Design and Evaluation of a Bioelectric Guidewire

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1 Background

As common vascular procedures become less invasive, the need for advanced catheter navigation techniques grows. Endovascular procedures depend on accurate navigation of the interventional device, but the clinical state of the art presents significant challenges. In practice, the interventionalist plans the path to the area of interest based on pre-interventional images, inserts the guide wires and catheters, and navigates to area of interest using fluoroscopy. However, it is difficult to identify bifurcations for navigation, and the difficulty is compounded by anatomic irregularities. Furthermore, fluoroscopy presents disadvantages in the form of radiation exposure to the patient [2] and interventionalist [7] and possible reaction to the nephrotoxic contrast agent [9].

In a recent paper, we proposed a radically new solution, Bioelectric Navigation [3]. It was inspired by weakly electric fishes who use specialized electrosense to sense and discriminate subtle features of nearby objects (i.e. distance, material, motion, and size [8]). The fish creates a weak electric field, and objects in the field of different impedance than the water distort the electric field. The fish measures the disturbance using voltage-sensitive receptors distributed across the body surface, providing a highly localized measurement of its surroundings.

Our technique combines local bioimpedance measurements with estimates from preinterventional imaging to determine the position of the interventional device within the vascular tree (Fig. 2). Instead of the interventionalist navigating based on fluoroscopy, the catheter itself is equipped with electrodes. One or more of the electrodes emits a weak electric signal and measures the change to the resulting electric field as the catheter is advanced through the vessel tree. The impedance of blood is much lower than that of vessel walls and surrounding tissue [4], so the catheter detects local vessel geometry (e.g. bifurcations, stenoses) from changes in the impedance measurement. For instance, as the device is advanced through a blood vessel, a significant disturbance to the electric field caused by the dramatic increase in vessel cross-sectional area is detected.

BN bridges the gap between catheter-based sensing and catheter navigation. The local measurement from the catheter is compared to predicted measurements from a pre-interventional image to identify the global position of the catheter relative to the vessel tree. Experiments in a synthetic vessel tree and *ex vivo* biological tissue showed the potential of the proposed technology to navigate catheters. Bioelectric Navigation's foremost benefit would be the reduction of radiation exposure for the patient, interventionalist, and staff. Furthermore, it is unaffected by movement and manipulation of the surrounding tissue and therefore does require 2D/3D deformable registration.

1.1 Project Goal

The state of the art for intravascular navigation is to first navigate a guidewire under fluoroscopy to the area of interest then advance a catheter over the guidewire (Fig. 1). Guidewires are used for navigation because they are smaller in diameter and more flexible, so theres less chance of puncturing a vessel or getting stuck in a small artery. The current BN prototype uses a commercially available, non-irrigated 6F catheter, too large to be used as a guidewire. The goal of this project is to create a guidewire based on the BN technology.

1.2 Relevance

While results with Bioelectric Navigation with the catheter indicate that it is a promising technology to reduce the dependence on x-ray guidance, its clinical utility is limited by the fact that the prototype is a catheter rather than a guidewire. Our clinical collaborator has specifically asked for a guidewire so that we can test the navigation capabilities of Bioelectric Navigation *in vivo*, and the success of this project is integral to the eventual adoption of the technology.

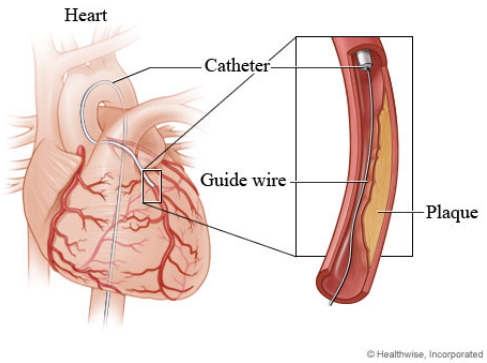

Figure 1: **Endovascular Navigation.** Catheters are advanced to a target by coaxial movements over a guidewire. In this illustration, the guidewire is inserted into the femoral artery, and advanced into the aortic arch. The catheter is pushed over the guidewire into the aortic arch. The surgeon uses the catheter to selectively stiffen the guidewire in order to navigate into the coronary artery. Then the guidewire crosses the lesion. From https://metrohealth.net/healthwise/coronary-angioplasty/.

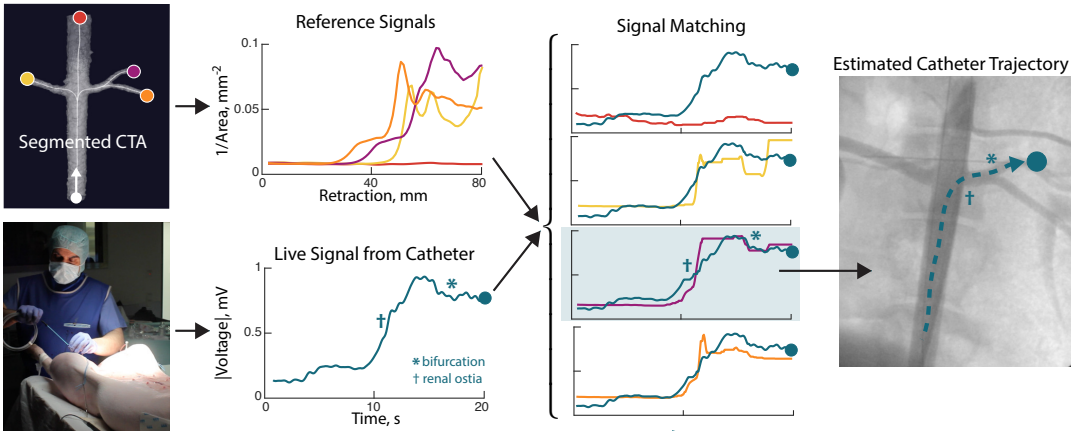

Figure 2: **Schematic diagram of Bioelectric Navigation.** Software registers the live bioelectric measurements from the catheter to the simulated signals from a pre-interventional image to determine the catheter's position.

2 Technical Background: Bioimpedance Acquisition

Like the fish, our guidewire uses measured changes to its electric field to detect changes in the geometry of its surroundings. The bioimpedance acquisition system consists of three main components: the guidewire, the electronics, and the signal processing. Almost any commercially available catheter equipped with electrodes can be used to measure bioimpedance. A function generator supplies a sinusoidal input to a custom-designed constant current source. The current source supplies a constant low-current signal to the emitting electrode on the guidewire, creating a weak electric field in its near surroundings. As such, the voltage measured from the guidewire is a function of the change in impedance. The technology requires very little signal processing; our software simply extracts the voltage magnitude at the input frequency as the catheter advances along a path.

3 Approach

First, I researched guidewire construction. I found an excellent article outlining how to construct custom guidewires [1]. Next, I created a guidewire simulation with configurable electrodes in COMSOLs electric currents module. I was interested in how the wires signal amplitude compares to the catheters. Next, I designed the guidewire. Working with the mentors, I defined the design constraints. I fully developed three designs. I will performed a decision analysis to pick the best design. I improved the embodiment design and created the bill of materials. Then I ordered all of the parts and constructed the prototype. Finally, I tested the guidewire in the acrylic phantom. I measured the voltage as the guidewire passes through six paths of the phantom, using video recordings as ground truth for the guidewire position. I compared the results to the catheters performance in the same phantom.

3.1 Clinical and Technical Literature

Clinical Guidewires There are many types of guidewires for different applications, but the most common for navigation is the "workhorse". These wires generally are made of an inner core and inserted into an outer helical hollow strand (Fig. 3). The stiff inner core tapers distally and does not extend to the guidewire tip to reduce trauma to vessel walls. The standard diameter for a workhorse guidewire is 0.035". The wire is usually made from ASTM 316L stainless steel, nitinol, or Platinum-Iridium. The three most important factors in choosing a wire are:

- Trackability: The wire must be able to follow the tip down a vessel, especially through tortuous vessels.
- Torquability: The ability to transfer a torque applied at the proximal end of the wire to the tip of the wire.
- Flexibility: The ability of the wire to flex on its longitudinal axis while maintaining torque and trackability.

Based on these factors, I have decided to use a commercially available 0.014" guidewire as the core of my prototype. While more flexible than a 0.035" guidewire, it will be stiffened slightly by the electrical wires required for bioelectric navigation. Furthermore, the core is guaranteed to be biocompatible.

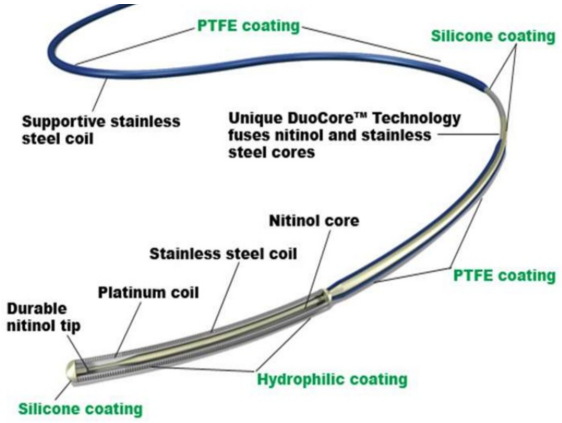

Figure 3: **Commercial Guidewire.** Schematic diagram of a commercially available workhorse guidewire (Runthrough NS, Terumo Interventional Systems, Somerset, New Jersey). From http://www.cathlabdigest.com/articles/Experience-a-New-Guidewire-The-Terumo-Runthrough-NS.

Conductance Guidewires While BN is a new concept, one study of an impedance-monitoring guidewire has been published. The goal of this research was to validate a conductance guidewire's placement of a peripherally inserted central catheter (PICC) *in vivo* [6]. The key result was that important anatomical landmarks were accurately and repeatedly located solely with the conductance guidewire system. In benchtop and *in vivo* tests, the system measured large conductance step increases when the wire advanced in the correct direction. When the guidewire was advanced in the incorrect direction the conductance dropped. When incorrect advancement occurred, the wire was retracted to the previous location in which the conductance was the highest. The guidewire was then advanced in the correct direction as evidenced by the step increases in conductance at each new location in the simulated anatomy. Once the simulated cavoatrial junction was identified, the wire was held stationary, and the PICC was advanced over the wire. When the PICC was placed, the conductance reading dropped almost to zero because of the small CSA of the PICC. Therefore, the authors' guidewire system enabled feedback during PICC placement, a procedure previously performed without guidance. Unfortunately, there was no information about the guidewire's construction, materials, or electrode spacing. While our guidewire could also be used for PICC placement, BN has broad applicability because it incorporates a pre-interventional model. Because our software maps conductance to that vessel model, without knowing the landscape of the arteries along the path to an area of interest, the interventionalist will be given the location of the device in the vessel tree.

Electrode Diameter and Spacing The same set of authors published an older study introducing the "conductance catheter" technology [5]. The goal of this research was to develop an accurate and reproducible method of vessel cross-sectional area (CSA) measurement with a conductance catheter. The key results were equations relating vessel and catheter diameter and *ex vivo* validation of the CSA measurement. In simulation, the authors found that the voltage potential tends to be fairly uniform in the vessel lumen domain followed by an exponential decay into the surrounding tissue for both concentrations of saline. The drop-off at the vessel wall seems relatively slow. This is encouraging for my experiments because it means that when the catheter is slightly off-center in the cross-section, we can still expect a reasonable impedance signal. The authors

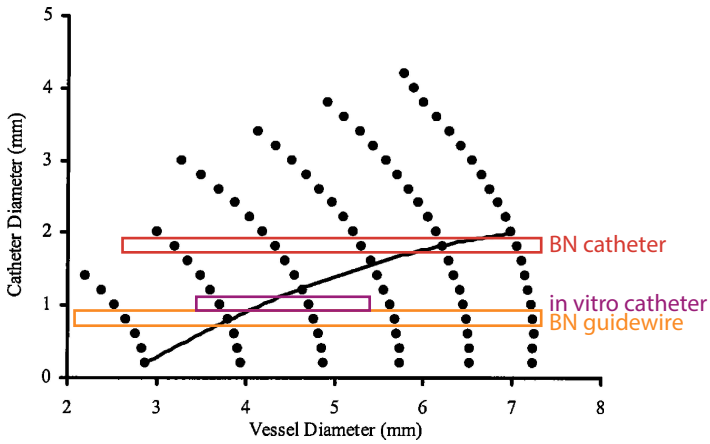

Figure 4: **Catheter-Vessel Diameter Relationship** The FEA was executed for a range of catheter and vessel diameters as shown by the six curves. The solid curve represents the optimized relationship between vessel and catheter diameter. I have highlighted the range of vessels we navigate with the BN catheter (red) and the range we proposed to navigate with the guidewire (orange). From [5], but colored annotations are mine.

combined all of their data and found the optimized relationship between vessel diameter, D_v, and catheter diameter, D_c:

$$D_c = -0.064D_v^2 + 1.07D_v - 2.35 \tag{1}$$

That equation and Figure 4 have been extremely useful to me. The model showed the best agreement with for a 0.8 mm catheter in a 3.8 mm (medium-sized) vessel. That means that we can expect accurate impedance measurements from our proposed 0.889 mm guidewire. The authors summarized their findings into three main points which I used as starting points for the guidewire design:

- The detection electrodes should be placed equidistant from the excitation electrodes.
- The distance between the current excitation electrodes should be much greater than the distance between the voltage detection electrodes.
- The distance between the detection and excitation electrodes should be comparable with the vessel diameter, or the diameter of the vessel should be small relative to the distance between the excitation electrodes.

3.2 Simulation

To test the performance of the guidewire under various electrode configurations, I simulated the voltage in a model of the vessel phantom. Extraction of a complete bioimpedance model requires the three-dimensional and multi-material solution of the generalized Poisson equation, assuming known permittivities of blood and tissue. Given a relatively simple geometry, one can use finite element analysis to numerically solve the generalized Poisson equation. For the first feasibility experiments, I designed an eight-path vessel phantom with two stenoses and one aneurysm. I imported the 3D CAD model into Comsol Multiphysics (COMSOL, Inc., Stockholm, Sweden) and simulated the signal as a two-electrode guidewire passed through the primary branch, measuring

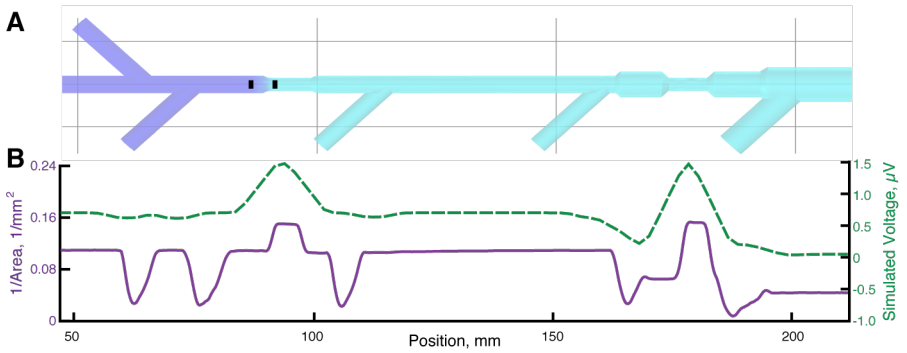

Figure 5: **A)** Simulation of synthetic vessel phantom based on imported CAD geometry. The electrodes (black) span the second bifurcation in this image. **B)** Voltage magnitude from simulation (dasged green), measured at 1 mm increments, and the inverse of the cross-sectional area (solid purple) extracted from CAD model.

once every 1 mm. The simulation yielded a voltage profile for the path. As expected, the simulated voltage at the emitting electrode was inversely proportional to the CSA extracted from the CAD model (Figure 5), and the results matched the profile generated by a catheter in the same geometry.

4 Guidewire Development

4.1 Guidewire Design Specifications

The guidewire must meet some general specifications for guidewires and the electrical needs of our specific application.

- Safety: biocompatible, atraumatic tip to avoid perforation and dissection
- Evidence: patents, literature, existing electrode-equipped vascular devices
- Electrode Surface Area: sufficient current transmission
- Durability: strong electrode/wire connection, corrosion-resistant
- Ease of Manufacture: prototype-able given my skills, available tools, off-the-shelf components
- Flexibility: able to withstand repeated bends in tortuous paths

4.2 Guidewire Design Selection

With these specifications in mind, I developed three design alternatives: Cylinder, Spring, and Braid (Fig. 6). Detailed drawings and Bills of Materials for each can be found in Appendix A. I quantitatively evaluated each design (Table).

Design 1: Cylinder. This guidewire is the closest to commercially available electrophysiology catheters. It has platinum-iridium cylinders soldered to stainless steel wires and threaded onto a commercial 0.014" guidwire core. It scored highest in evidence and electrode surface area. The most challenging part of this design is the manufacture of a prototype because the tiny (0.889 mm diameter) platinum cylinders might be difficult to solder to the wires.

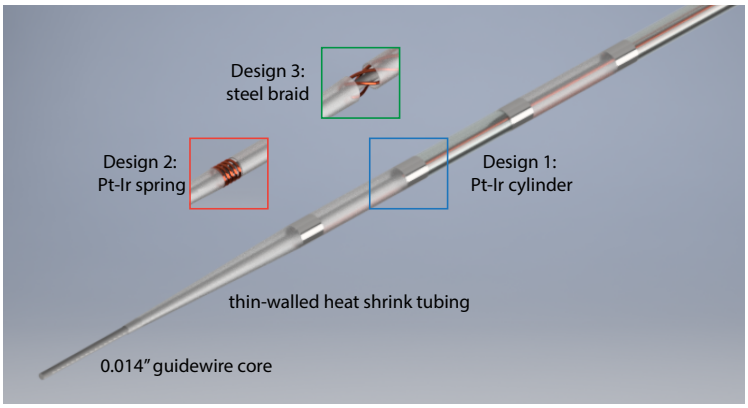

Figure 6: **Design Alternatives.** The three designs vary in the electrode design (inset).

Table 1: **Decision Analysis**

	Weight	Cylinder		Spring		Braid	
		Raw	**Weighted**	Raw	**Weighted**	Raw	**Weighted**
Safety	5	10	**50**	10	**50**	10	**50**
Evidence	5	10	**50**	7	**35**	3	**15**
Ease of Manufacture	4	5	**20**	8	**32**	6	**24**
Durability	4	8	**32**	4	**16**	3	**12**
Flexibility	3	5	**15**	7	**21**	7	**21**
Electrode Surface Area	5	10	**50**	6	**30**	3	**15**
Total			**217**		184		137

Design 2: Spring. This guidewire incorporates a Pt-Ir coil in place of the cylinder of Design 1. This design would be relatively easy to manufacture with Pt-Ir wire. However, it lacks durability because the wires may uncoil, and the electrode surface area is relatively small compared to the cylinder.

Design 3: Braid. This guidewire incorporates insulated stainless steel wires braided around the core. The insulation would be selectively removed from the wire, exposing the wire at intervals. This design is expected to be flexible, but I found no evidence to support this design, and the electrode surface area is the lowest of the three alternatives.

4.3 Prototype Construction

Based on my analysis, I chose Design 1: Cylinder as the embodiment design (Table 2). I first cut three 50 cm lengths of enameled copper wire. For each wire, I sanded 3 cm of enamel from both ends. I threaded one end through a platinum electrode and soldered it to the exterior of the electrode. I soldered a lead to the other end. Next, I threaded all three electrodes over the guidewire and applied a flew drops of silicone sealant between the electrodes to insulate them from each other and relieve some strain. Electrode spacing was adjustable but set to 7 mm. Finally, I manually braided the three strands of copper wire with the guidewire. Ideally, I would have covered the exposed wires in thin-walled heat shrink tubing as in [1], but I did not find a distributor with sufficiently small diameter tubing in stock. Furthermore, the 0.014" commercial guidewire core that

Table 2: **Prototype Bill of Materials**

Description	Manufacturer	Model	Quantity	Length	Part Number
0.014" guidewire	Abbott	Hi-Torque Traverse Guide Wire	1	120 cm	22379H
enameled Cu wire	Conrad	0.15 mm Küpferlakdraht	3	50 cm	605196
Pt-Ir marker band	NuTec Medical	.0315″ OD x .0285″ ID x .03937″ LONG 90Pt/10Ir	3	1 mm	n/a
silicone adhesive sealant	DAP	All-Purpose Silicone Adhesive Sealant	1	n/a	n/a

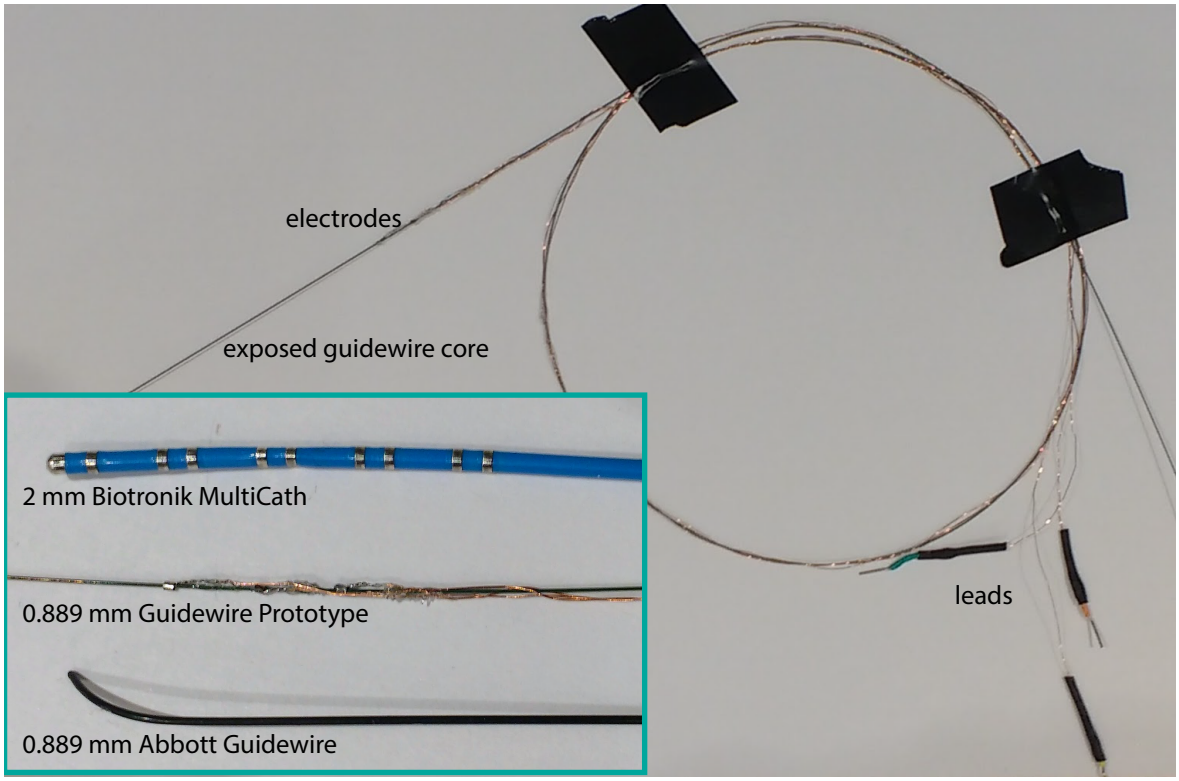

Figure 7: **Guidewire Prototype** The prototype guidewire was constructed around a 0.014" guidewire core. Its diameter matches that of a 0.035" workhorse guidewire (inset).

I used has an extremely long atraumatic tip at 20 cm, so I threaded the electrodes onto the stiffer proximal end of guidewire. Therefore, this prototype is non-biocompatible and lacks an atraumatic tip, so it will only be used in the synthetic phantom. The prototype (Fig. 7) meets the other design specifications.

5 Experimental Validation

The objective of this experiment was to test if the prototype guidewire detects bifurcations, widenings, and stenoses as expected in a synthetic phantom.

5.1 Experimental Setup

For comparison with the prototype guidewire, we used a 6F cardiac electrophysiology catheter (MutliCath 10J, Biotronik, Berlin, Germany). Its ten ring electrodes are 2mm wide with 5mm

spacing. For the guidewire and the catheter, the input to the current source was ± 5 mV at 430 Hz, and the current source supplied a constant 18 μA to the emitting electrode on the catheter. A neighboring electrode is grounded. The signal between the two electrodes is amplified and filtered by a low-power biosignal acquisition system (RHD2000, Intan Technologies, Los Angeles, USA). The Intan software (Intan Interface 1.4.2, Intan Technologies, Los Angeles, USA) logs the AC voltage measurement from the electrodes and filters the signals 8. Finally, a sliding window discrete Fourier transform converts the signal into the frequency domain, and the magnitude at the input frequency is extracted for each window. We performed the first validation experiments in a custom-designed phantom immersed in 0.9% saline (Fig 9). A camera recorded the trajectory of the guidewire and the catheter as it was drawn through the six paths at $1 - 2$mm/s.

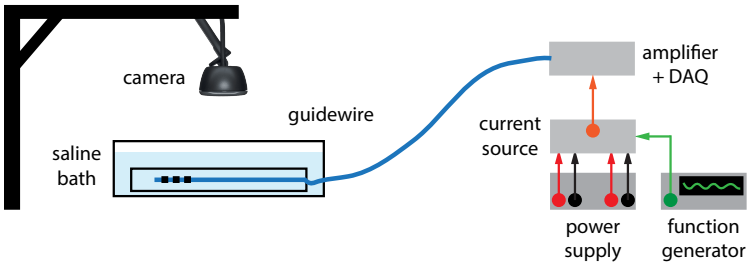

Figure 8: **Experimental Setup** The phantom is placed in a saline bath. A camera captures video as the guidewire advances through the phantom. A power supply powers the constant current source, and a function generator provides the input AC signal to the current source. The measured signal from the guidewire is amplified and recorded by a DAQ. The voltage data collection and the video recording are synchronized such that the position of the guidewire is verified by the video throughout each trial.

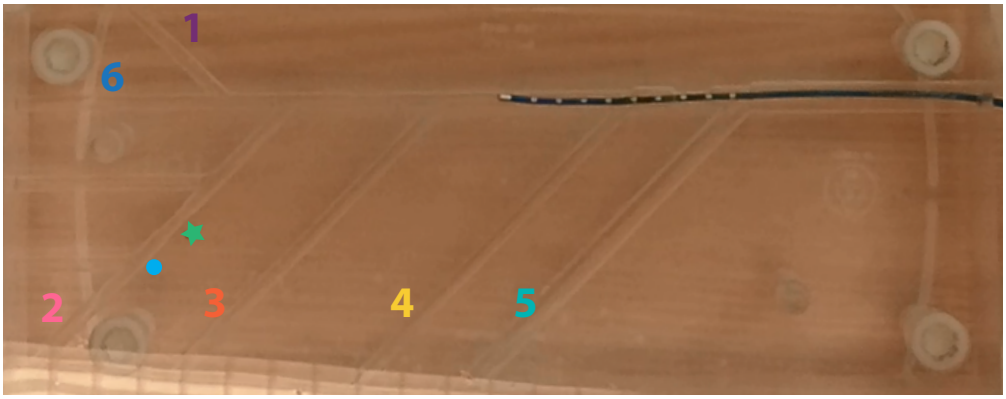

Figure 9: **Synthetic phantom with labeled paths.** The two halves of the phantom were machined from acrylic and sealed with a thin layer of transparent waterproof grease. When assembled, it measures 10 cm × 25.4 cm × 5 cm. The paths are 2.5-10 mm diameter.

5.2 Results

The guidewire behaved as expected in the phantom, based on the literature and simulations. The catheter and the prototype guidewire had very similar performance in the phantom (Fig. 10). The guidewire even out-performed the catheter in the detection of a side branch, possibly because the guidewire's slightly smaller electrode spacing. These results suggest that this guidewire design could be pursued as an option for non-fluoroscopic guidewire navigation.

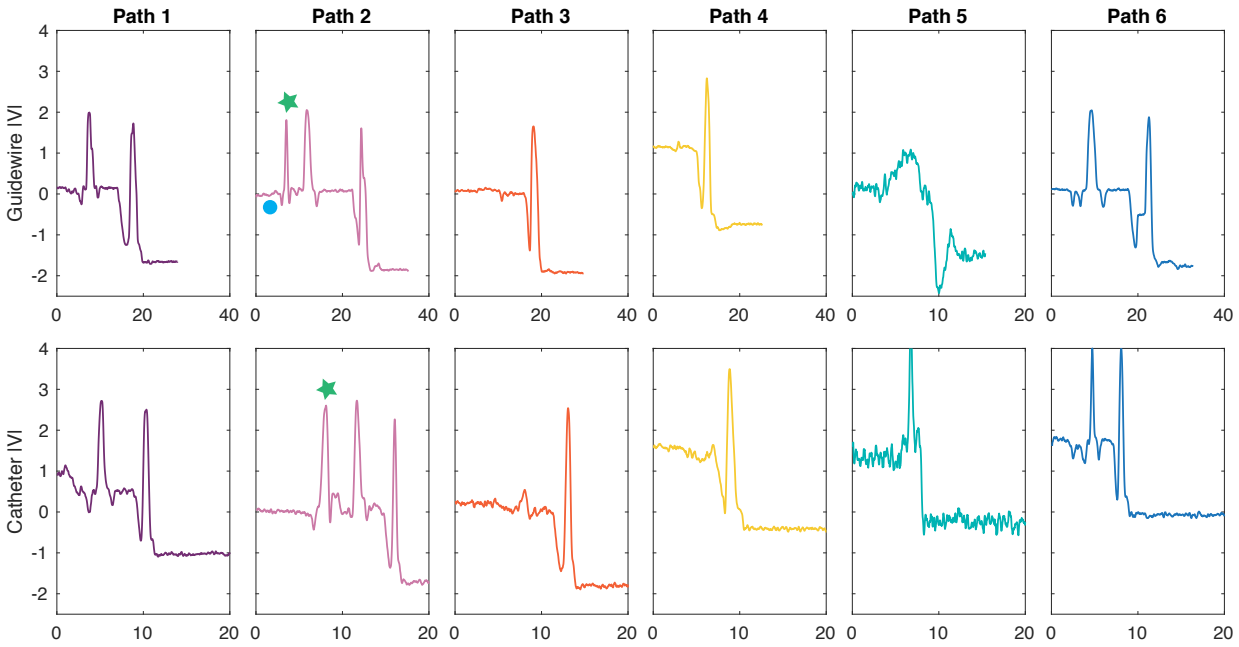

Figure 10: **Results.** Measured voltage from the guidewire (top) agrees with the catheter (bottom) in 6 paths of the phantom. Peaks (e.g. star) indicate that the device is at a stenosis and valleys (e.g. circle) indicate bifurcations, as confirmed by the video recordings. In Path 2, the guidewire detected a 2.5 mm diameter side branch (star) not detected by the catheter.

6 Management Summary

6.1 Duties

As the single student working on this project, I was responsible for all of the deliverables. I discussed my progress in person with Dr. Noah Cowan at our weekly meetings. I met with Dr. Nassir Navab over Skype approximately once a month. Until April, Dr. Bernhard Fuerst attended the weekly CAMP CIS II meeting. After Dr. Fuerst left, I continued attending that weekly meeting to check in with the other CAMP CIS II teams.

6.2 Accomplished vs Planned

As outlined below, I completed all of the Minimum and Expected deliverables. For the Maximum deliverables, I did not conduct an experiment in a gelatin phantom or design a new constant current source. Because the prototype was not biocompatible or easy to clean, I would have had to dispose of it after conducting a gelatin test, so I decided to forego that experiment. I simply ran out of time to design a new current source, but I obtained replacements for our broken sources. All of the other tasks were completed on time, as reflected in the schedule posted on the project webpage.

Minimum Deliverables

- Project Plan report and presentation (online)
- Simulation of three-electrode guidewire in single stenosis in COMSOL
- Repaired current sources
- Seminar report and presentation (online)
- Single CAD design of guidewire, including Bill of Materials (Appendix A)
- Checkpoint presentation (online)
- Experiment Design report (Appendix B)
- Results from experiment in acrylic phantom
- Final report and poster presentation

Expected Deliverables

- Simulation of three-electrode guidewire acrylic phantom's main path
- Replacement current sources (Appendix C)
- Several CAD designs of guidewire with 0.014" commercial guidewire core (Appendix A)
- Final presentation to LIMBS Laboratory (online)

Maximum Deliverables

- Simulation of guidewire with several electrode configurations
- *New design for the constant current source in Eagle*
- *Results from experiment in gelatin phantom*
- Experiment design for in vivo test, ready to submit to ACUC (Appendix D)

6.3 Next Steps

The next step in this project is to manufacture a biocompatible prototype. While infeasible to construct in-house, I have designed a slightly more complex prototype capable of detecting side-dependent bifurcations to aid navigation (Fig. 11). I would perform mechanical testing for trackability and torqueability for this guidewire to ensure that it meets the ASTM guidelines. Similar tests are outlined in [1]. Then, the design should be subjected to clinically relevant navigation testing in tissue with a guiding catheter. A modified version of this report will appear in my PhD thesis. All files (data, code, CAD, etc) relating to this project are located in a private Google Drive directory to be accessed by the mentors and future researchers.

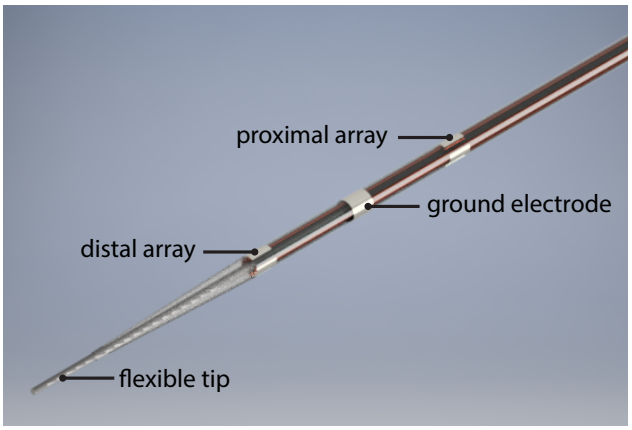

Figure 11: **Proposed Guidewire Design.** Electrode "arrays" consisting of four electrodes each are distributed around the guidewire core at two locations to measure side-dependent voltage changes.

6.4 What I Learned

I started this project with very little knowledge about guidewires, so the literature review I conducted early in the project was instrumental to the project's success.

I also learned how to order PCB's, including making a detailed bill of materials. I did make a rookie mistake by not checking the dimensions of electronic components (Fig 12). Now, I'll need to either replace those capacitors and that one resistor or flip the headers over.

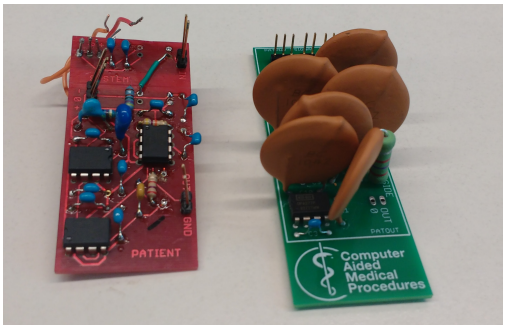

Figure 12: Broken current source from 2013 (left) and replacement current source (right). Lesson: Always check dimensions of electronic components!

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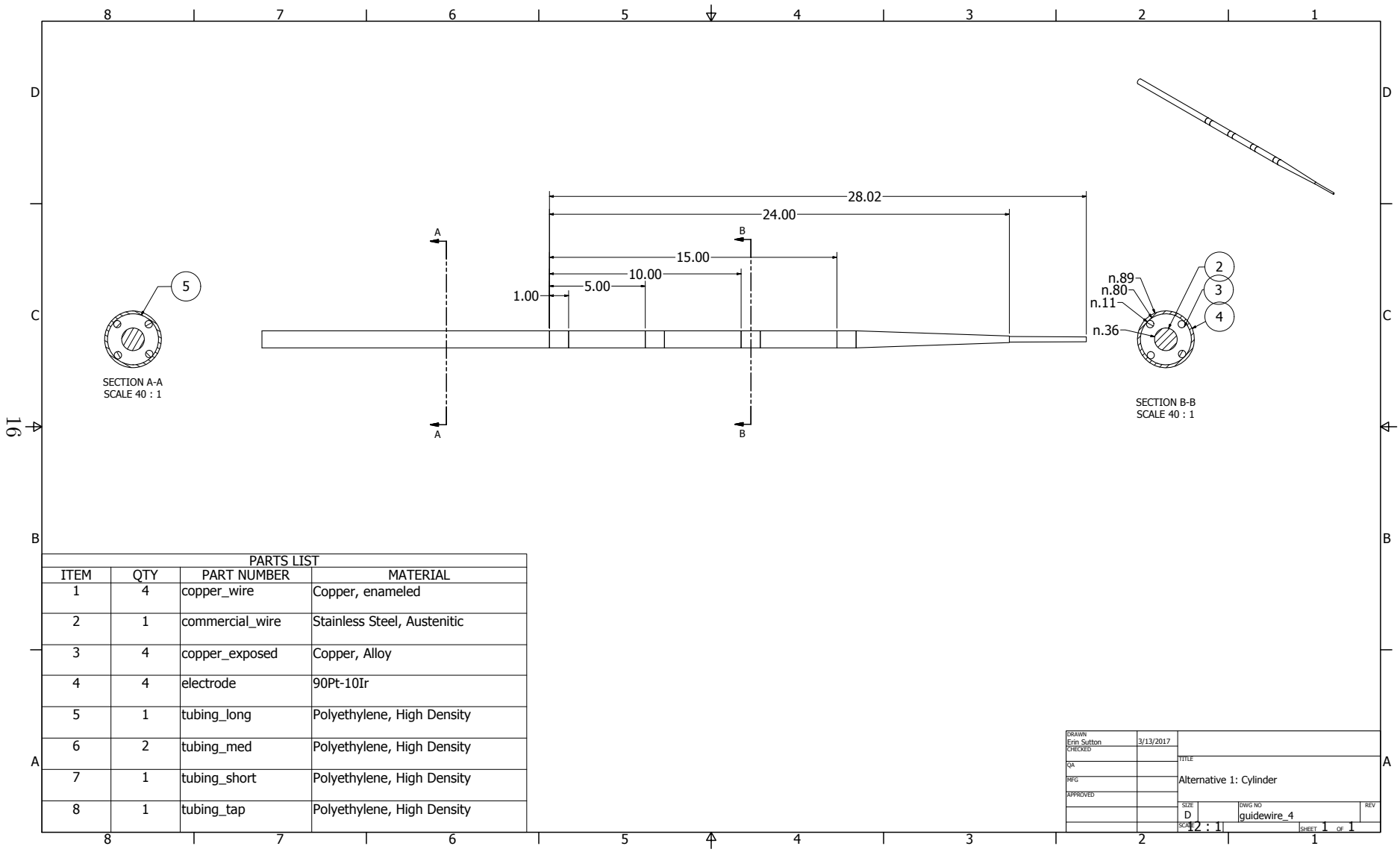


PARTS LIST			
ITEM	QTY	PART NUMBER	MATERIAL
1	4	copper_wire	Copper, enameled
2	1	commercial_wire	Stainless Steel, Austenitic
3	4	copper_exposed	Copper, Alloy
4	4	electrode	90Pt-10Ir
5	1	tubing_long	Polyethylene, High Density
6	2	tubing_med	Polyethylene, High Density
7	1	tubing_short	Polyethylene, High Density
8	1	tubing_tap	Polyethylene, High Density

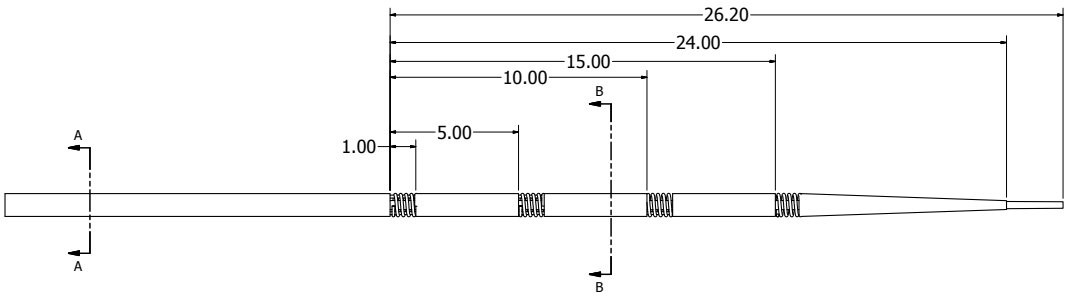
DRAWN	Erin Sutton	3/13/2017
CHECKED		
QA		
MFG		
APPROVED		

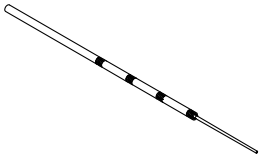
TITLE: Alternative 1: Cylinder

SIZE: D | DWG NO: guidewire_4 | REV:

SCALE: 12 : 1 | SHEET 1 OF 1

SECTION A-A
SCALE 40 : 1





SECTION B-B
SCALE 40 : 1

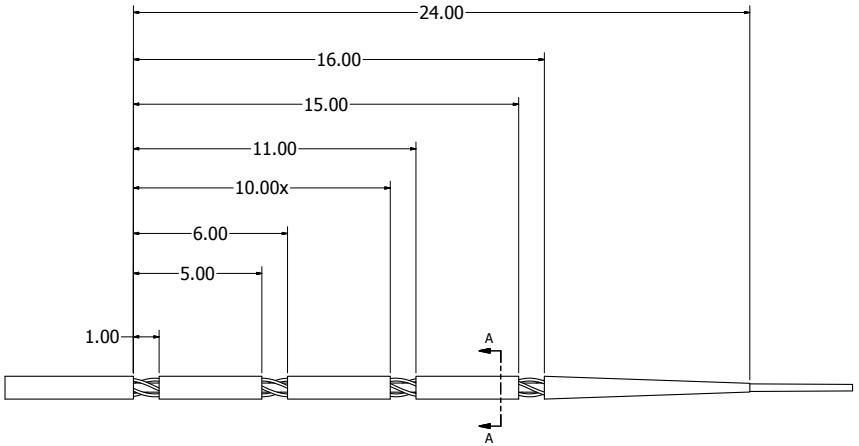
PARTS LIST			
ITEM	QTY	PART NUMBER	MATERIAL
1	4	copper_wire	Copper, enameled
2	1	commercial_wire	Stainless Steel, Austenitic
3	1	tubing_long	Polyethylene, High Density
4	2	tubing_med	Polyethylene, High Density
5	1	tubing_short	Polyethylene, High Density
6	1	tubing_tap	Polyethylene, High Density
7	4	spring	90Pt-10Ir

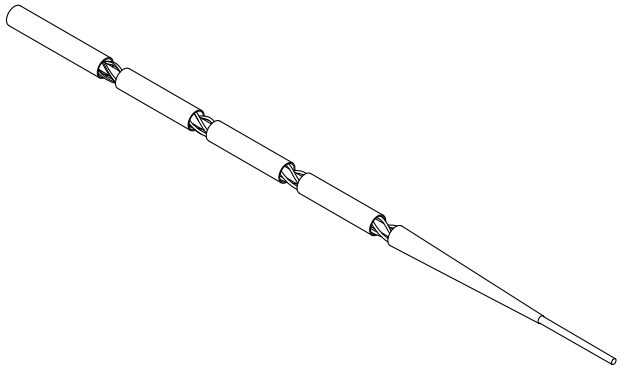
DRAWN	Erin Sutton	3/13/2017
CHECKED		
QA		
MFG		
APPROVED		

TITLE: Alternative 2: Spring

SIZE: D | DWG NO: guidewire_spring | REV:

SCALE: 12 : 1 | SHEET 1 OF 1





SECTION A-A
SCALE 40 : 1

PARTS LIST			
ITEM	QTY	PART NUMBER	MATERIAL
1	1	braid	Copper, enameled
2	1	commercial_wire	Stainless Steel, Austenitic
3	1	tubing_long	Polyethylene, High Density
4	2	tubing_med	Polyethylene, High Density
5	1	tubing_short	Polyethylene, High Density
6	1	tubing_tap	Polyethylene, High Density

DRAWN	Erin Sutton	3/16/2017
CHECKED		
QA		
MFG		
APPROVED		

TITLE: Alternative 3: Braid

SIZE: D | DWG NO: guidewire_braid | REV:

SCALE: 12 : 1 | SHEET 1 OF 1

B Experiment Design Report

Erin Sutton
Bioelectric Sensing and Navigation
April 3, 2017

Experimental Design: Synthetic Phantom

Objective: Test if the prototype guidewire detects bifurcations, widenings, and stenoses as expected in a synthetic phantom.

I. Setup

The phantom is placed in a bath of 0.9% saline solution. A camera records the trajectory of the guidewire through the phantom as it is drawn through the six main paths at 1-2 mm/s.

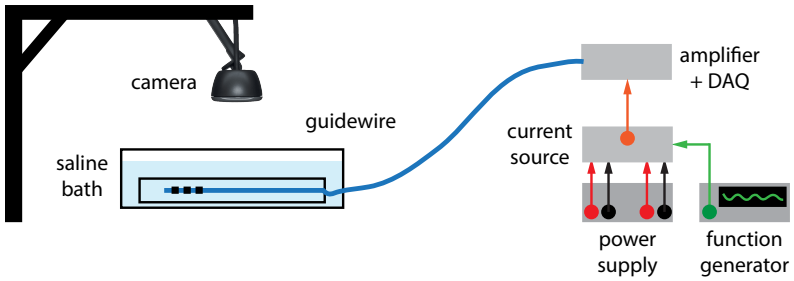


Figure 1. *Experimental Setup*. The phantom is placed in a saline bath. A camera captures video as the guidewire advances through the phantom. A power supply powers the constant current source, and a function generator provides the input AC signal to the current source. The measured signal from the guidewire is amplified and recorded by a DAQ.

II. Electronic Hardware

The input to the current source is ±5 mV at 730 Hz, and the current source supplied a constant 18 µA to the emitting electrode on the catheter. A neighboring electrode is grounded. The signal between the two electrodes is amplified and filtered by a low-power biosignal acquisition system (RHD2000, Intan Technologies, Los Angeles, USA). The Intan software (Intan Interface 1.4.2, Intan Technologies, Los Angeles, USA) logs the AC voltage measurement from the electrodes and filters the signals.

III. Phantom

The phantom for this experiment was custom-designed. The two halves of the phantom were machined from acrylic and sealed with a thin layer of transparent waterproof grease. When assembled, it measures 10 cm x 25.4 cm x 5 cm. It has eight paths, but only six are accessible with the non-steerable guidewire.

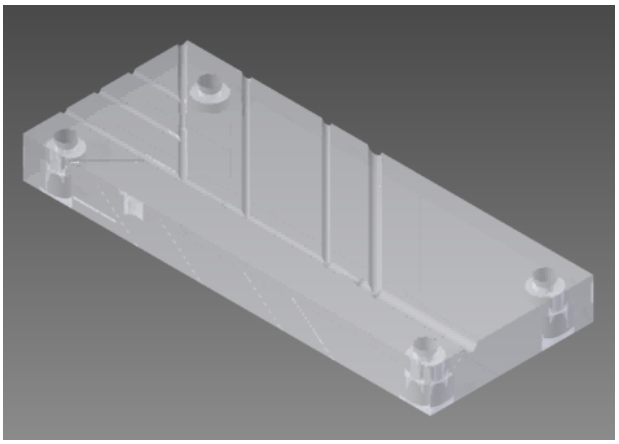
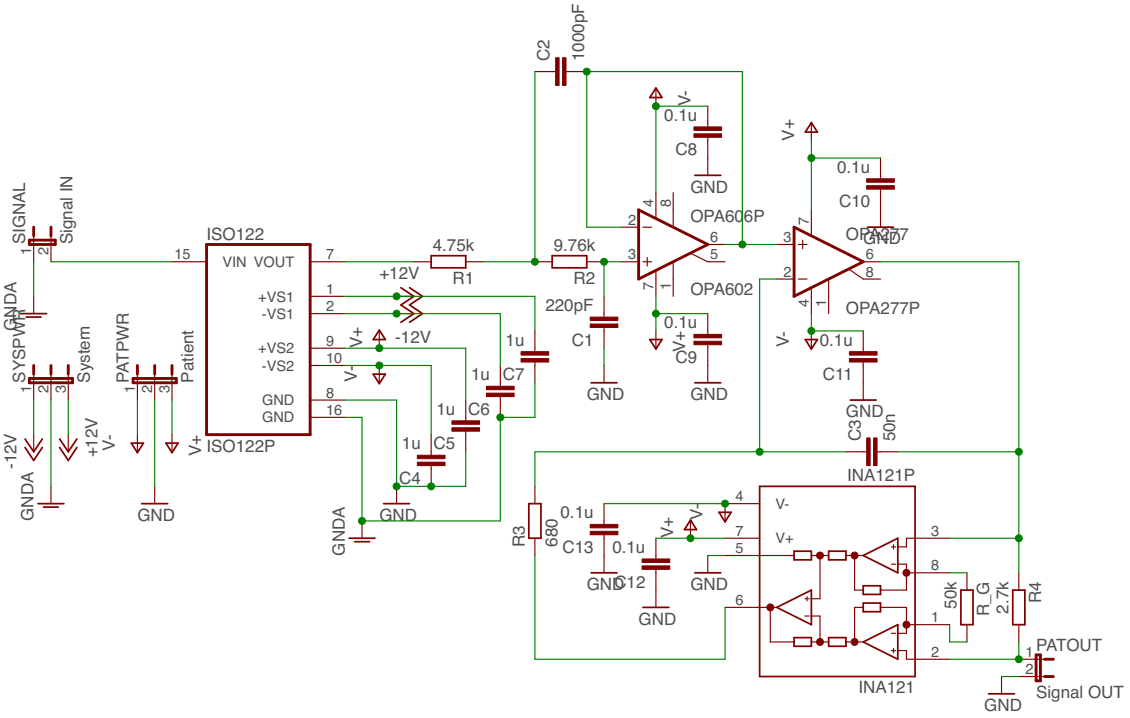


Figure 2. *Bottom Half of Vascular Phantom*.

V. Data Analysis

For each trial, the data is loaded into a custom Matlab script. A sliding window discrete Fourier transform converts the signal into the frequency domain, and the magnitude at the input frequency is extracted for each window. In this fashion, the input signal enables relatively simple path identification.

C Current Source Schematic



D Live Animal Surgical Plan

A Description of Procedures

All animal housing and procedures will be performed at the Johns Hopkins University Medical Center in the facilities of Research Animal Resources (RAR). Three domestic swine (*sus scrofa domestica*) of either sex will be housed in the RAR facilities. For both experiments, the animal will undergo one day of imaging, rest for approximately one week, then one of the minimally invasive procedure will be conducted. On the imaging day, full-body soft tissue CTA and MRA scans will be acquired in in the RAR radiology suite. While the animal rests for a week, we will segment the CTA and MRA images to extract a 3D model of the vasculature. The centerlines of the vessels in that model become reference signals for our sensing system. We propose two distinct surgical procedures: Bioelectric Sensing, and Bioelectric Navigation.

A.1 Bioelectric Sensing

This experiment requires one animal. In the operating room, the animal will be anesthetized and ventilated, and femoral access will be obtained by a cutdown of the femoral artery. The artery will be cannulated with a 6F sheath. Our guidewire will be inserted into the sheath and a 4-5F catheter regularly used in human angiography will be advanced over the guidewire to mechanically support it. During the procedure, we will take continuous fluoroscopy and bioimpedance recordings while our clinical collaborator oversees the advancement of the guidewire by a linear actuator at a constant speed from the femoral artery into the aortic arch, providing torque as necessary to steer the wire. If needed for navigation, contrast material (300-330 mg/mL iodine) will be injected through the catheter. After the procedure, we will compare the bioimpedance signal to the surrounding geometry ground truth from the CTA and fluoroscopic image series. We expect that the guidewire will detect all major branching arteries (brachiocephalic, left subclavian, celiac, cranial mesenteric, renal, caudal mesenteric, contralateral external iliac, and internal iliac trunk).

A.2 Bioelectric Navigation

This experiment requires two animals. The user will perform *in vivo* navigation using only our navigation GUI from femoral access to carotid arteries, blind to fluoroscopic images acquired simultaneously with the bioimpedance signal. In the operating room, the animal will be anesthetized and ventilated, and femoral access will be obtained by a cutdown of the femoral artery. The artery will be cannulated with a 6F sheath. Our guidewire will be inserted into the sheath and a 4-5F catheter regularly used in human angiography will be advanced over the guidewire to mechanically support it. When the carotid artery is cannulated, the user will take a fluoroscopic image with contrast (300-330 mg/mL idoine) as a final ground truth image to measure accuracy (carotid artery placement, inserted past the proximal electrode). In the same animal, we will repeat navigation with fluoroscopic guidance available to surgeon. We will compare time to goal and placement accuracy for the bioimpedance-only and fluoroscopy-only conditions.

B Justifications

Domestic swine was selected based on the similarities between human and porcine anatomy and physiology, especially the cardiovascular anatomy. Domestic swine have been shown to be especially useful in the testing of novel endovascular devices, and our research team has performed many previous studies in this model system. These *in vivo* procedures are only a part of our research plan, which also includes simulation, synthetic, gelatin, and *ex vivo* validation. However, they are crucial to investigate the safety and effectiveness of our novel device, because the electrical environment inside a live animal is more complicated than simulations and benchtop phantoms can replicate. For instance, we have a peristaltic pump to approximate bloodflow through our phantoms, but it lacks surrounding tissues like organs and fat deposits that might influence the electric field of our guidewire.

C Minimization of Pain and Distress

All animals will be premedicated by an intramuscular injection of atropine (0.05 mg/kg), midazolam (0.1 mg/kg), and ketamine (20 mg/kg). General anesthesia will be induced 15 min after premedication by an intravenous injection of thiopental (5 mg/kg), and maintained with mechanical ventilation and a mixture of ethrane (1.5$\pm$2%) and oxygen (1.5L/min). At the end of both experiments, sacrifice of the anesthetized animal will be carried out in accordance with the AVMA guidelines. If, after the imaging study or during the surgical procedure, an animal contracts a severe infection, undergoes respiratory distress, or fails to eat, it will be humanely euthanized.