2D out-of-plane ultrasound probe to provide a cross-sectional view of the target vessel (Telemed Linear Transducer L18-10L30H-4). (device set-up can be seen in **Appendix A.1**). The US probe provides a 30mm field of view of the imaged area, with a frequency range of 10-18 MHz, suitable for superficial and deep US imaging (0-40mm). The vessels center depth and Y-position relative to the transducers surface is recorded and used to determine the kinematics necessary for properly aligning the needle's trajectory with the imaged vessel center. The injection-DOF is responsible for performing the actual needle insertion and is driven using a Maxon RE ϕ8mm DC screw drive motor. Device calibration for needle placement control is explained in **Appendix A.2.**

To evaluate the needle placement accuracy of the hand-held device compared to the previous bench-top device, a phantom arm study was conducted. A phantom arm is used to mimic the vessel and surrounding tissue during live venipunctures [43]. The phantom arm's tissue was comprised of 18% porcine gelatin to match elastic properties of hypodermis tissue in literature [43], and the vessels were made of Silastic tubing (3 and 2mm diameter). This study involved tasking the robot to successfully insert a needle to the center of a synthetic vessel, simulating a successful venipuncture. The difference between

the desired needle tip position (center of vessel) and the actual position was recorded via ultrasound imaging. The hand-held device demonstrated a 97% successful first stick rate (62/64) with an RMS error of 0.25±0.2 and 0.46±0.2 mm for the 3 and 2mm veins (n=64), respectively. The two failed attempts were possibly the result of the vessel compressing from the needle attempting to puncture the vein, which may have resulted due to the needle becoming blunt during each set of 8 trials (8 trials total with 8 needle sticks per trial). During this same experiment previously completed, the previous benchtop device demonstrated a 0.3±0.2 and 0.4±0.2 mm placement accuracy for the 3 and 2mm diameter vein, respectively, and a 100% first-stick success rate (n=16) [40]. Compared to the previous benchtop device, the miniaturized, hand-held device shows comparative placement and first-stick accuracy, especially given the higher sample size (n=64 to n = 16).

<u>Objective 1.2:</u> Develop catheter insertion sub-system for hand-held device. While the device does demonstrate capabilities of placing an attached needle into a target vessel, it currently lacks capabilities of inserting a catheter sheath into the vessel for either fluid delivery or intravenous therapy. Performing catheter insertions requires additional steps and functionality that go beyond just needle insertion; once the guide needle has properly punctured the vein, the angle of insertion must be lowered and the catheter sheath then must be driven forward to assure the sheath is properly inserted into the vessel. During this, the guide needle is retracted back simultaneously until it is

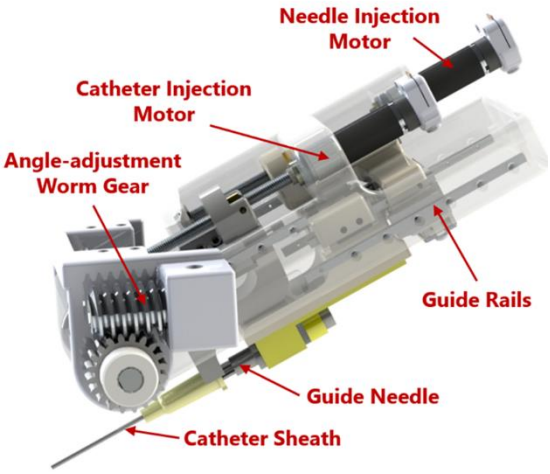


Figure 3: Catheter Insertion Manipulator. Features 2 DC spindle motors for independent needle and catheter sheath actuation, along with a worm gear mechanism for precise angle adjustments between 0 and 40 degrees.

removed from the sheath. The major steps of operation can be seen in **Appendix A.3.** So far, the current device lacks the capabilities of performing these mechanical translations, and as such cannot perform peripheral intravenous catheter (PIVC) insertions; an essential step for patient treatment in hospital and emergency situations.

To achieve these mechanisms, we have developed initial concepts for catheter insertion manipulation (**Figure 3**). A dual DC screw-drive gearhead will be utilized to control both guide needle and catheter sheath movement independently, allowing proper catheter sheath injection into the vessel while also simultaneously retracting the guide needle. A worm-spur gear model will be used to control the angle of insertion during injection, allowing the device to lower the angle of attack to assure proper vessel cannulation once the vessel has been punctured. The device will feature a 35mm needle insertion stroke distance and a 5 N thrust; sufficient to puncture and cannulate deep veins in high BMI patients of up to 20 mm in depth. Catheter placement capabilities will be evaluated by utilizing tunable phantom arms to simulate PIVC insertions, the details of which can be found here: [43]. We aim to achieve needle tip placement accuracies of <0.25 mm to assure sufficient precision in cannulating infant vessels, which typically have vein diameters of around 1.0 mm. The result of this objective will be a sub-system capable of performing the necessary modes of action to place PIVCs.

Objective 1.3: Perform human pilot study to evaluate needle placement capabilities and obtain in-human data. While the device has shown high accuracy and first-stick accuracy in phantom trials (96% first-stick success), it is difficult to relate these results to real-world, patient applications. This is because phantom arms do not truly mimic the patient's vessel and surrounding tissue anatomy or morphology; live veins are more prone

to roll, move, and deform than they are in the phantom arms. Additionally, the acoustic properties of the phantom vessel and surrounding tissue are not accurately represented, giving misleading ultrasound imaging results that would otherwise have large amounts of noise and artifacts when imaged on live tissue, vessels, and blood. Because of these discrepancies in phantom arm testing, this objective will focus on evaluating the devices capabilities at performing simple routine blood draws on human patients.

The purpose of this study was to evaluate the device's capability to robotically align and insert an attached needle towards a pre-chosen vessel center. This study is not an evaluation or comparison study of the hand-held device in actual clinical use, but rather an evaluation of the ultrasound imaging capabilities and robotic placement accuracy of the needle in a fixed, non-moving state. As such, the device faced certain limitations. The device was fixed to a benchtop by using a passive arm device that allowed the hand-held device to be suspended above the patients arm during the procedure. Additionally, the clinician was tasked with selecting the vessel center from streaming ultrasound images, as the device lacks vessel segmentation and tracking capabilities.

Patient	Success?	Procedure time	Skin Tone	Sex	Reason for Missed Stick
1	Yes	1m 55s	Type III	M	
2	Yes	2m 1s	Type II	M	
3	Yes	1m 40s	Type II	F	
4	Yes	50s	Type IV	F	
5	Yes	1m 18s	Type IV	F	
6	Yes	1m 8s	Type III	F	
7	No	1m 50s	Type III	F	Vein rolled out of way
8	Yes	3m 22s	Type V	M	
9	Yes	1m 9s	Type V	F	
10	Yes	1m 20s	Type II	M	
11	No	52s	Type II	M	Vein compressed, no puncture
12	Yes	1m 16s	Type II	M	
13	Yes	1m 18s	Type II	M	

Figure 3: a) Hand-held venipuncture device prototype and setup; b) Results from device use in human pilot study. Average procedure time = 94s. 85% first-stick success rate (11/13). 25G Exel brand needle was used. Skin tone based on Fitzpatrick scale. 12 of 13 patients noted little to no pain during the procedure.

The first half of an IRB approved human pilot study has been completed to validate the accuracy and efficacy of the miniaturized, hand-held device. Thirteen random patients were recruited for the study, in which the device (**Figure 3a)** was tasked with drawing a small sample of blood (3 cc) from a suitable vein selected by the attending clinician. A successful first-stick was determined if the following criteria were met: continuous blood flow visibly seen from needle to Vacuette tube; no vessel back-wall puncture; no bruising/internal bleeding post-stick. The device demonstrated an 85% first-stick success rate (11/13) with no complications or injuries to the patient or clinician in all trials (**Figure 3b)**. Average procedure time for obtaining venous access using the device was 94 seconds. A 25G Exel brand needle was used. 12 of 13 patients noted little to no pain during the procedure. Discussion of results from this trial are described in the following section.

Future Work and Alternative Approaches for Aim1:

The majority of aim1 has been accomplished, including the development of the hand-held venipuncture device and the first half of the human pilot study. The following is future work to be done, as well as alternative approaches that will be investigated to improve device performance.

A major challenge in device operation and hand-held use is assuring there is proper needle alignment with the imaged vessel and the attached needle in the Y-direction. If the needle is not properly aligned with the US imaged subcutaneous vessel during insertion, then the needle will not reach its target and will instead fall either to the right or left of the vessel. To remedy this, we will investigate implementing an additional degree-of-freedom (DOF) to the device to auto-align the needle with the US imaged vessel in the Y-direction. A preliminary design has been created and can be seen in **Appendix**

A.4. A rack and pinion method of translation is actuated by a fixed miniature DC motor, and is used to translate the needle insertion component along the Y-axis. By tracking the vessel center position via ultrasound relative to the needle insertion path, the device could then quickly auto-adjust the trajectory path to compensate for any position changes either due to user, patient, or vessel movement during the procedure. We aim to achieve submillimeter needle-to-vessel alignment accuracy of <0.5mm and response times >0.01 seconds in response to vessel movements. This objective will obviate the users need to align the device exactly with the imaged vessel, requiring only device placement in the general region-of-interest to obtain venous access.

Device miniaturization and performance can also be improved. Currently, we are working with a commercially available research probe (Telemed) that features a transducer for imaging and a main body for handling. By removing the main body and integrating just the essential transducer component of the US probe, we can greatly reduce device size either further (30% reduction). Furthermore, we are also investigating possible alternative device embodiments for improved device handling, stability, and performance during in-patient use. One such design is an “arm-cuff” device, in which the device can tightly grip itself around the patient’s upper forearm to provide stability during the procedure. Additionally, with sufficient force, the “arm cuff” can also act as a tourniquet for the patient, providing additionally stability and dilation to vessels for increased first-stick accuracy. Initial concept designs have begun for this, with ongoing work on developing computer aided drafting (CAD) models.

During the human pilot study, the device demonstrated notable needle positioning and placement accuracy. However, there are several limitations that the device still faces that limit its potential for clinical translation; the major including its inability to determine when the needle tip has successfully reached the vessel center. Furthermore, the device

could not adjust for variations in vessel movement during insertion, as was the cause for failure in patient 7 and 11 (**Figure 2b, Figure 4**). As a result, the vessel rolled out of the way of the needle insertion path. This was because the device has no way of predicting whether an attempted insertion would be successful during insertion, and thus could not adjust for these vessel deformations. Additionally, the device is not truly hand-held nor autonomous, as it was mounted to a fixed surface with a passive arm device to assure proper needle-to-vessel alignment, and could not autonomously segment and classify US imaged veins, as the clinician was required to identify them beforehand.

These limitations of US imaging and puncture detection will be addressed in aim 2, where we will investigate applying machine learning algorithms for auto-vein US segmentation and a force sensor-based puncture detection system for predicting successful punctures in real-time during the procedure.

Aim 2: Combined ultrasound and force feedback system for automating venipunctures.

The greatest challenges in obtaining venous access are properly identifying a vein for insertion and assuring the needle tip safely reaches the vessel center [13]. The major reasons for failed venipunctures are because of vessel rolling/deformation and an inability to identify Experienced clinicians rely on both US image and tactile force-feedback to guide the needle and determine whether puncture

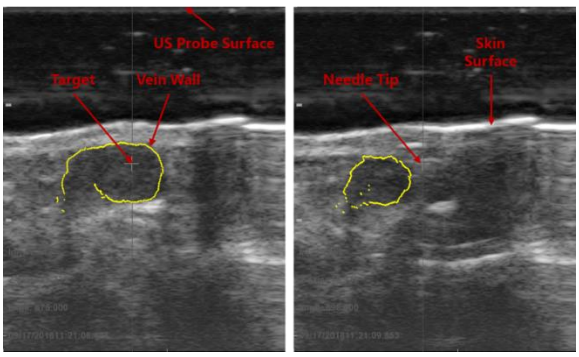


Figure 4: Vein rolling during needle insertion. (Left): Vein position before needle insertion. (Right): Vein position after needle has reached its desired target. Vein rolled out of the insertion path of the needle, resulting in a missed-stick.

has occurred during insertion; Additionally, experienced clinicians, can “feel” when the needle has punctured the initial vessel wall, indicated that the needle tip has reach the lumen center. As of now, the current hand-held device has no method of predicting whether a needle insertion will be successful or not and relies solely on driving the attached needle towards the intended target. As such, the device lacks capabilities of adjusting needle control to compensate for unpredictable vein deformation and movement, as was observed in the human pilot study. In **Figure 4**, US images from the human study show that failed venipunctures were the result of vein deformation / vein rolling as the needle attempted to puncture the vein wall and failed. Additionally, tracking vein positions manually via US can be challenging and time consuming, as veins are difficult to identify from the noisy images and small movements, can create challenges in properly aligning the imaged vein with the needle path. The goal of this aim is to automate and optimize vessel tracking/classification and puncture prediction utilizing real-time vessel tracking and puncture-detection algorithms. The hypothesis is that the challenges of vein identification/tracking and puncture detection can be remedied by utilizing a combined US imaging and force-feedback puncture detection system to automate both vein segmentation and puncture detection during real-time needle insertions. The applications of such a system extend beyond just the venipuncture device, but can be adapted to other surgical applications that require precise needle placements in junction with real-time ultrasound imaging.

Objective 2.1: Vessel segmentation and classification from temporal ultrasound image sequences. Previously, we developed an algorithm to segment vessels that used a modified Gradient Vector Flow active contour model. We evaluated this approach in nine subjects and showed an RMS error of 4.9% compared to manual segmentation [44]. While

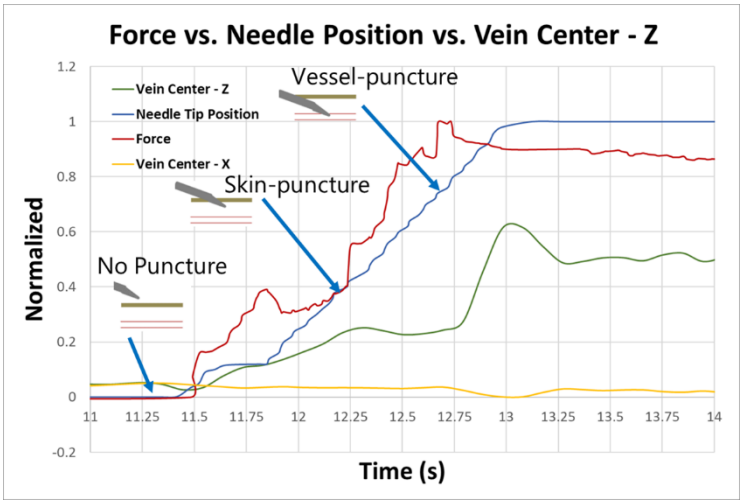


Figure 5: Force vs. Needle Position vs. Vein Center–Z during live insertion in patient. Needle Tip Position (Blue): the distance traveled by the needle to reach the vessel center, normalized (0-21mm to 0-1); **Force (Red)**: The force along the needle axis during insertion, normalized; **Vein Center – Z (Green)**: The percent change in depth of the vessel center relative to its resting position (indicates vessel deformation; **Vein Center – X (Yellow)**: The percent change of the vessel center relative to its resting position (indicates vessel rolling). A trend in force and vein center-z is seen at the moment of initial vessel puncture (time = 12.65s)

performance was sufficient, the method required manual initialization and processing speeds were slow (42.2 ms). Additionally, the procedure required fixed probe placement during imaging and relied on Color Doppler to differentiate between veins and arteries. Color Doppler is not available on all probes, is costly, and suffers from low vessel detection sensitivity. We will compare the above image processing approach to learning-based methods that jointly compute the segmentation and vein/artery classification. In particular, we will investigate the use of deep neural networks, which are capable of directly learning image features that optimize for segmentation and classification accuracy. We hypothesize that such methods will allow real-time predictions that require no initialization and have no dependence on Color Doppler imaging. The model architecture we will investigate makes use of a contracting path to capture context and a symmetric expanding path for specific localization [45]. This convolutional network, termed as U-Net, has been chosen because of its state-of-art performance on biomedical image datasets, small training sample size requirement (~30), and its fast processing time (25 FPS for a 512x512 image) [45]. We will adapt this U-Net system to segment vessel images from a 2-D out-of-plane US imaging probe (same set-up as hand-held device; example of vessel image from US can be seen in **Appendix A1**). We will also investigate

modifications to the architecture that exploit the temporal aspect of US video sequences by adding time-dependent recurrent nodes to individual layers in the network. This allows information to propagate from previous image frames to influence the live prediction, as well as identify key features for vessel location prediction. [46]. We hypothesize this will improve robustness to motion, deformation, jitter, image artifacts, loss of acoustic coupling, and other challenges. Finally, from the segmented vessel image, we will calculate the vessel diameter to determine if the imaged vessel is suitable for cannulation by comparing it to a pre-determined diameter threshold value. The final results of objective 1 will be a segmentation algorithm capable of identifying veins from streaming real-time US, as well as classifying between veins and arteries and determining suitable veins for cannulation. Through retrospective analysis of the previously acquired ultrasound image stream from the human trials, we will assess the vessel segmentation algorithm's by measuring accuracy, robustness to overfitting, and processing time. This new U-Net method will be compared to both the previous approach used and manual segmentation. Our goal is to obtain an RMS comparable to the previous method (~4.9%) and a processing time <50 ms (20 FPS), suitable for real-time imaging using the ultrasound imaging probe.

Objective 2.2: Combined framework for simultaneous vessel tracking and puncture prediction. A characteristic vein deformation and displacement at the initiation of vessel puncture was observed from the human study US images **(Figure 5)**. Additionally, axial forces (red) at the needle tip demonstrate a characteristic rise and drop in force once the needle successfully punctured the vein wall. However, these force profiles and vessel deformations, indicative of vessel puncture, varies among patients and is difficult to isolate a specific threshold that would satisfy across multiple procedures and demographics.

From the initial clinical trial results, standard deviation between force peaks and force drops after the peak force were 44.6% and 20.7% from the max, respectively. This indicates a large variability in force profiles between patients, however more data is required for statistical significance, and it is expected that these percent differences will decrease drastically with more data. Ultimately, the goal of this objective is to develop an algorithm that utilizes both force and US imaging modalities to predict, with confidence, whether the needle will successfully puncture the vessel in real-time. We will investigate utilizing machine learning algorithms to determine the optimal features for predicting a successful puncture, while also possessing capabilities of learning and optimizing its parameters through future procedures and data-sets. By determining the probability of a successful insertion and tracking vein positions via US in real-time, the device can

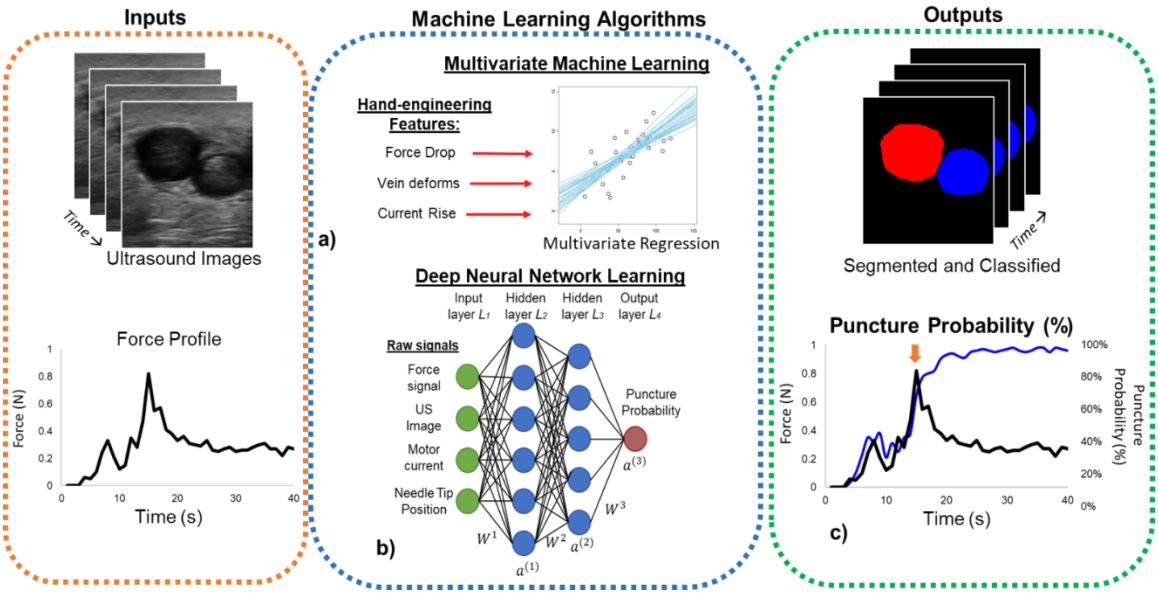


Figure 6: Architecture of the puncture predication and vessel segmentation algorithm. The objective of this system is to both segment and track suitable vessels for cannulation, and determine, in real-time, whether the inserted needle has punctured the vessel wall. The inputs to this algorithm include the raw US images and force profiles during the insertion, as well as needle tip position and motor current. **a) Multivariate Machine Learning:** Takes in relevant "hand-engineered" features for predicting puncture, such as drop in force or vein deformation from needle contact to optimize vessel puncture probability over time. **b) Deep Neural Network Learning:** Takes in raw input signals over time and extracts the best features to maximize puncture probability mid-insertion. **c) Outputs:** The outputs of the system are the probability of vessel puncture over time and US vessel segmentation and classification.

optimize its first-stick performance for difficult venous access patients, especially in vein rolling/deformation cases.

We will compare two methods of predicting vessel puncture during robotic cannulation using machine learning models (**Figure 6)**:

1. Multivariate machine learning: We will develop and train multivariate classifiers that operate on “hand-engineered” metrics extracted from raw signals (**Figure 6a)**. The “hand-engineered” features to detect puncture include the vein position changes (deformations) from US images, axial forces at the needle tip, as well as needle tip position and motor current values, all within a given time window. These features will be combined into one input vector that is then sent through our multivariate machine learning models to predict puncture probability over time. The benefit of traditional machine learning is the ability to hand-pick features for optimizing puncture detection, allowing us to make future modifications to the device for improved performance. Additionally, traditional machine learning is much quicker then compared to deep learning, which is essential for our requirements for real-time.

2. Deep learning, with multimodal inputs: Unlike traditional machine learning classifiers, the deep learning approach will operate on raw signal inputs directly, and extract the best features that optimize predication accuracy, as well as update its prediction accuracy in future procedures. We will focus on deep networks with recurrent operations that are able to capture salient temporal signatures. **Figure 6b** shows an example of such an architecture with raw signals as the inputs, which are used widely to predict on time series data [47]. Again, needle tip position and motor current values are also incorporated into this model as well to increase puncture prediction. The benefit of deep learning is its improved performance and accuracy compared to traditional machine learning. However, deep learning algorithms have a “blackbox” operation (**Figure 6b (hidden layers)**, where

in it can sometimes be difficult to view which features it is considering important for puncture detection.

The results of this system (**Figure 6c**) shows an example of a probability of puncture at each time point during cannulation. When the probability exceeds a threshold, the device will halt the cannulation, as the needle has successfully punctured the vein. This model will also output the US vessel segmentation and vein/artery classification from objective 1, along with the puncture prediction over time, all in an end-to-end manner (**Figure 6c)**. We will also investigate developing models that output not only the probability of puncture, but other possible states of puncture/no-puncture, including: vessel rolling; vessel deformation; needle overshoot; needle undershoot. We will investigate multimodal input models with and without the incorporation of time-dependent recurrent nodes as well. To increase the training size for both the traditional and deep learning approaches, we will also implement data augmentation on the raw data and introduce various modes of noise. Finally, we will evaluate whether pre-training on simulated force data improves system performance for outputting a successful puncture.

Objective 2.3: Train and evaluate the puncture detection and vessel segmentation framework: The machine learning models above require data sets for supervised training and validation. The prediction algorithms, for both the ultrasound and force profiles, will be trained retrospectively on the US imaging and force profile results from the previous human pilot study (~30 patients total). If more ultrasound data sets are required, we will explore the impact of pre-training the US segmentation algorithm on publicly available US datasets that are found from Zukral et al. at the *Signal Processing Library* [48]. After training is sufficiently complete, we will assess the algorithms capabilities of successfully predicting punctures and segmenting/classifying vessels. Evaluation of this system will be

done prospectively on human patients in a future clinical trial (aim 3). However, before that is done, evaluation will be done utilizing 10 human arm cadavers as models, obtained from the Robert Wood Johnson Cadaver Lab at Rutgers University, with assistance from Dr. George W. Mulheron, Program Director of the RWJMS Anatomical Association. These human arm cadaver models can be perfused with saline to mimic active vessels with matching elastic and anatomical properties of that of live tissue. If human arm cadaver models do not prove to be a sufficient model for live patients, we will investigate using a multilayered tissue mimicking skin and vessel phantom with tunable mechanical, optical, and acoustic properties that has been previously developed in our lab by Chen *et al.* [43]. Lastly, we will evaluate system performance retrospectively on the previously acquired human study data (not used in training the system). In the healthcare field, previous studies have shown first-stick success rates for non-DVA patients to be 86% [7]. With this puncture detection algorithm, we expect to achieve a first-stick success rate of >95%.

Summary and Alternative Approaches: The completion of this aim will provide a framework for automated US vessel segmentation, along with a puncture prediction system for improved needle placement and first-stick accuracy. This framework will utilize machine learning algorithms, along the device to optimize its puncture prediction and vessel segmentation capabilities from future venipunctures. This system will be trained utilizing the previously acquired US image sets and force profiles from aim 1. However, the quantity of data sets may not be sufficient enough to determine reliable features for predicting puncture or classifying vessels. We will explore the impact of pre-training the US segmentation algorithm on publicly available US datasets that are found from Zukral et al. at the *Signal Processing Library* [48]. If processing times for the combined framework are higher than expected (<5 ms), we will investigate utilizing localized search areas

(region-of-interests) on raw input signals to reduce computational workload on the puncture prediction and vessel segmentation algorithm. In objective 2.3, cadaver arms will be used to evaluate the puncture detection framework. If the cadaver arm models prove to not be a reliable model, we will investigate using a multilayered tissue mimicking skin and vessel phantom with tunable mechanical, optical, and acoustic properties previously developed in our lab [43].

Aim 3: In-human comparison study comparing the efficacy of a hand-held venipuncture device to manual venipuncture.

The objective for this aim is to compare the hand-held device at drawing blood against the traditional manual approach in a prospective comparative study on difficult venous access patients. For manual venipuncture, previous studies have reported blood draw failure rates at 14% for non-DVA patients, 27% for patients without visible veins, 40% for patients without palpable veins, and 60% for patients who were emaciated [7]. Long procedure times have also been reported for obtaining venous access in difficult patients, with times ranging anywhere from 15 minutes to two hours and requiring alternative methods for cannulation, including ultrasound-guided venipuncture [12]. The goal for this aim is to show an improved first-stick accuracy and procedure time using the hand-held device compared against the traditional manual approach. We aim for the device to obtain a first-stick accuracy of >95% for both DVA and non-DVA patients, and an average procedure time of < 1 minute. The results of this aim will validate the efficacy of a hand-held venipuncture device for obtaining venous access in a real-world, clinical setting.

<u>Objective 3.1</u>: Compare hand-held device against manual venipuncture for obtaining venous access. This study will aim to recruit a sample patient population that has history or likelihood of having difficult venous access. Difficulties in obtaining venous access are the result of a number of patient factors, including: age (elderly and pediatrics; dark skin pigment; both high and low BMI (obese/emaciated). Other factors, not specific to demographics, include prior vessel damage and vessel stability/likeliness to roll or deform, either from previous venous damage or excess fluid in surrounding tissue. We will aim to recruit 40 patients, including both male and female, to evaluate the device compared to manual venipuncture. Protocol for recruitment will include: age range from 18 to 70 years, body mass index in the range of <18 (underweight) and >30 (obese), and skin tone ranging between Fitzpatrick Type I and Fitzpatrick Type VI. This recruitment protocol is to focus patients that would be considered to have difficult venous access (DVA). All proposed human subject research will be reviewed by the Rutgers University Institutional Review Board (IRB) prior to initiation. Recruitment will be taken place at the Robert Wood Johnson Hospital (RWJH) in New Brunswick. Clinical supervision and consulting during this study will be conducted by Dr. Enrique Pantin of RWJH.

The study will involve a direct comparison between the hand-held device and clinician in performing routine blood draws on patients. Here, the device and the manual approach will each attempt to draw blood from the same patient's upper forearm. This will allow a direct comparison between the device and manual approach for each individual patient, allowing for a more in-depth comparison between the two approaches in terms of venous access safety and time-to-completion. Before venipuncture begins, the clinician will record the level of difficulty to obtain venous access on the patient. This will be accomplished by ranking the degree of vessel visibility and palpability on a "1-10" scale, as well as indicate the number of available insertion sites found on each arm. This will

allow for a more in-depth comparison between manual and device when obtaining venous access.

Device protocol and the major steps of operation during this study can be seen in **Figure 7**. Here the clinician, having previously been trained in using the device on phantom arms first, will place the hand-held device over the intended insertion site, this site being the upper forearm. Once in place, the device will identify a suitable vessel for cannulation and prompt to the clinician to begin the procedure if he or she agrees with the choose vessel for puncture. Once initiated, the device will proceed to attempt to puncture the vessel for blood retrieval. The novel puncture detection system, previously developed in aim 2, will then attempt to successfully predict when the needle tip has reached the vessel center. Once detected, the device will halt motor movement and will begin blood retrieval. Once 10 ccs of blood are collected, the needle will be retracted and the device will be removed from the patient. Manual approach will follow traditional blood retrieval protocol, the specifics of which are stated in the World Health Organization [42].

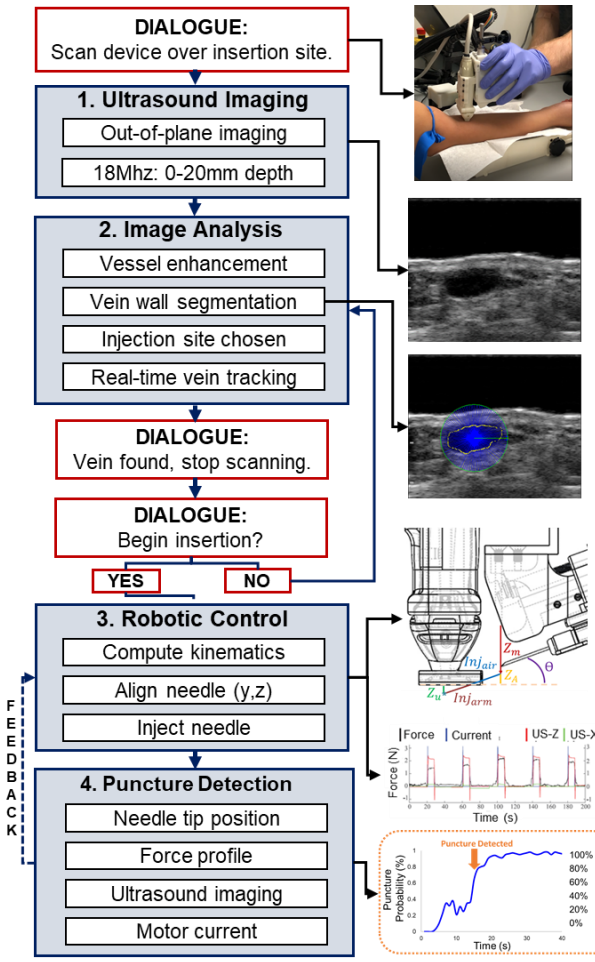


Figure 7: Essential device operations during use. 1) *Ultrasound Imaging:* Ultrasound probe is scanned across insertion site to image peripheral veins; 2) *Image Analysis:* Vein cross-section is segmented, the center calculated, and tracked in real-time during scanning; 3) *Robotic Control:* Once injection site is chosen, kinematics are computed and needle is aligned then injected towards target (Figure from *[40]*); 4) *Puncture detection*: Incorporates motor information, force-feedback, ultrasound, and needle tip US visualization into a machine learning algorithm to predict and confirm a successful puncture.

Expected Outcomes and Alternative Approaches:

Previous studies indicate failure rates in the clinic reported at 14% for non-DVA patients, 27% for patients without visible veins, 40% for patients without palpable veins, and 60% for patients who were emaciated [7]. Additionally, procedure times for non-DVA averaged 1-5 minutes, 2-3 sticks averaged 15 minutes, and for patients that required ultrasound assistance ranged anywhere from 15 minutes to 2 hours [24]. With this in mind, we aim to achieve a first-stick success rate of >95% among all patient demographics, with a procedure time of <1 minute. We will also investigate comparing the device against ultrasound assisted manual venipuncture, the gold standard for obtaining venous access in difficult situations for obese patients [23] [13]. If performing device and manual venipuncture on same arm of the patient proves ineffective, we will investigate a “double-arm” approach, where the device and manual approach will each attempt to draw blood from a separate arm. This assumes that vessel structure is symmetric and similar between arms. However, choice of arm will be randomized to avoid bias, as preferential venous access may be given to a certain arm by clinicians, depending on vein visibility and palpability. If human subject recruitment proves inefficient or difficult for this comparison study, we will investigate recruiting random patients with no preference given to those that are considered to have difficult venous access. In this approach, we will aim to show first-stick accuracies and procedure times that are equivalent to the manual approach.

Conclusion

The work proposed here is to develop and clinically validate a hand-held, robotic venipuncture device that can quickly, efficiently, and safely obtain venous access in a broad demographic of patients. The specifics of this research plan follow: 1) Develop a compact, hand-held prototype for precise needle actuation; 2) Develop an US imaging

and force-based puncture detection system for optimizing automated venipuncture; and 3) Clinically validate the device in a comparative study against manual venipuncture.

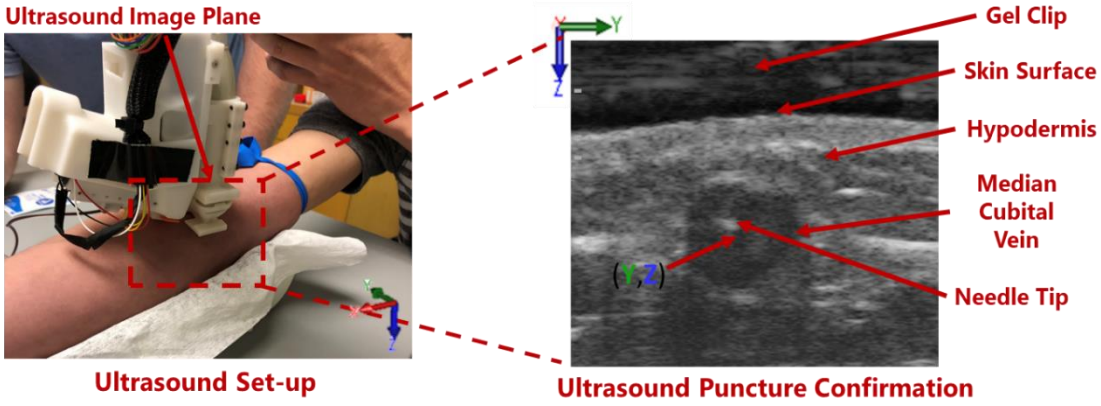
The majority of aim 1 has been completed, with more cannulation testing still being conducted, specifically for needle placement accuracy in phantom arms with vessel diameters of 1mm, a vessel size typically seen in infants. Additionally, the first half of a human pilot study has been completed, where we have obtained in-human ultrasound and force-profile data that will be utilized further in aim 2. The second half of the study is currently underway, with 25 patients being recruited for a total of ~35, and is expected to complete in early April. Once in-human data is collected, aim 2 will begin by investigating both models of machine learning algorithms (feature based / neural network) to develop a system to segment, classify, and track imaged vessels, as well as autonomously determine vessel puncture in real-time. Completion of this aim will improve device performance, allowing it to autonomously identify suitable vessels for cannulation while simultaneously assuring a successful first-stick. Aim 3 will involve the combination of aim 1, the hand-held device, with aim 2, software for automated US and real-time puncture detection, and a comparative human study against manual venipuncture in drawing blood on patients with DVA.

Specifics of cost have not been discussed, however an important consideration in device development is clinically viability and translation in the healthcare workflow. This includes the device to be cost-effective such that the results of improved venous access are not outweighed by the limits of cost. Furthermore, the work here is not stand alone, but may also have potential applications. For example, the framework for combined US and force sensing puncture detection algorithms (aim 2) can also provide a basis for future medical robotic applications that require real-time feedback control, such as in robotically

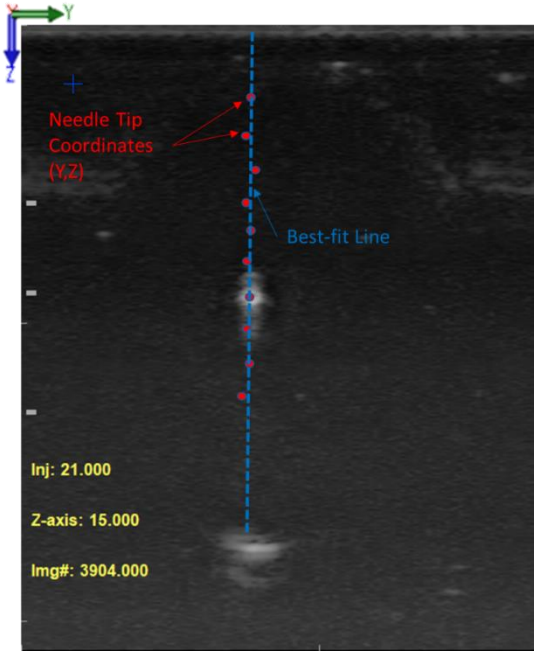
assisted invasive surgeries that require ultrasound imaging and precise, real-time, needle control.

The proposed work here would develop a device for blood retrieval and catheter placement for peripheral venous access. However, future work could involve adapting the device to specific venipuncture applications, such as arterial line placements, deep venous access, and other areas of surgery involved with precise needle placement and free mobility. In conclusion, the results of this proposed project will be a hand-held device capable of aiding clinicians in obtaining venous access in patients. Our goal with this is to improve patient care by reducing needle-stick injuries as a result of failed venipunctures, as well as improve clinical workflow in obtaining venous access for either blood sampling or intravenous therapy, thereby improving patient healthcare while simultaneously reducing difficult venous access related costs hospitals.

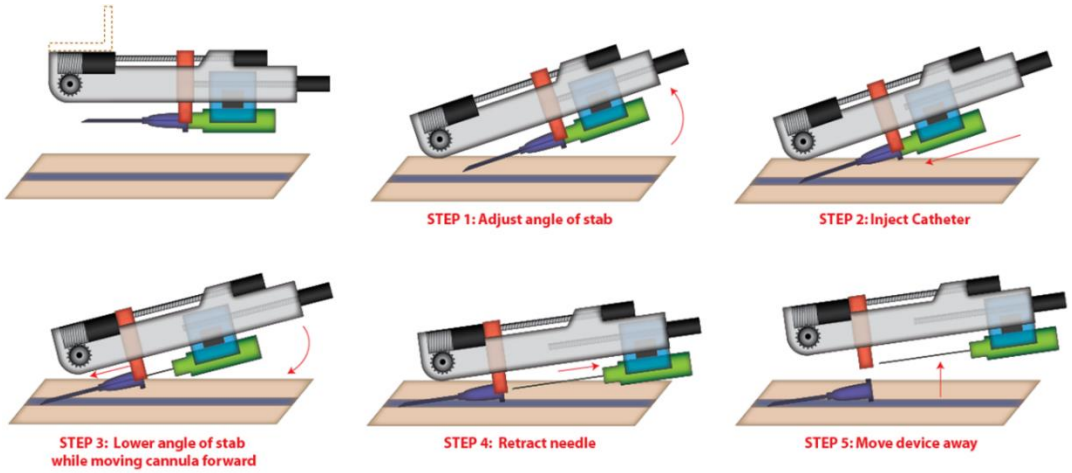
Appendix A



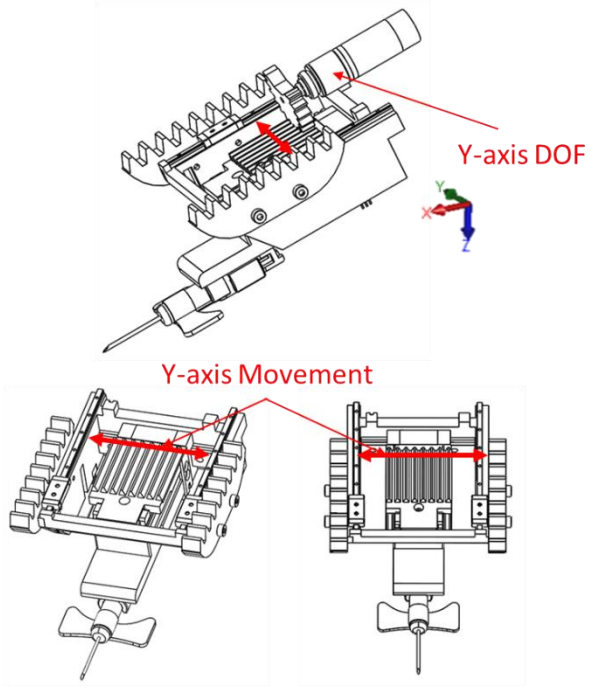
Appendix 2: Hand-held device set-up over upper forearm and resulting ultrasound image. Left: The hand-held device (left) is placed over the intended insertion site, where the attached ultrasound probe provides a cross-sectional view of the underlying vessel (right). Note, probe is assumed to be perpendicular to underlying vessel and needle insertion path to be parallel to underlying vessel. **Right:** Ultrasound image displaying a successful puncture, as indicated by the needle tip in the vessel lumen center.



Appendix 1: Pre-calibration of the hand-held device. Ultrasound image depicting the needle tip points (coordinates) of the calibration. Repeating this process 10 times and varying the depth (Z-axis) each time, it is possible to determine a linear relationship between the US depth (Z) and the required Z-axis position to reach that depth. The result of this calibration is a best-fit line for all recorded needle tip positions, which is then used to determine what the Z-axis motor must descend in order the needle to cross the US imaging plane at that point. Note that the needle trajectory will only travel a pre-destined path in the US image because the needle lacks a Y-axis DOF. In this case, 10 points were recorded, along with the corresponding Inj and Z-axis motor positions (in mm's). Using these points, a best-fit line was found (y = mx+b), which is used to determine what the Z-axis and Inj motor positions must be in order for the needle tip to reach a certain depth (Z) and position (Y).



Appendix 3: Major operational steps during catheter insertion for the hand-held device. First, the device is positioned above the target vessel and the needle trajectory is robotically aligned with vessel. 1) The angle of insertion is adjusted to 25 degrees. 2) The catheter and guide needle are simultaneously injected towards the target vessel. 3) The angle of attack is lowered to 15 degrees. Once lowered, the catheter sheath is independently pushed forward while, simultaneously, the guide needle is retracted back and out of the punctured vessel. 4) The guide needle is retracted back fully until it has completely cleared the catheter sheath. 5) The device is robotically moved away while the catheter sheath is firmly secured to the patient using an adhesive tape.



Appendix 4: Y-Axis Degree of Freedom (DOF) for automatic needle to vessel alignment. The Y-axis DOF features a rack and pinion mode of translation, and is powered via a Maxon RE8 DC motor. This DOF allows for the device to autonomously align the needle trajectory with the underlying vessel, assuring the needle path will directly meet with the vessel during insertion. This DOF will reduce set-up time and will reduce errors and mis-sticks as a result of vessel movement prior to needle injection.

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