Biosensor for Ischemic Stroke Detection

Major Qualifying Project

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Abstract

Each year 795,000 Americans suffer from a stroke, 87% of them being ischemic where a blood clot travels from the heart to the brain causing irreparable damage. The potentially fatal consequences of these strokes could be avoided with early detection and removal of the clot. The team developed phantom models of the neck and carotid artery for testing. Artificial blood and clots were pumped through the model, and an ultrasound probe connected to a computer running a computer vision algorithm was used to detect them. This proof of concept shows that a wearable device could be created to preemptively detect ischemic strokes for at risk patients.

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Chapter 4: Design Process	All	All
Chapter 5: Design Verification	Trevor	Rachel, Trevor
Chapter 6: Final Design and Validation	Rachel, Trevor	All
Chapter 7: Discussion	Rachel, Trevor	All
Chapter 8: Conclusion and Recommendations	Rachel, Chloe	Rachel, Trevor

FIGURE **Page**

CHAPTER 1

INTRODUCTION

Thousands of people are affected by ischemic strokes every year, and many of these patients suffer long term ailments or death as a result. Various prevention methods exist, such as blood thinners, but these are not always an effective or viable option for the patient. Those at a higher risk of stroke, such as people with atrial fibrillation (AFib), high blood pressure, or other afflictions, should not only have access to prevention methods, but early detection methods available to lower their risk of stroke. Ischemic strokes take up the majority of total strokes occurring each year within the United States. There are almost 800,000 strokes each year and 87% of those are ischemic [1]. Although there are prevention and detection methods already on the market, they do not satisfy real-time detection methods, ultimately revealing the growing need for such a device.

The inspiration for this project comes from one of the team member's grandfather, William (Bill) Bygrave, who is accomplished in academia, an amazing gardener, and most of all a loving grandfather. In the fall of 2019, he suffered from an ischemic stroke as a result of his atrial fibrillation (AFib) diagnosis that he has had since birth. He survived, but not without brain damage that severely impacted his cognitive skills. The team member's grandfather had been unable to use traditional methods of prevention, namely blood thinners, because he experienced gastrointestinal bleeds as a side effect. Furthermore, he did not recognize that he was having a stroke in time because he did not exhibit the typical signs of a stroke until the following morning, around 24 hours after the first signs of a stroke had occurred. His ischemic stroke, like many others, could have been easily and effectively treated if there was a real-time detection method that was readily accessible for individuals like him.

The overall goal of the project was to create a wearable biosensor to detect blood clots traveling through the carotid artery using real-time monitoring and alert the patient that medical attention is needed in order to remove the clot in a timely manner. The team's original plan was to utilize a capacitive micromachined ultrasonic transducer (CMUT) in the development of a small sensor that could be worn on the neck and constantly monitor the common carotid artery in real time, but it did not come to fruition. Although the team contacted several companies about purchasing a CMUT, they were denied their request because this technology is not commercialized on the market yet. Instead, the team developed a proof of concept model to test if their original idea was feasible. To accomplish this task, the team divided it into three smaller sections with attainable objectives. This allowed the team to understand and assess the scope of their project. The first

objective was to create phantom models to accurately represent the acoustic properties of a human neck and common carotid artery. The phantom models were used to test the real-time imaging capabilities of an ultrasound probe while blood mimicking fluid and blood clot mimics were passed through. It was necessary for the phantom models to have similar acoustic properties to that of a human neck and artery to get the most accurate data possible. The second objective was to pass a blood-mimicking fluid and blood clot mimics through the phantom model. This allowed the team to see how the clots look on the images from the ultrasound probe as they passed through the phantom artery. The last objective was to process the images from the ultrasound probe in real time to demonstrate that the team's original goal was feasible. To meet this objective, the collected data from the phantom model imaging was processed and used to create an algorithm to detect blood clots in real time.

The first objective, creating phantom models, was completed in two steps. The first was to design and fabricate molds to shape the phantom models and the second was to develop the correct composition of material to be used in the models. Two molds were designed: one being the artery and the other the neck. These molds were created to be as realistic as possible, taking into account the average size and location of a human neck, carotid artery, and neck vertebrae. Once the molds were modeled using Solidworks, they were 3-D printed and then placed in an acetone bath to reduce their surface roughness for better molding quality. The phantom material was then made by mixing polyvinyl alcohol (PVA) with deionized (DI) water and Sigmacell cellulose powder to gain similar acoustic properties to that of a human neck and carotid artery. Once made, it was poured into the molds, undergoing freeze-thaw cycles to obtain better acoustic properties before testing. Blood mimicking Doppler fluid was then pumped through the phantom model along with small pieces of the phantom model material, representative of blood clots. The Clarius L7 ultrasound probe was then placed over the model and images of the Doppler fluid and blood clot mimics were recorded. Cast API was used to take the ultrasound images and sent them to a computer running an OpenCV algorithm which was used to locate the carotid artery, display it in real time, and detect when a blood clot passes through.

To design this system, background research was conducted on ischemic strokes, the carotid artery, and image processing techniques. A strategy to decide on the requirements of the project was created and a needs analysis for the final product was made. Designs were drafted and tested compared to alternative designs, at which point a final design was selected. The final designs were verified and then validated, then discussed. Finally, a conclusion was drawn and recommendations for future work were made.

CHAPTER 2

LITERATURE REVIEW

2.1 Ischemic Strokes

Each year in the United States alone, approximately 795,000 individuals suffer from a stroke, killing over 142,000 people in 2019, making strokes the fifth leading cause of death in the United States that year [1]. Put into perspective, someone in the United States has a stroke every 40 seconds, and every four minutes someone dies [2]. Although the majority of stroke patients survive the stroke itself, 15-30% of them become permanently disabled after the stroke, which leads to long-term health complications and possibly death [3]. It is estimated that 1 in 4 of the survivors will have another stroke in their lifetime [4] and that 80% of all strokes can be prevented with medications and healthy lifestyles [4].

An ischemic stroke is one in which a blood clot travels from the heart to the brain, passing through the carotid artery and continues flowing through until it blocks blood flow to a portion of the brain, accounting for approximately 87% of the total strokes per year [1]. When the clot blocks flow, it can prevent a portion of the brain from receiving the nutrients it needs to function, which eventually causes that area of the brain to die. The rest of the body will be impacted by this blockage and, like the brain, will not be able to function as it should, causing a stroke [5]. This can result in a multitude of problems for the patient, such as physical disability, cognitive impairment, or even death.

2.2 Risk Factors

There are many known factors that put an individual more at risk for having at least one stroke in their lifetime. Approximately 60-80% of strokes can be directly linked to increased blood pressure (hypertension), increased blood cholesterol, cigarette smoking, and carotid stenosis [6]. In addition, 10-20% of strokes are linked to an increased apolipoproteinB - apolipoproteinA1 ratio, obesity, physical inactivity, psychosocial stress, and low fruit and vegetable intake, amongst many others [6]. Other individuals at risk for stroke include individuals suffering from atrial fibrillation, sickle cell disease, coronary artery disease, and diabetes [6].

2.3 Preventative Measures

2.3.1 Medicine

To mitigate the risk of having a stroke, there are a multitude of preventative measures individuals can take. At-risk patients, especially with atrial fibrillation, are generally prescribed anticoagulants such as Aspirin or Warfarin to thin the blood and reduce the risk of blood clot formation. People who have sickle cell disease can undergo transfusion therapy to reduce their risk of stroke. Other preventative medicines include beta-blockers, which slows the heart rate and decreases blood pressure, decreasing the heart's demand for oxygen, or angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), which work to decrease the blood pressure [7].

2.3.1.1 Limitations of Medicine

Although the current medications available to patients help with reducing the risk of stroke, there are also limitations to them that could harm the patient. For example, anticoagulants, like Aspirin, are found to obstruct the proper functioning of platelets and cause the exfoliation of renal epithelial cells [8], amongst other limitations. Also, medications like beta-blockers can increase the risk of heart failure by slowing the heart rate too much, and could also increase the chance of having lung disease [9]. Medications used to prevent the chance of stroke have the potential to cause other health complications and not be the best option for some individuals.

2.3.2 Healthy Lifestyle

Preventative measures that do not require medication include improving glucose control and intake for diabetic individuals, at least 30 minutes of moderate daily exercise, a well-balanced diet of five or more servings of fruits and vegetables per day, reducing alcohol consumption to no more than two drinks a day for men and one drink a day for women, ceasing drug use, and avoiding tobacco products [3].

2.4 Methods of Detection

There are multiple methods of stroke detection that can be used ff the stroke cannot be prevented. When patients experience symptoms of stroke the methods of detection that are used today fall into three categories: imaging tests, electrical activity tests, and blood flow tests [10]. Imaging tests include computed tomography (CT) and magnetic resonance imaging (MRI). Imaging tests are helpful in detecting a blood clot, however, a blood clot may be seen in an MRI and not in a CT scan, based on where it is in the artery or brain [10]. Electrical activity tests include an electroencephalogram (EEG) which reads electrical impulses in the brain through electrodes placed on the scalp, and those impulses are printed as brain waves. Another electrical activity

test is the evoke response test which measures how the brain responds to different sensory information, where electrodes record the electrical impulses related to the senses. The last category of detection methods is blood flow tests, such as an angiography or ultrasound technology. An angiography is performed by injecting dye into the brain's blood vessels and using an x-ray image to show the flow of blood through the vessels, determining the size and location of the blockage from there [10]. Lastly, the most commonly used type of detection method is ultrasound technology. Ultrasound probes are placed over an artery and the amount of blood flowing through the artery can be determined. This method is preferred because it is noninvasive and poses minimal additional risks to the patient [10].

2.4.1 Applications of Ultrasound

Ultrasound is one of the most commonly used methods of blood clot and stroke detection. It has many applications in the medical field, such as for cardiac, gynecological, urological, abdominal, and cerebrovascular examinations [11]. It has also been used for real-time monitoring during orthopedic surgeries. Specifically, transcranial Doppler ultrasonography (TCD) has been used to count microemboli in the cerebral circulation during orthopedic surgery. A review on 14 studies that used TCD for real-time detection of microemboli concluded that microemboli are detectable in the middle cerebral artery (MCA) [12]. This allowed the team to conclude that real-time monitoring using ultrasound was feasible and has been successfully done before. While most ultrasound monitoring is done using a probe, a research team led by Dr. Sheng Xu at the University of California San Diego has developed a wearable ultrasound patch that allowed for blood pressure measurements to be taken within an artery or vein as deep as 4 cm beneath the skin [13]. They used an ultrasound transducer in order to get an accurate reading of the blood pressure. The high frequency sound waves that rebound off blood vessels are produced by the ultrasound transducers. The transducers then take the rebound sound waves and turn them into waveforms via a computer and can be calibrated to detect changes in the blood pressure [13]. Although the device is still in the design phase, it has not yet been compared with catheterization methods to measure blood pressure accurately and precisely. It is also not wireless at the current phase of development [13].

2.5 Treatment Methods

If a blood clot has been detected then the patient can undergo a medical treatment with Alteplase IV r-tPA (which must be done within 4 hours of onset) [14] or a mechanical treatment like mechanical thrombectomy where a doctor would use a stent retriever to remove the clot from the artery (which must be done within 24 hours of onset) [14]. Alteplase IV r-tPA is administered through an intravenous, commonly known as an IV, and works to dissolve the clot, improving the flow of blood to all parts of the brain. A thrombectomy is a procedure to remove the blood clot

in patients with large vessel occlusions where doctors use a stent retriever, thread a catheter through an artery in the groin up to the blocked artery in the brain, open the stent and grab the clot. A suction tube can also be used to remove the clot [14]. As most individuals do not know they are having a stroke until they are experiencing symptoms, there becomes an increasingly small window to seek medical attention before serious, and sometimes fatal, consequences occur. As with the saying “time is brain,” the therapeutic window that stroke patients have to seek treatment and reverse the neurological effects of a stroke is limited and cannot be overstated [15]. The earlier the detection is, the more likely the patient is able to get the clot removed without any side effects or long lasting disabilities that can result from a stroke.

CHAPTER 3

PROJECT STRATEGY

3.1 Initial Mission Statement

Although the team did not have a client to base their project on, they did get inspiration from one of the teammate's grandfather, as mentioned previously, and devised their mission statement with him in mind. The team wanted to create a wearable biosensor to detect blood clots, through real-time monitoring, as they travel through the carotid artery, and alert the patient that medical attention is needed in order to remove the clot in a timely manner.

3.2 Technical Design Requirements

3.2.1 Objectives

The team wanted to obtain a capacitive micromachined ultrasound transducer (CMUT) to create a small, non-invasive, wearable device that could use the CMUT to detect blood clots in the carotid artery. The device would be worn around the neck or chest near the carotid artery and would be monitoring the patient's blood flow in the carotid artery at all times. If a blood clot, or abnormality, is detected flowing through the artery, the device would notify the patient through an app on a smart device to alert them that medical attention is needed. Upon receiving said notification, the patient can be brought to the hospital well within the window of time needed to remove the clot from their body before it causes irreparable damage to the patient.

3.2.2 Constraints

Once the team had an idea of what they wanted to accomplish, they then contacted various companies who manufacture CMUTs to identify if any one of the companies would loan or sell their CMUTs to the project team. The cost of the CMUT was not easily accessible on any of the companies' websites, and therefore was assumed to be well outside of the team's budget of $600. Once in contact with the companies, specifically Phillips and Micralyne, the team was led to find out that the CMUTs they manufacture are not yet commercially available and therefore cannot be loaned out to an undergraduate project team. The team then had to revise their project goal, because what they originally wanted to do was outside the feasible timeline (seven weeks) and budget ($600) of their project.

3.2.3 Functions

Because the team was unable to gain access to a CMUT, as previously mentioned, they were confined to developing a proof of concept for the functionality of the device they proposed to create. The team gained access to a Clarius L7 ultrasound probe which was used to demonstrate the theory behind the team's original device design and functionality. The probe was handheld and wireless which would help with ease of transportation and allow the team to view and analyze the ultrasound on a computer when the ultrasound is wirelessly connected. A phantom model of the neck and carotid artery can be constructed so that the ultrasound probe could be used on the model to demonstrate the concept of the original device design. Blood mimicking fluid and a clot mimic could be passed through the phantom model to confirm that the fluid and blood clot appear on an ultrasound. Once that was confirmed, a computer algorithm can be developed to recognize the difference between normal blood flow and a blood clot. By doing this, a successful proof of concept could be fabricated, showing that an wearable ultrasound device could be developed to monitor blood flow through the carotid artery in real time and alert the patient if a blood clot is detected in the carotid artery.

3.2.4 Specifications

To ensure proper functionality of the proof of concept, certain specifications were taken into account before making the phantom models. For example, the size of the phantom neck and carotid artery were accurate to that of the average human. In a healthy adult, the diameter of the common carotid artery lumen ranges from 4.3 mm to 7.7 mm. The intima-media thickness tends to be between 0.4 mm to 0.8 mm, meaning the total wall thickness could be estimated as slightly larger than that, closer to 1mm [16]. Based on these findings, the inner diameter of the modeled artery would be 6 mm and the wall thickness would be 1 mm, which the team determined was an appropriate approximation for the purposes of this proof of concept. The phantom model of the neck would be more loosely based, taking the measurements of an average human neck and creating an elliptical mold to fit the general shape. However, the neck mold would have more accurate positioning of both the cervical spine model and the artery. In the average human, the common carotid artery is positioned 23.5 ±6.9 mm from the skin and is approximately 7.36 ±3.8 mm close to vertebrae in the cervical spine [17]. Using these dimensions, the team would place the cervical spine and common carotid artery accordingly within the neck mold.

The phantom models should share similar acoustic properties to that of human tissue, which has a speed of sound of approximately 1,540 m/s [18]. Similar acoustic properties are most important when determining what material should be used for the phantom model as the detection of blood clot is achieved via ultrasound and without the proper material, the scattering effects would be vastly different, producing inaccurate results. Depending on the material chosen for the phantom model, there needs to be a way to properly store the model when not in use to ensure dehydration does not occur. In order to flow blood mimicking fluid and clot mimics through

the phantom, the average flow rate of blood through the carotid artery should be considered, which is approximately 7 ml/s [19]. Because blood clots can range in size and shape so often, it was decided that multiple sizes of blood clot mimics should be used while detecting with the ultrasound probe.

The team decided it could be best to use the Clarius L7 probe and Cast API to take ultrasound images and sent them to a computer running an OpenCV algorithm. The location of the artery phantom could be identified and displayed in real time. Using the Clarius L7 probe would allow the team to use the Clarius developed Cast API to take in images in real time. An Application Programming Interface (API) would allow one program to send data to another program. Clarius built an API that can be used with the device to send data to a connected computer. OpenCV, an open source computer vision library, would be used to analyse the images, as it is robust and well documented and one of the largest and most widely used computer vision libraries available.

3.3 Revised Mission Statement

Due to the unfortunate fact that the team was unable to obtain a CMUT to create a wearable biosensor, the team had to revise their mission statement to fit their current projected goal. The team wanted to develop an acoustically accurate phantom model of a human neck and carotid artery in order to demonstrate how their proposed device would function, creating an algorithm to detect blood clots as they pass through the carotid artery.

3.4 Management Approach

To organize their activities, the team first created a Work Breakdown Structure (WBS) to have a general overview of the project as a whole, seen in Figure 3.1. From here, the team realized that the project could be broken down into three distinct areas: design of phantom molds, fabrication of phantom models, and creation of a clot detection algorithm. Using this knowledge, the team then created a Gantt chart seen in Appendix A, detailing the individual activities that needed to be accomplished within the timeline of the project.

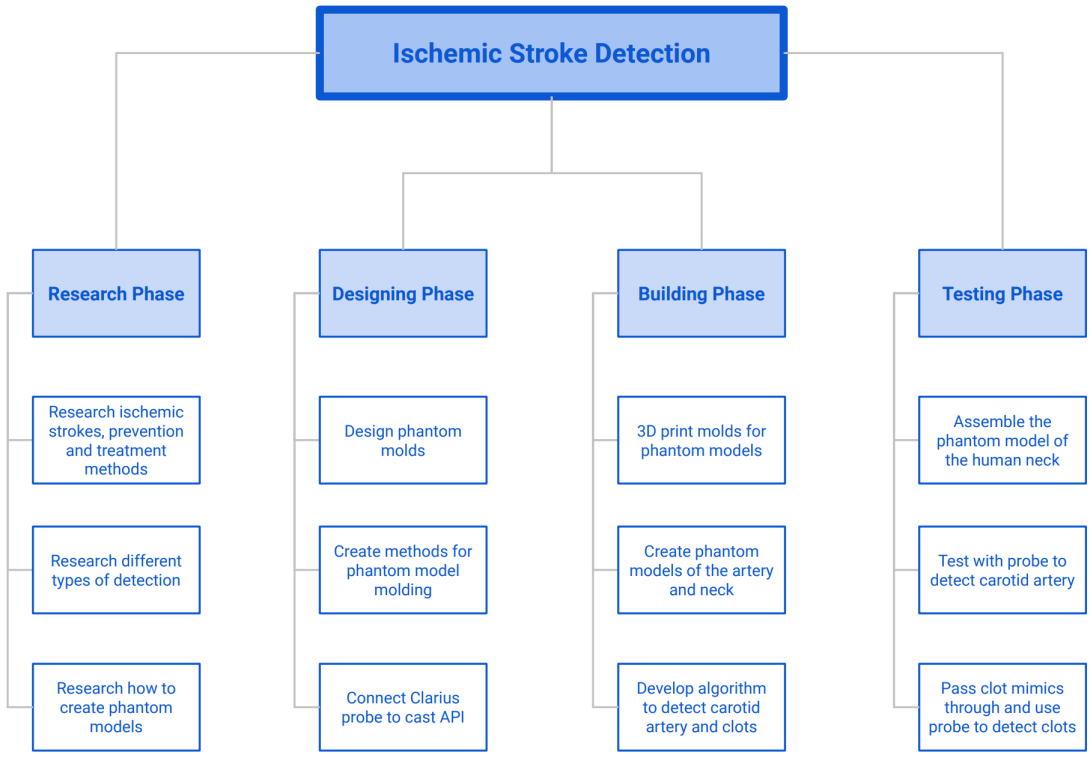


Figure 3.1: *Work breakdown structure*

CHAPTER 4

DESIGN PROCESS

4.1 Needs Analysis & Limitations

4.1.1 Molding Needs

To create the phantom models, the team first needed to design molds that would form the shape of the common carotid artery and a human neck. While designing these molds, the team looked at a few possible solutions and using a selection matrix, determined what the best option would be. The first design used a CT scan to create an artery that is shaped exactly like the common carotid artery in the human body. This design had two separate portions, one that had a model of the carotid artery and a top portion that slid over it, creating a shell that had a gap between for filling with molding material, which can be seen in Figure 4.1.

The second artery design, which can be seen in Figure 4.2, was simplified to allow for ease of injection molding. This design modeled the artery as a cylinder with dimensions approximate to that of the carotid artery's inner diameter and wall thickness. It separated into two halves, but instead of a top and bottom portion, it was split lengthwise with two sides coming together to form a cylindrical shape.

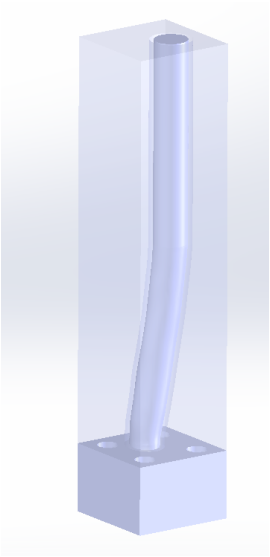


Figure 4.1: *Artery mold design 1*

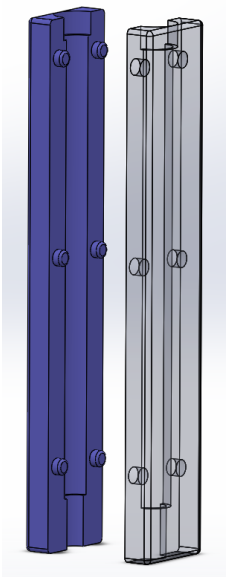


Figure 4.2: *Artery mold design 2*

While the neck mold went through several design iterations, there were not distinct designs that the team selected from. The neck mold was designed around the design of the carotid artery phantom and was redesigned to allow for different considerations such as printing time, 3D printer filament usage, and the placement of the artery and cervical spine model. When selecting the best phantom artery mold, some specifications were considered. These included ease of molding, dimensional accuracy, quality of the mold, ease of manufacturing, and cost to print. Using this criteria, the two artery mold designs were compared using a selection matrix, as seen in Figure 4.3, and design two was chosen as it ranked higher than design one.

	Requirement	Weight	Design 1: CT Scan Mold	Design 2: Simplified Mold
Needs	Dimensional Accuracy	6	+1	0
	Ease of Molding	5	-1	+1
	Quality of the Mold	4	0	0
	Ease of Manufacturing	3	-1	+1
Wants	Inexpensive to Print	2	0	0
	Short Printing Time	1	0	+1
	Rank Score		**-2**	**9**

Figure 4.3: *CAD Model selection matrix*

Once the simplified artery mold was chosen, the team reviewed the physical limitations of this mold. Two factors were considered in these limitations: the material used to print the mold and how injection molding would work with the mold. When looking at 3D printing, the team explored various possible avenues such as using the Foise Makerspace, asking a peer for use of their printer, and using the Formlabs Form2 printer in WPI's advanced rapid prototyping lab. For the artery model, since it was small and vitally important that the phantom model had the correct dimensions and a good surface finish, the Form2 printer with resin filament was chosen. Despite higher manufacturing time and cost than a fused deposition modeling (FDM) printer, the team chose to use the the Form2 because the artery mold was small and required precision. The next consideration involved the injection molding process. Once the mold was printed, it would have to be filled with phantom model material and then contain that material while it sets. For this process to work correctly, the mold would have to have an opening that material could be poured into while the mold kept the proper shape for the phantom model. For this reason, the mold was designed with a counterbored hole in the top that had a wider opening, both allowing material to be injected using a small syringe and creating a reservoir that allowed extra material to collect at the top once the rest of the mold was filled.

4.1.2 Phantom Material Needs

After conducting preliminary research, the team found that there were four popular materials used to create a phantom model of a human neck: polyvinyl chloride (PVC) [20], polyvinyl alcohol (PVA) [21], silicone [22], and gelatin [23]. In order to determine which material was best suited for making a phantom model of the neck and artery, the team had to first determine what the most important requirements were for the specific material. The team found that the following requirements were most important to consider, ranked from most important to least important: acoustic and mechanical properties, reusability, perishability, transparency, portability, cost, ease of making, and curing time. The team then split the requirements up into two groups, needs and wants, to determine which requirements are crucial in the successful completion of the project. It was decided that the phantom material needs to be acoustically and mechanically similar to human tissue and it has to be reusable. All other requirements were determined to be a want for the chosen material, as they were determined to be not crucial in creating a working phantom model. Once the requirements were established, ranked, and divided, the team then created a selection matrix to determine which of the four materials would be best suited for what the team needs, shown below in Figure 4.4. After determining the score of each material, it was decided that PVA was the material of choice and the team proceeded with that material in mind.

	Requirement	Weight	Material 1: Polyvinyl Chloride (PVC)	Material 2: Polyvinyl Alcohol (PVA)	Material 3: Silicone	Material 4: Gelatin
Needs	Acoustically Similar	9	0	+1	0	+1
	Mechanically Similar	8	+1	+1	-1	-1
	Reusable	7	+1	+1	+1	0
Wants	Nonperishable	6	+1	0	+1	-1
	Transparent	5	-1	-1	+1	+1
	Portable	4	0	0	0	-1
	Affordable	3	0	+1	0	+1
	Easy to make	2	-1	+1	+1	+1
	Quick curing time	1	+1	-1	-1	0
	Rank Score		**15**	**23**	**11**	**1**

Figure 4.4: *Phantom model material selection matrix*

After determining that the best option for the phantom material was PVA, the physical requirements of PVA were discussed. The team recognized that since the model's size would need to be anatomically accurate, the team would need to obtain enough PVA to make at least three or four phantom neck models, because the team prepared for prototyping of their final model. The PVA model would also require being stored in deionized water at 5°C to prevent dehydration,

which could be viewed as a limitation.

4.1.3 Algorithm Needs

The clot detection algorithm is a very open-ended product of this project, and as such could be configured in many different ways. The clot detection algorithm is the core element in alerting users that they may soon experience a stroke. The algorithm needs to be robust enough to effectively identify the carotid artery through movements and at different times of the day. If a user was to lay down, go for a walk, or eat food, it would be imperative that the detection algorithm did not lose track of the carotid artery. If the algorithm cannot find the carotid artery, it would be impossible to attempt to identify any clots passing through it. The detection algorithm also needs to be inexpensive enough to run in real time. For the project to be developed into a product, it would require the algorithm to run on a microprocessor with low enough power usage to be used on a daily basis as a wearable device, and to run all the time, analyzing ultrasound data constantly. If the algorithm were to slow down and get behind, it is possible that a blood clot could pass through the lumen while the device tries to catch up. For this reason, the algorithm must run quickly enough in relation to the processor that it will not miss any deadlines. Finally, the algorithm must also be robust enough to detect all variations of clots that could be seen in the carotid artery. Clots in the center of the carotid would likely be easy to detect, whereas clots that sit on the edge of the carotid artery would be much more difficult to differentiate from the edge of the carotid artery itself. This idea is further complicated by the need to identify the carotid while moving, further demonstrating the robustness required in every algorithm.

Ultrasound is a very versatile technology, allowing itself to be used in many different ways. For this reason, the team would ideally incorporate a few extra features into the project to increase its appeal as a product. Blood pressure measurements would be one addition to the project that might be possible, based on some research done [13]. Heart rate measurements, based on tracking the increasing and decreasing size of the carotid would also be an addition to the algorithm that would add another feature to the project. Increasing the feature set could increase its appeal and help to make it a more interesting product to consumers or medical professionals.

4.2 Design Concept Prototyping

4.2.1 CAD Model Review Process

The CAD models for the artery and neck molds went through a thorough review process. Over a two week period, the team drafted designs for both the artery and neck molds in Solidworks and revised these designs based on feedback from their advisor. The artery mold underwent particular scrutiny, as it was an integral component to the final phantom model. Originally, the team proposed using a CT scan to create a realistically shaped model, seen in Figure 4.1, but that

was determined to be too complex for use in molding. This feedback resulted in a more simplified model that represented the artery as a cylinder with a 1 mm wall thickness, which is based off of prior research in chapter 3. The neck mold underwent a similar review process, but not as rigorous as the particulars were not as crucial in this design. Some redesigns that were included were cutting down the design to use less material, changing the slots where the artery and neck would be inserted, and adjusting the height of the model.

4.2.2 Test Mold Prototyping

Before printing the neck mold, a test mold was printed using the same Ultimaker printer with ABS filament so that the team could determine if this printer would meet their needs. The test mold also served as a trial run for using an acetone vapor bath to smooth out the layer lines that occur in FDM prints. Once this process was tested, the test mold was then used to create the first phantom model so that the team could practice the molding process before creating a final phantom model. This allowed the team to gain experience in the molding process before going into the final design.

4.2.3 Algorithm Prototyping

In order to create and test the algorithm, a computer running MATLAB was used for its ease of rapid prototyping using digital image processing techniques. MATLAB has functionality very similar to OpenCV, but makes it very easy to run many iterations of the same program and to display different results at the same time. For this reason, the algorithm was prototyped in MATLAB rather than Python, which it would eventually be translated into in order to run seamlessly with the Cast API. To decide how to write the detection algorithms, various image processing techniques were tested and evaluated qualitatively using test images of a group member's carotid artery and images of the phantom carotid artery.

4.3 Alternative Designs

4.3.1 CAD Model Designs

Before the final mold design was selected, the team created and reviewed multiple potential designs. Two for the artery were discussed in the needs analysis section, and these were the two main design options for the artery. The neck mold also went through some design iterations, such as removing excess material to allow for efficient 3D printing, changing the location of slots for the artery and cervical spine models to be more accurate, and having the mold be split in two halves to allow for easy removal of the completed phantom model.

4.3.2 Phantom Material Designs

Although PVC, silicone, and gelatin were not chosen to fabricate the phantom model, they were considered as alternative designs. With different additives, they can achieve similar acoustic properties to human tissue. For example, adding glass beads or powdered fiber can help with acoustic scattering. With this in mind, they all have been shown to serve as a good material to be used for a phantom model for a human neck.

4.4 Final Design Selection

After conversing with the project advisor and considering the results of applicable needs analyses, the team came up with the following final design components.

4.4.1 Phantom Mold Selection

The simplified artery design and corresponding neck mold were chosen as the final design because they met all of the requirements the team was aiming for. While the simplified design did not look exactly like a common carotid artery, it shared similar qualities such as the wall thickness and inner diameter, which the team felt met the specifications needed for this proof of concept. The simplified model made the molding process easier, both for injecting the material and for removing the finished phantom artery. This design was also easy to incorporate into the neck mold, allowing for an accurate distance from the “skin” as well as from the cervical spine model. Overall, this design was cost effective, easy to manufacture, allowed for injection molding, had high quality, and was dimensionally accurate for the purposes of a proof of concept.

4.4.2 Phantom Material Selection

PVA was chosen as the final phantom material mainly because it met all of the team’s desired requirements for finding a suitable phantom material. It shares very similar acoustic properties with a human neck and its mechanical properties can be altered based on the amount of freeze-thaw cycles the model undergoes [21]. Once molded, PVA can also be reused as many times as desired as long as it is stored in deionized water at 5°C to prevent dehydration. The process for fabricating a PVA phantom model also seemed to be fairly easy and the process did not require any special equipment, besides standard laboratory equipment, like a heated stir plate, beakers, and a scale, to name a few. With all of this in mind, the team moved forward with creating a process to make the PVA phantom model.

4.4.3 Algorithm Selection

The final algorithm implements the key steps discussed above to identify the carotid artery and clots within it. First, images have an adaptive histogram equalization applied to bring out details,

then a Gaussian and median blur are applied in order to make background details easier to ignore. Otsu's binarization algorithm is applied, which allows the following contouring algorithm to easily find data, the contours are searched based on calibration data from test images of the carotid artery being used, and then the carotid can be effectively found and tracked in real time. Finally, a masking image is created and the inside of it is searched for blood clots, at which point any clots detected are drawn on the original image and the user can be alerted.

CHAPTER 5

DESIGN VERIFICATION

5.1 Core Design

Through MATLAB, the first step taken was to increase the contrast of the image in such a way that the important details (the carotid and the clot) were emphasized more, and the surrounding tissue and features were still present but not the focus of the image. Increasing contrast globally would have led to an image that would be difficult to analyze, as it would just get brighter or dimmer without emphasizing any features specifically, which can be seen in Figure 5.1 and Figure 5.2. Using adaptive histogram equalization algorithms proved to be much more successful, such as contrast limited adaptive histogram equalization [24] which can be seen in Figure 5.3. Once the detail in the image was increased, a blur was added in order to remove the finer details, especially in the background of the image, so that tissues surrounding the carotid artery were not overtly visible, as seen in Figure 5.4. Median and Gaussian blurs were experimented with, and both were used to achieve the goal of blurring the surrounding details. After blurring the image, the image was binarized in order to create clearly defined shapes with definite edges. This was used instead of Canny [25] or Sobel [26] edge detection, as they introduced too much noise. Instead of applying a globally thresholded binarization [27] to the image, in which every pixel with a value above or below a given threshold value is set to either black or white as seen in Figure 5.5 the images were subjected Otsu's method, a binarization algorithm that works similarly to the adaptive histogram equalization, except that instead of equalizing the entire histogram, it does the opposite in order to show the image as two colors, seen in Figure 5.6 [28].

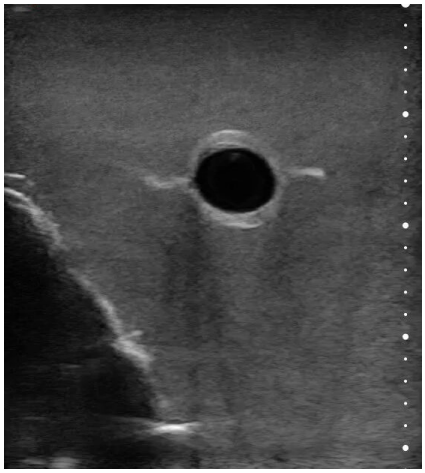


Figure 5.1: *Original phantom image*

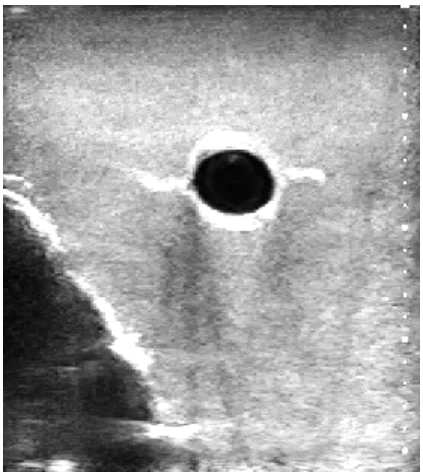


Figure 5.2: *Contrast boosted globally*

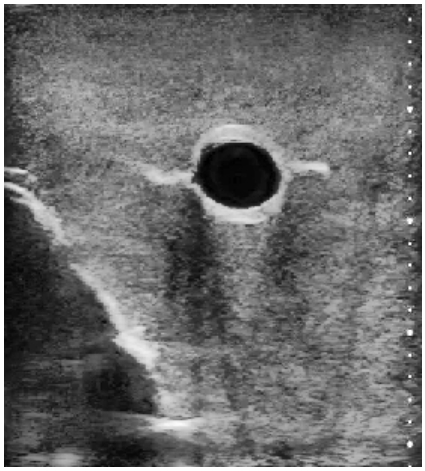


Figure 5.3: *CLAHE image*

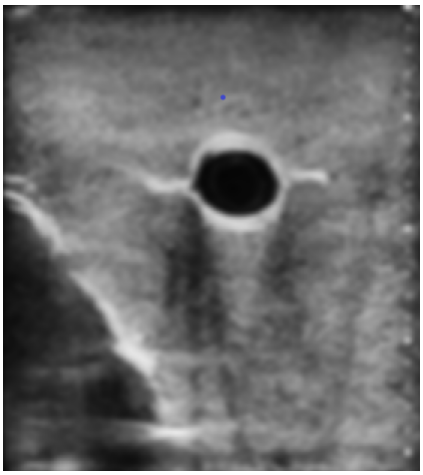


Figure 5.4: *Median and Gaussian blur*

Figure 5.5: *Global binarization*

Figure 5.6: *Otsu's binarization*

5.2 Carotid Detection

Once the image is binarized and easy to work with, the carotid artery (and any clots that may exist within) is made clear and well-defined. To identify the carotid artery, the first approach used was to try a Hough circle transform to the image. In ideal situations such as in Figure 5.7, it would identify the carotid easily. Despite that, identifying the carotid artery while moving or in non-ideal situations (lying down, eating, moving, etc.) showed the flaws in using the Hough transform [29], as the carotid's shape became more elliptical and less circular. To solve this, a contouring algorithm was used instead. Using OpenCV, contours [30] in the image are identified and added to a list, then based on the size and area of the contours, they are filtered to find the carotid artery. This design worked best such that the algorithm can be modified to work on different people with varying carotid artery sizes. The contour(s) identified as the carotid artery are then drawn on the original image, which shows where the algorithm detects the carotid artery, seen below in Figure 5.9.

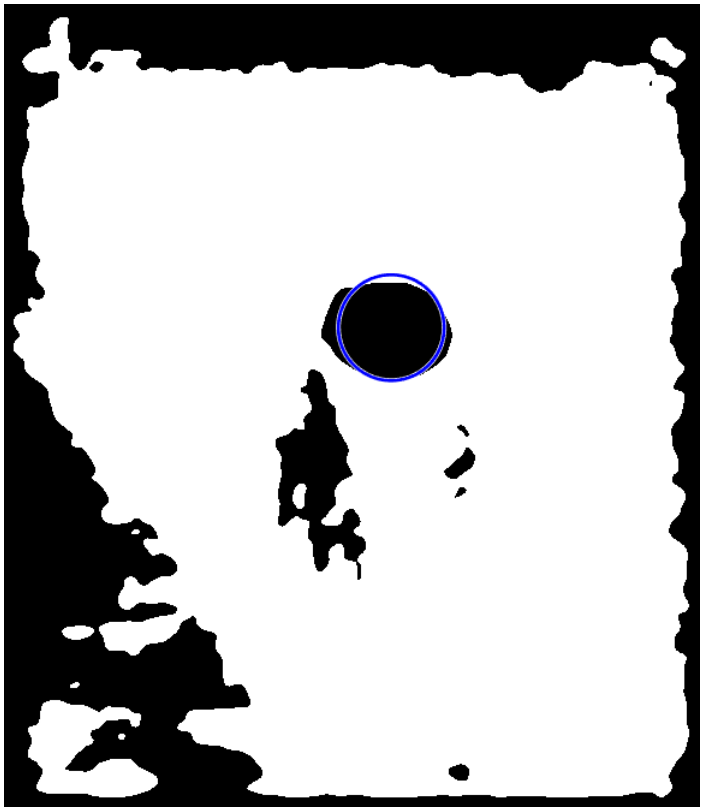


Figure 5.7: *Hough transform success*

5.3 Clot Detection

To identify clots within the carotid artery, a very similar algorithm was used. Since the image processing has already been done, the efforts are focused within the area identified to be the carotid artery. Using the contour(s) defined as the carotid artery, an image mask [31] as seen in Figure 5.8 is created and applied to the binarized image, to isolate only the data inside of the defined carotid artery. The contouring algorithm is run within that area, searching for any contours within the carotid artery. Due to the accuracy of the contouring algorithm, it finds very small contours that are effectively combined with larger contours, so small contours are ignored as errors and not any legitimate risk. Using test data with phantom blood clots allowed for a filter to be devised that identifies any clots of dangerous size and drawn on the original image, similar to the carotid artery, as seen in Figure 5.9. Once the clot is detected, a flag can be raised that would save the frames of video and alert the user that a clot has been detected.

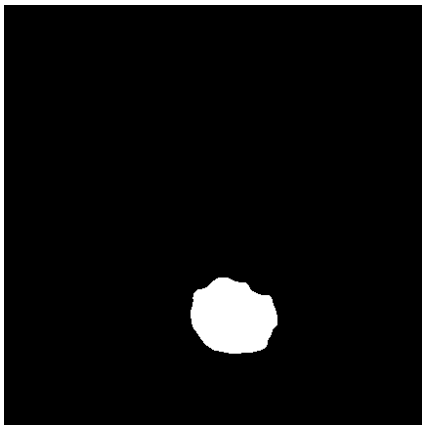


Figure 5.8: *Image mask*

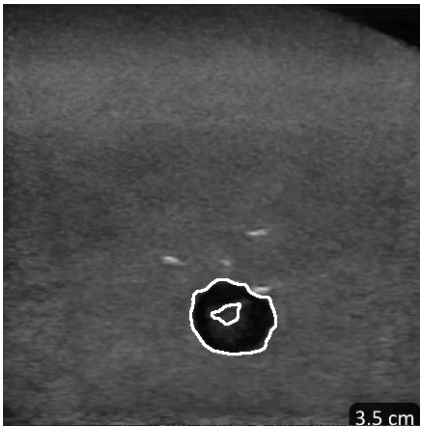


Figure 5.9: *Contours drawn on image*

CHAPTER 6

FINAL DESIGN AND VALIDATION

6.1 Experimental Methods

6.1.1 Fabricating the Molds

Before creating the phantom models, the team first had to create molds of both the common carotid artery and the neck. These molds were first drafted on paper, and then designed as CAD models using Solidworks. They were designed for manufacturability, ease of injection molding, time and cost of 3D printing, and dimensional accuracy. The artery mold was dimensioned to allow for a 1 mm wall thickness on the final phantom artery. This was accomplished by dimensioning the cylindrical portion of the artery mold, seen in Figure 6.1, as 8 mm. This left space for a 6 mm aluminum rod to be placed in the middle of the mold, held in place on either end, to create the center of the artery. A counterbored reservoir in the top of the mold allowed for excess material to collect there during injection molding, which gave the team an indication of when the mold was completely filled. A cap was designed to be placed over the top of the mold when completely filled, holding the aluminum rod vertically so that the artery would maintain the correct shape during molding.

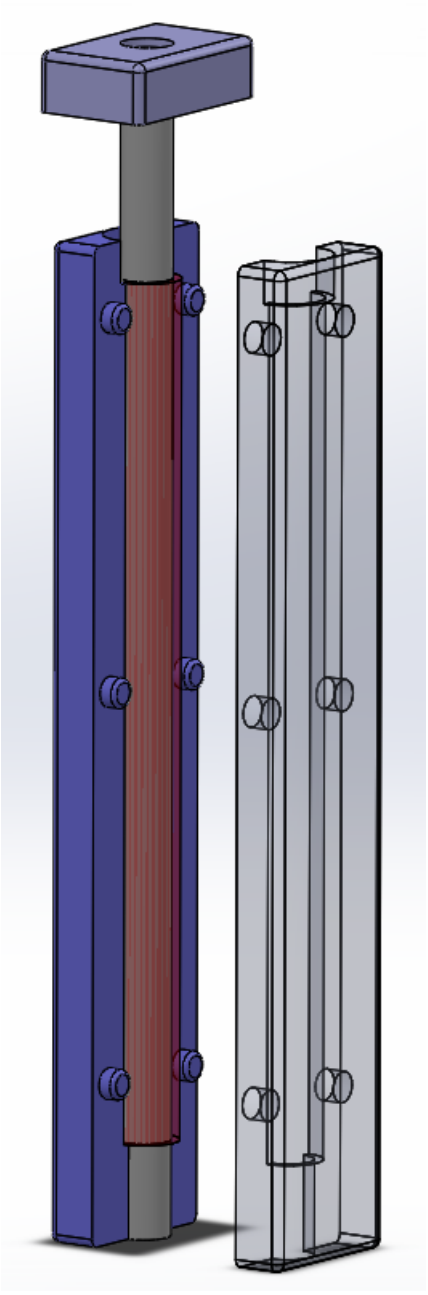


Figure 6.1: *CAD model of the artery mold*

The neck mold, shown in Figure 6.2, was designed with the artery mold in mind as it needed to receive the completed artery mold during the phantom fabrication process. This mold was designed as an ellipse with dimensions modeled approximately after a human neck as the measurements for this aspect of the phantom model were not crucial. This model also had slots in the bottom to accept the 6 mm aluminum rod from the artery model as well as an 8 mm rod from a cervical spine model. The locations of these slots were important as the artery and cervical spine models needed to be in the correct locations to allow for a reasonable anatomically accurate representation of the human neck. They were dimensioned using the specifications laid out in Chapter 3, detailing how far the common carotid artery is both from the skin and from the cervical spine. In order to ensure these molds were being modeled correctly, a final phantom mold was assembled in Solidworks to see if the dimensions were accurate to the specifications the team needed.

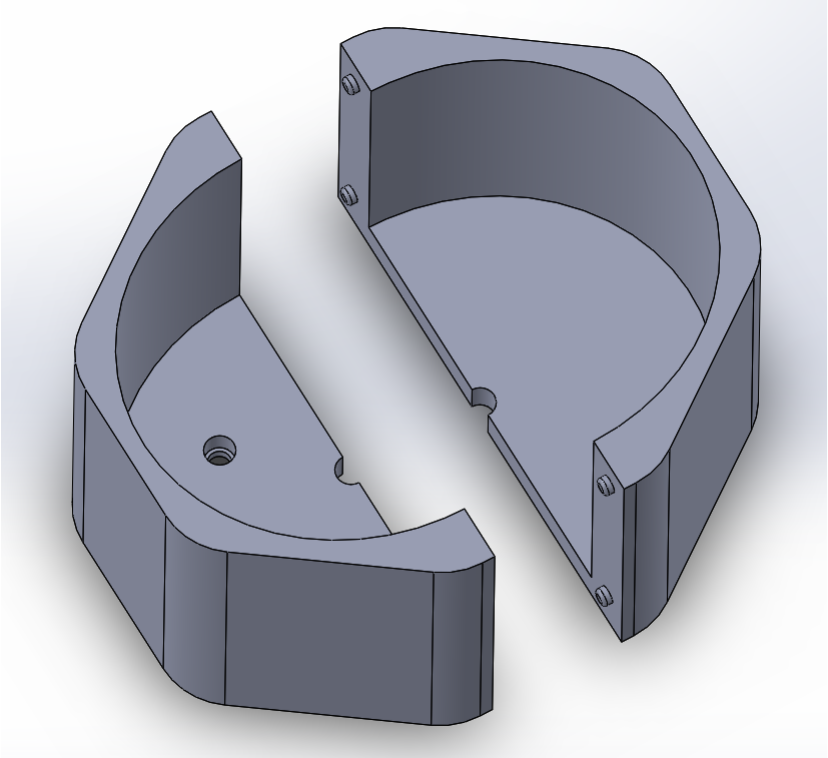


Figure 6.2: *CAD model of the neck mold*

Once the molds were fully modeled in Solidworks, the team decided which 3D printers they would use for manufacturing the molds. After some consideration, it was decided that the artery mold would be printed using a Formlabs Form2 printer in WPI's advanced rapid prototyping lab because a resin printer would provide a quality surface finish, even though it would take longer and be more expensive than an FDM printer. Since the artery model was both small and dimensionally important, the time and money could be spent to use the resin printer. The neck

mold, being larger and not as dimensionally important, was printed in the Foise Makerspace on an Ultimaker printer using acrylonitrile butadiene styrene (ABS) filament. While ABS leaves layer lines, it was determined that ABS would be okay for the purposes of the neck mold. Also, ABS can be smoothed out using an acetone vapor bath. The vapor bath was created using a pot, hotplate, acetone, raised platform, and a lid. The neck mold was placed inside of a pot that was on a hotplate and had around a tablespoon of acetone in the bottom. The mold was not in contact with the bottom of the pot, but rather on a slightly raised platform so that it would not touch acetone directly. A lid was placed over the pot, and when the heat was turned on, the acetone would vaporize and gently smooth out the layer lines on the ABS print. This was done using a test mold first to practice the timing for this process, as there is no specific amount of time to leave the mold in the vapor bath. Once the mold was removed, the layers were melded and smoothed out, which allowed for the phantom model to be easily removed after molding, and created a better surface finish.

Once both 3D printed molds were printed and in the case of the neck mold, smoothed out using acetone, they were ready for molding.

6.1.2 Creating the Phantom Models

After the molds were ready to use, the phantom material was made and poured into the molds to set. The phantom artery was made by mixing 10 wt% percent polyvinyl alcohol (PVA) [32] with 87 wt% deionized (DI) water for 30 minutes on a stir plate with a magnetic stir bar. While still stirring, the mixture was then covered and heated in a water bath at 90°C for one hour. It was then removed from the water bath and stirred with a magnetic stir bar for another hour. The cover was kept on to keep water vapor from escaping. 3 wt% Sigmacell cellulose powder [33] was then added and stirred for 15 minutes, or until the mixtures look uniform. The entire beaker, or container holding the mixture, was then put into a vacuum chamber and monitored until all air bubbles rose to the surface. Once all air bubbles were on the surface, the mixture was taken out of the vacuum chamber and the bubbles were scraped off. A syringe was then used to inject the mixture into both sides of the artery mold. A 6 mm diameter aluminum rod was placed on top of one of the sides of the mold, pushed into position, then both sides were put together and clamped to stay together. More of the mixture was injected into the top of the mold to ensure it was completely full. The cap was then put on the mold to ensure the rod would stay in place and the filled mold was left upright for 12 hours to let any extra air bubbles rise to the surface. Once the air bubbles were scraped off, the mold was put into the freezer to freeze at -20°C for 12 hours then thawed at room temperature for another 12 hours, completing one freeze thaw cycle. The mold was then taken out of the clamp and opened to reveal the PVA mixture to be molded around the aluminum rod. The rod and the phantom artery was placed in DI water and stored at 5°C to prevent dehydration.

To make the phantom neck, the same method was used, however, the amounts of each material changed to be 8 wt% PVA, 91 wt% DI water, and 1 wt% Sigmacell cellulose powder. Once the mixture was made, the phantom artery, with the rod, and the neck vertebrae, were placed in their respective positions in the neck mold. After degassing the mixture, it was poured into the neck mold and left to set for 12 hours. The filled mold went through two freeze/thaw cycles, each cycle containing 24 hours freezing at -20°C and 24 hours thawing at room temperature. Once the two freeze/thaw cycles were complete, the rod was taken out of the phantom artery and the neck phantom was taken out of the mold and stored in 5°C DI water to prevent dehydration. The final neck phantom model is shown below in Figure 6.3.

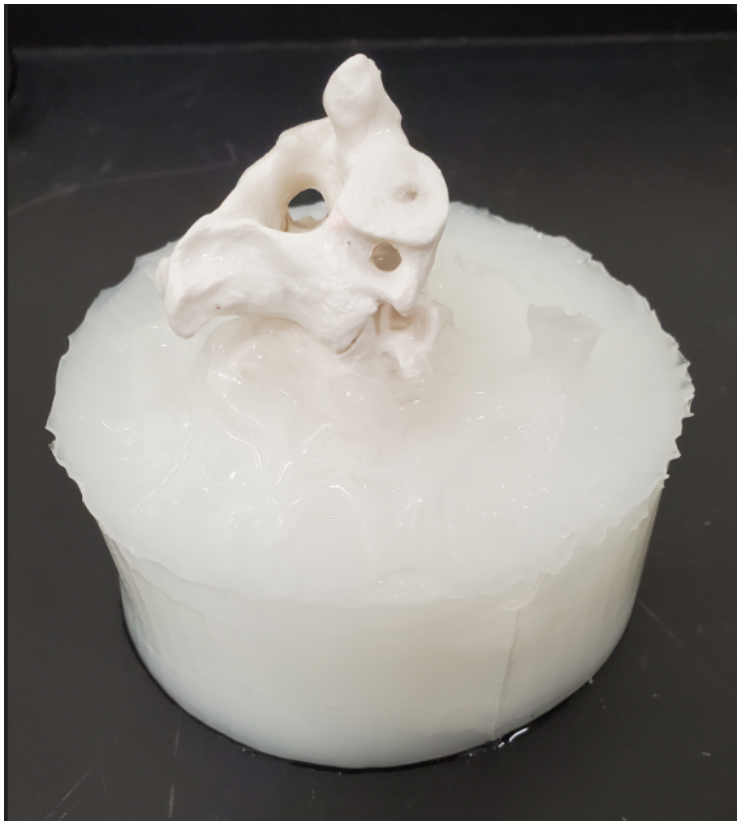


Figure 6.3: *Final phantom model*

6.1.3 Administering Blood Mimicking Fluid

To achieve the second goal of passing a blood-mimicking fluid through the phantom model along with blood clot mimics, the team acquired 6 mm (outer diameter) polyvinyl chloride (PVC) tubing, a 10 mL syringe, Doppler refill fluid [34], and small 5 mm pieces of phantom model material to use as clot mimics. The syringe was filled with Doppler fluid and then attached to one end of the tubing while the other end of the tubing was fitted into the phantom artery. The piece of the phantom material was placed in the tubing, so that once the syringe was depressed, the Doppler

fluid and the clot mimic would flow through the phantom model. This process can be repeated as necessary to obtain the desired amount of data collected through the ultrasound probe, that was placed on the side of the phantom model as the Doppler fluid and blood clot mimic was passed through the artery. The set up for administering the blood mimicking fluid through the phantom model is shown below in Figure 6.4.

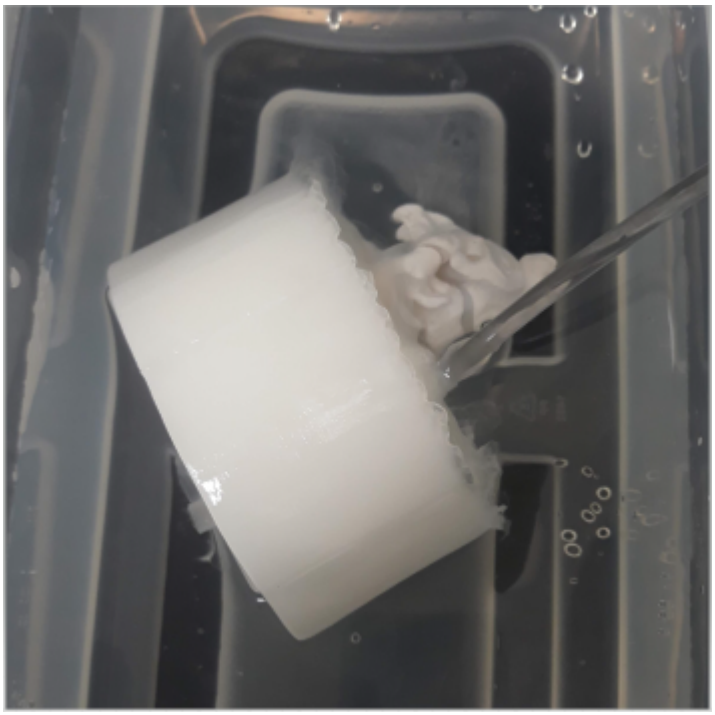


Figure 6.4: *Phantom model set up for blood flow test*

6.1.4 Algorithm Setup

In order to ensure that the algorithm used to detect blood clots would run successfully, there are numerous specifications and precautions that were taken. The setup of the computer running the algorithm was important in order to ensure proper functioning of the Cast API, and the computer hardware was also important to ensuring real-time processing of the images. The ultrasound probe also played a factor in the success of the clot detection algorithm. In order to guarantee success of the real-time processing of the images and detection of blood clots, the hardware and software must be adequately configured.

Setting up the Cast API proved to be fairly challenging, the first attempt was using an Ubuntu virtual machine on Windows, but the video transmission seemed to be blocked by the Windows firewall, despite all attempts to turn it off. The next step was to use a native Ubuntu install to run the Cast API which was set up in the same way as the virtual machine (VM). Running the Cast API on a native install avoided any problems encountered due to the Windows firewall on

the VM. Naturally, OpenCV for Python was installed, along with a few other libraries necessary for the Cast API to function, such as QT5. To complete the setup, the computer running Ubuntu had to be connected to the Wi-Fi network that the Clarius L7 created. By connecting a phone or tablet running Android or iOS and the Clarius ultrasound application, the L7 was used in cast mode. This allowed the L7 to create its own WAN connection with the computer and phone on the same network. The Clarius app gives an IP address and port which are put into the Cast API application to establish the connection, after using the given WPA key to connect to the network. In summary, to create a connection using the Cast API, a phone or tablet, the Clarius ultrasound scanner, and a computer (ideally running a native install of Ubuntu) are required.

6.1.5 Analyzing Data

The final algorithm was derived from an algorithm prototyped in MATLAB, then adapted to run using OpenCV on Python. The algorithm pipeline works by intercepting the frame from the Clarius L7 then converting it to a format which can be manipulated by OpenCV. The algorithm adjusts the contrast to enhance details, blurs the image to reduce noise, binarizes the image to identify the lumen, identifies contours in the image, identifies the carotid artery contours by size parameters specific to a given lumen, masks the image based on the identified carotid contours, and searches for the clot inside using a similar contour identification algorithm tuned for clots within the carotid. This pipeline can be seen below in Figure 6.5. The algorithm works well for the carotid phantom the team built, but more testing with different sized phantom arteries and more complex phantom models would likely improve the robustness of the algorithm by allowing the algorithm to be tested in a wider variety of settings and with varying test conditions.

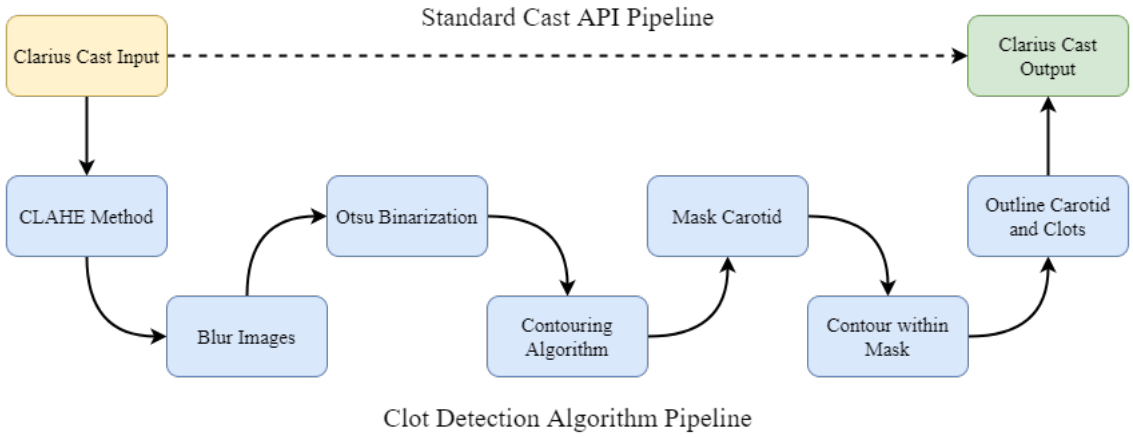


Figure 6.5: *Detection Algorithm Pipeline*

6.2 Standards

6.2.1 Coding Standards

Python Enhancement Proposal 8 (PEP-8) is the key standard required for writing code in Python. It dictates the style in which Python code should be written in order to improve the readability of code. Writing readable code is particularly important in professional and collaborative settings, where many different people may need to read and interpret the same code that only one person has written. For this reason, following PEP-8 style guidelines was necessary to ensure that the clot detection algorithm was easy to understand and will be easy to modify in the future if desired.

6.2.2 Engineering Standards

Because the team's project is a proof of concept for a medical device, there were not any engineering standards directly applied to the design. However, if the proof of concept were to be implemented to create the wearable biosensor, then certain standards should be taken into consideration while fabricating the final design of the device. Such standards include the American Society for Testing and Material (ASTM) standards such as STP1260-EB Validation Practices for Biotechnology Products [35], STP800-EB Medical Devices: Measurements, Quality Assurance, and Standards [36], and F748-16 Standard Practice for Selecting Generic Biological Test Methods for Materials and Devices [37]. Food and Drug Administration (FDA) standards that should also be considered while fabricating the wearable biosensor should include FDA-2019-D-4048 Safer Technologies Program for Medical Devices [38], FDA-2017-D-5372 Marketing Clearance of Diagnostic Ultrasound Systems and Transducers [39], FDA-2013-D-0350 Select Updates for Biocompatibility of Certain Devices in Contact with Intact Skin [40], and FDA-2019-D-3805 Biocompatibility Testing of Medical Devices - Standards Specific Information for the Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program [41].

6.2.3 Ethical Standards

There are multiple ethical standards that should also be considered if the proof of concept is to be implemented into a wearable biosensor. The team would follow rules set by the Health Insurance Portability and Accountability Act (HIPAA) which include the privacy rule, security rule, enforcement rule, and the breach notification rule [42], as the device would have access to the patient's blood flow patterns and personal health information. Risk assessments would also be necessary to complete if the device were to be made, as it could interfere with the health and safety of the patient. There is also assumed liability with missing a blood clot, so rigorous testing would also have to be done in order to insure that there are limited cases where the clot would go undetected. Lastly, there are FDA safety regulations to ensure the well-being of the patient is not compromised such as FDA-2016-D-1495 Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions [43] and FDA-2013-D-0350

Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" [44].

6.3 Impact of Project

The team determined the impact of the project by basing it on the prediction that their proof of concept will be implemented to create a wearable biosensor. This biosensor would then be manufactured and distributed to patients in need. The following areas of impact were predicted to be affected by the medical device.

6.3.1 Economics

One impact of this device could be that with early detection and removal of a clot, people would be less likely to have to pay medical expenses for the long term health problems that result from a stroke. Those expenses often include medication, rehabilitation, or other long-term medical needs. Another potential impact is that high risk patients would not have to pay for more expensive prevention methods, such as the Watchman device, which requires an invasive procedure. They also would not have to pay for constant medication such as blood thinners, which is a lifetime expense for those at high risk of stroke.

6.3.2 Environmental Impact

The environmental impact of the project is difficult to predict, but if it were to become a product that was used commonly, then it would be largely dependent on the manufacturing processes used. Most of the components used would utilise standard electronics manufacturing techniques, so the environmental ramifications would be tied primarily to the standard that factories are held to. Most manufacturing produces waste, but if companies are held responsible by their governments, the people, and consumers, then they can be pushed to implement various techniques to offset their actions, such as using carbon credits, or improving their efficiency. The product itself could become a type of e-waste over time, but given that the product would be designed to have a long lifespan when compared to consumer electronics, and would likely be fairly expensive, it would not be an item as disposable as a phone or laptop for example, and likely not be a significant contributor to e-waste.

6.3.3 Societal Influence

The creation of this device has the potential to ease the minds of many people affected by strokes each year. For those who are not able to use typical prevention methods, such as blood thinner, this device would provide an alternative option. With constant monitoring, both the patient and family and friends would feel at ease knowing the patient is safe. Another impact is that the

patient does not need to wait for the signs of a stroke in order for this device to be effective. It will detect a clot passing through before it reaches the brain, so the patient and their loved ones can have peace of mind knowing that they do not have to worry about looking for signs of a stroke, whether obvious or subtle.

6.3.4 Political Ramifications

The amount of patients with access to the team's proposed device could be limited to those with access to smart devices. If the patient is unable to gain access to a smart device, then the biosensor would not be able to function as intended. More specifically, individuals in third-world countries who do not have any access to smart devices will not be able to use the proposed biosensor and would still face the problem of having ischemic strokes without a way of detecting them before side effects occur, leaving the patient with potentially fatal or long term health complications. On the contrary, the project would be able to aid in the health and well-being of patients in countries who are technologically developed and have access to smart devices, whom the biosensor would be marketed towards.

6.3.5 Ethical Concerns

The team's project will allow patients and their friends and family to have ease of mind knowing that their good health is the main priority when it comes to the fabrication of this device. The device would be monitoring their blood flow patterns at every hour of the day and will allow the patient to feel relieved knowing that blood clots will not go undetected. Because it is extremely important that the blood clot is detected in the patient's carotid artery, there needs to be liability if there is any chance a blood clot goes undetected or if there is a false detection of one, as the patient's health is the top priority.

6.3.6 Health and Safety Issues

The project will influence the health and personal safety of individuals by allowing them to be assured that there is instant detection and alert of a blood clot in their carotid artery so they can seek medical attention in a short amount of time, well before the blood clot reaches the brain and causes potentially fatal side effects. With this device, the patient also does not have to wait for the signs of a stroke in order to know that they are having one. In some instances, when signs are noticed, there is not enough time to seek medical attention and remove the clot, resulting in an easily preventable death.

6.3.7 Manufacturability

The manufacturing techniques involved in commercializing the project would be mostly standard electronics manufacturing, with the exception of the CMUT. There are several techniques used for

producing CMUTs [45–47], but until they become more widely manufactured and more available, the manufacturing techniques specifically will need refinement. This was the biggest obstacle faced in this project, and time will be required to allow the technology needed to manufacture these components to become more advanced and for their cost to decrease. Other components needed would follow fairly standard electronics and medical device manufacturing processes, and would not be prohibitive to production.

6.3.8 Sustainability

Sustainability is primarily dependent on the product's manufacturing methods and product lifespan. A product designed with planned obsolescence in mind is inherently unsustainable, but a medical device designed with a long lifespan and serviceability in mind are very important in creating a sustainable product and image.

CHAPTER 7

DISCUSSION

7.1 Discussion of Results

The results of collecting data using the phantom artery and neck mold show that the algorithm developed can consistently detect the carotid artery. When passing the simulated blood clot through the phantom mold, the algorithm was able to detect the clot in real time, proving that the concept works as intended. This shows that a wearable biosensor could be developed with an ultrasound transducer and portable microprocessor that would allow the project to be adapted into a more realistic wearable device.

7.2 Limitations

Although the team met each of their revised goals and were successful in creating a working proof of concept, there were limitations that set the team back and did not allow them to reach their overall goal of creating a wearable biosensor. Firstly, the team did not have access to a CMUT and therefore was not able to create their wearable prototype the way they wanted to. Although they had contacted Philips and Micralyne, the CMUTs were not commercially available and were extremely expensive when the team reached out in hopes of loaning one. Because of this, they resorted to their proof of concept and used an ultrasound probe as their method of detection.

The fabrication of the PVA phantom model also came with limitations. While molding the phantom artery, if there were any air bubbles created while pouring the PVA mixture into the mold, it would be extremely noticeable when the mixture cures, shown in Figure 7.1 below, and would interfere with accurate ultrasound imaging. Additionally, if the cured phantom artery does not have a long enough freeze-thaw cycle, then the artery will not reach the desired stiffness and fall apart if removed from the rod. Lastly, if the molded PVA mixture does not freeze fully, while going through the freezing portion of its freeze-thaw cycles, then it will not be able to cure as desired and will not be able to hold its shape, as shown in Figure 7.2.

The Clarius L7 probe and associated Cast API also caused a few limiting constraints on the project overall. The Cast API only gives and receives certain image formats and must use QT to display images, which caused problems when sending images to or from OpenCV, which uses a different image format. Using OpenCV in conjunction with QT5 was fairly problematic, and would probably not run well on a mobile device, due to various expensive functions used in

Figure 7.1: *Artery with air bubbles*

Figure 7.2: *Uncured PVA mold*

OpenCV, such as the adaptive histogram equalization and Otsu binarization method. Wireless communications were another limitation, which required constant troubleshooting in order to ensure reliable transmission of the data. Using a wired probe would have made the prototyping phase of this project much simpler, but using the Cast API allowed for more flexibility to use the Clarius L7 in the future. The clot and carotid identification algorithm are limited by their flexibility in searching for specific contours. To find the carotid requires tuning the length and area parameters of the algorithm until a balance is found which correctly identifies the carotid artery and ignores other data in the ultrasound scan. Problems can arise when the carotid artery changes in size and becomes smaller or larger due to movements in the neck or surrounding tissue. This is one aspect of the algorithm that future work would likely improve upon, in order to make the algorithm more robust for daily use.

Lastly, the team had limited access to space and equipment while carrying out their project. While they were able to access the equipment they required, it was housed in multiple buildings, creating difficulties when transporting their models during the molding process. Furthermore, the freezer required to freeze the mold during the freeze thaw cycles was housed in a laboratory that the team had limited access to, which constrained the team to using it during weekdays from 8am to 6pm. This added further challenges because the team had to time the molding process perfectly in order to allow the phantom models to freeze for the correct amount of time. Although these limitations proved difficult, the team was able to work around them to the best of their ability and create a working proof of concept in the end.

CHAPTER 8

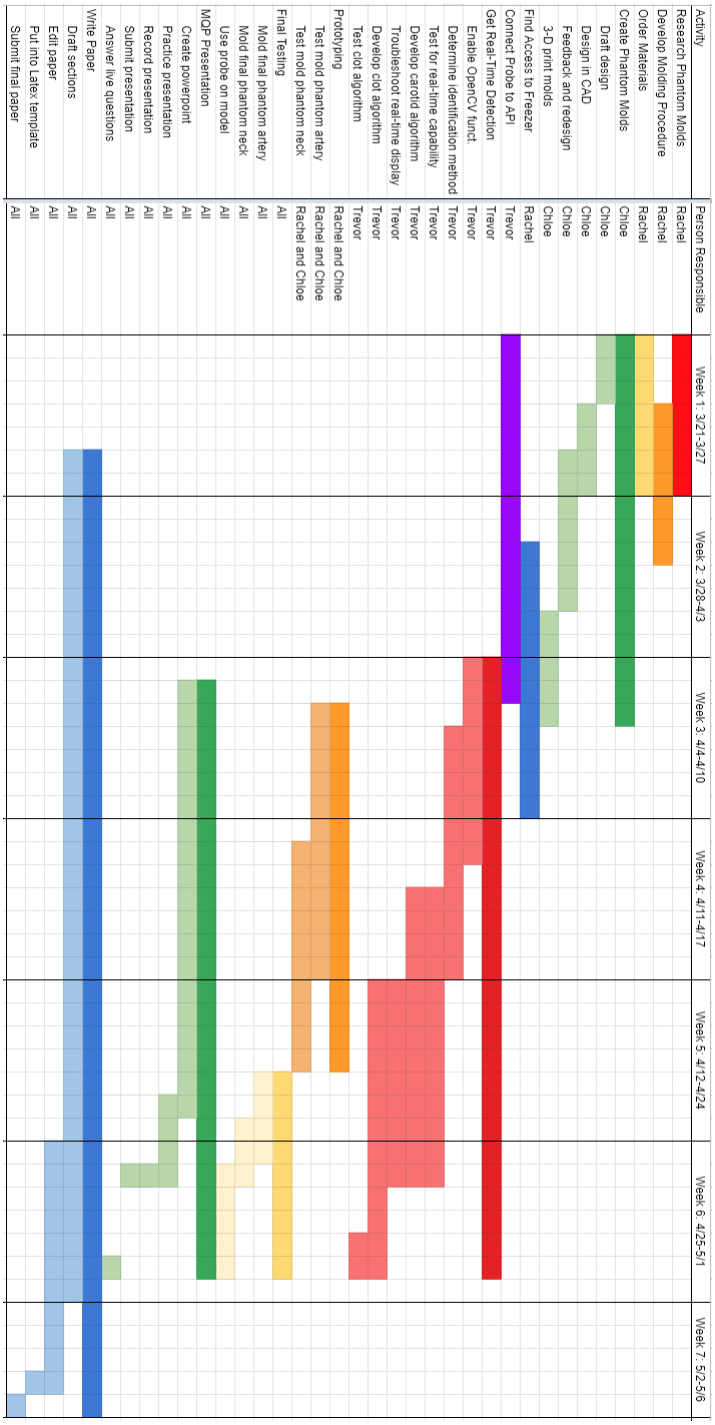
Conclusion and Recommendations

Strokes affect thousands of people every year, with the majority of those being ischemic. While prevention and treatment methods exist, there is not a real-time detection method currently available. What the team initially proposed to do was to fill that gap by creating a wearable biosensor that would detect clots traveling through the carotid artery in real time. Although this idea did not come to fruition because the team could not require a CMUT, they were able to develop a proof of concept model that demonstrated their original idea is feasible. To create the proof of concept, the team first created phantom models of both the neck and the carotid artery. They did this by designing and printing molds for the phantom artery and neck. Once the molds were complete, the phantom material was fabricated by mixing PVA with DI water and cellulose powder to obtain a material that shares similar acoustic properties to that of human tissue. The phantom material was poured into the artery mold and when ready, the artery was put in place in the neck mold, along with a cervical spine model, and the uncured phantom material was poured in to create the phantom model used for the project. After the phantom model was fabricated, the team then wanted to pass blood-mimicking fluid and clot mimics through the phantom model to model what a blood clot would look like in real-time via ultrasound. Doppler fluid was used to achieve blood-like fluid and small pieces of PVA phantom material were used for clot mimics. The Clarius L7 ultrasound probe was placed on the phantom and the clot passing through the artery was observed. In order to process the images from the ultrasound probe in real time, the team used Cast API, along with the probe, to send the ultrasound images to a computer running an OpenCV algorithm, and displayed the phantom carotid artery in real time.

Although limitations such as not having access to a CMUT, a quick prototyping and design phase, a limited budget, and limited access to space and necessary equipment may have been minor setbacks for the team, they were still able to reach their goal of creating a proof of concept for a wearable biosensor to detect blood clots in the carotid artery before reaching the brain, causing an ischemic stroke.

The proof of concept result of this project shows that there is hope for individuals at risk of ischemic strokes, and that one day a non-invasive, wearable, real-time monitoring device could be available to allow for early detection of an ischemic stroke. The device could greatly impact many people who are at risk of stroke, saving them from easily preventable and potentially fatal consequences that come with ischemic strokes.

A: Gantt Chart



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