Early-Stage Research and Design of a Diagnostic Sensor for Peripheral Vascular Disease

by
Hannah K. Mahaffey

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Signature of Author: _____
Department of Mechanical Engineering
June 2021

Certified by: _____
Ellen Roche
Associate Professor
Thesis Supervisor

Accepted by: _____
Kenneth Kamrin
Associate Professor of Mechanical Engineering
Undergraduate Officer

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Abstract

Peripheral Vascular Disease (PVD) is a blood circulation disorder that involves the narrowing and blocking of arteries in the lower extremities of the body. Symptoms of PVD include pain and restricted mobility, and as the disease progresses, it can lead to high risk of heart attack and stroke. PVD is underdiagnosed due the high amount of asymptomatic cases as well as issues with the current diagnosis process. The current process relies heavily on. The Ankle-Brachial Index (ABI). While ABI is an effective test, it is not widely preformed because it is time consuming and requires technical expertise. This project seeks to evaluate the possibility of developing a new diagnostic sensor or device to fill a similar role as ABI in the PVD diagnosis process. For evaluating the design space in the PVD diagnosis process, this project established clinical need for a new device, evaluates prior art, and then explores potential solutions. One potential solution identified is a modified digital ABI device that uses cuffless blood pressure measurements. Additionally, pulse oximetry is identified as a possible solution that would provide the fastest test time and greatest ease of use. Given the research done in this project, the recommendation for continuation is to pursue both potential solutions, but with an emphasis on expanding research into a pulse oximetry based device. If pulse oximetry is validated as a PVD screening method with similar accuracy to ABI, then it has the potential to be a fast and effective tool that will expand PVD screening in both primary care and hospital settings.

Thesis supervisor: Ellen Roche
Title: Associate Professor

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1. Introduction

Peripheral Vascular Disease (PVD), also known as Peripheral Artery Disease, is a blood circulation disorder involving the blocking and narrowing of blood vessels in the peripheral parts of the body, particularly the lower extremities [1]. PVD is a common disease, especially among the elderly, and cases are increasing as life expectancy increases. However, PVD is underdiagnosed, which is cause for concern considering the diminished quality of life and risk of heart attack and stroke that accompany the disease. Underdiagnosis results from a variety of factors including lack of symptoms in early stages as well as challenges in the current diagnosis process. Given the consequences of undiagnosed and unmanaged PVD, an efficient and widely used diagnosis process is critical to optimizing patient outcomes.

This project seeks to evaluate the current PVD diagnosis process as well as explore the possibility of designing a new sensor or device to assist in the diagnosis of PVD. By establishing clinical need, comparing prior art, and exploring potential technologies for the device, we can understand the design space for PVD diagnostic devices and create a recommendation for further work.

2. Background

2.1 Overview of Peripheral Vascular Disease

Peripheral Vascular Disease (PVD) is a disorder involving the narrowing, blocking, and/or spasming of blood vessels in the peripheral circulatory system, particularly the lower extremities. The changes to blood vessels is caused by a buildup of plaque, which results in both narrowing and possible blockage of the artery as blood flow becomes more strained [1]. PVD primarily affects elderly populations, but in addition to age, risk factors include smoking, diabetes, and obesity. Increase in prevalence of risk factors like diabetes and obesity in the U.S. contributes to the increasing number of cases. Additionally, life expectancy is rising, which means a greater percentage of our population is at risk for PVD as well as other types of vascular disorders.

PVD symptoms can manifest in many forms, but the most common one is pain in the lower extremities. Symptoms also include numbness and weakness in the legs, changes in skin, and restricted mobility. These symptoms have a direct impact on quality of life, and often the disease

goes unnoticed until symptoms set in and begin to disrupt a patient's day to day life. Complications that can arise as a result of PVD include pain and restricted mobility at lower stages of disease progression but can escalate to amputations, stroke, and heart attacks [2].

2.2 Current Diagnosis Process

The current diagnosis process for PVD generally involves a clinical screening for symptoms and risk factors, an Ankle-Brachial Index (ABI) test, and then an angiogram. Angiography is understood to be the gold standard for diagnosis since it allows doctors to see the full extent of disease progression and have full confirmation in diagnosis. However, angiography is invasive and time-consuming. Excluding preparation and set up, angiographies can take 2-3 hours, whereas ABI tests are on the order of minutes [3]. Therefore, providers use the clinical screening and ABI as tools to streamline the process and avoid angiographies unless necessary.

Clinical screening, or examination, for PVD includes assessing risk factors and symptoms that can easily be checked by a provider. The risk factors are often used as the first way of determining if further examination is needed. The American Heart Association lists the 4 main risk patient groups as follows:

1. Patients 65 years of age or older.
2. Patients 50 to 64 years of age with risk factors for atherosclerosis (history of smoking, diabetes mellitus, hyperlipidemia, hypertension) or family history of PAD.
3. Patients younger than 50 years with diabetes mellitus and one or more additional risk factors for atherosclerosis.
4. Patients with known atherosclerotic disease in another vascular bed (coronary, carotid, subclavian, renal, mesenteric artery stenosis, or abdominal aortic aneurysm). [4]

Within these patient groups deemed high risk, clinical examination proceeds with checking for signs like changes in hair or skin, unhealed wounds, or weak pulse [4]. Clinical When the clinical examination shows high risk and signs of PVD, patients will usually move on to an ABI test.

Ankle-Brachial Index (ABI) is used to screen for PVD because it serves as a gauge for blood circulation throughout the body. ABI is the ratio of blood pressure in the leg to blood pressure in the arm, thus providing a comparison of blood flow throughout the body [5]. The test is most often conducted manually by a physician in office. Prior to the test, the patient must lie at rest for about 10 minutes [5]. Lying at rest prior to the test is a critical component because blood pressure is easily affected by movement and activity. The doctor then uses inflatable blood pressure cuffs and a handheld doppler (an ultrasound device used to listen to the blood flow) to take the patient's systolic blood pressure. For the arm, the cuff is placed around the upper arm as with general blood pressure measurements. For the ankle, the cuff is fitted around the lower calf. Blood pressure measurements are taken in both arms and both legs and then ABI is calculated as follows:

$$ABI = \frac{P_{Leg}}{P_{Arm}}$$

$$P_{Leg} = systolic\ blood\ pressure\ at\ ankle,$$

$$P_{Arm} = highest\ systolic\ blood\ pressure\ of\ right/left\ arm$$

ABI is calculated for both the right and left leg, since the value can vary as the state of arteries in each leg also differ. An ABI of 0.9-1.3 is considered normal, but anything above or below requires further consideration. In the case of PVD, an ABI of below 0.9 is expected because it indicates that blood flow is weaker in the legs than compared to the upper body. Patients will be referred to a vascular specialist if ABI is low. The range for ABI values and the corresponding interpretations are shown below.

ABI Value	Interpretation	Recommendation
Greater than 1.4	Calcification / Vessel Hardening	Refer to vascular specialist
1.0 - 1.4	Normal	None
0.9 - 1.0	Acceptable	
0.8 - 0.9	Some Arterial Disease	Treat risk factors
0.5 - 0.8	Moderate Arterial Disease	Refer to vascular specialist
Less then 0.5	Severe Arterial Disease	Refer to vascular specialist

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Figure 2.1: Chart showing the breakdown of ABI values and the interpretation of each value. [5]

If a patient receives an ABI that indicates PVD, then the patient might next undergo a peripheral angiogram. An angiogram is an x-ray procedure where contrast material is injected into the veins of suspected narrowing and/or blockage [6]. This procedure allows physicians to view the extent of PVD progression because the contrast dye will highlight where plaque has built up in the veins. The angiogram can be used to determine next steps in managing and treating a patient's PVD.

Following diagnosis, most PVD patients are directed to manage their disease with lifestyle changes to address risk factors. For instance, many patients respond well to changes in diet and exercise [1]. In more severe cases, surgical intervention, called revascularization, is an option to remove the blockages throughout the legs [1]. However, revascularization comes with a variety of risks since it is an invasive procedure. Therefore, the focus for PVD patients is on preventing further progression and managing present symptoms of the disease rather than undergoing specific treatment for the blockages. Due to the emphasis on preventative care for PVD, this project focuses on early diagnostic screening in both primary care and hospital settings. Ideally,

improving the PVD diagnosis process will achieve earlier diagnosis on average for patients, which in turn will improve patient outcomes since early intervention can foster successful management of the disease.

3. Clinical Need

When exploring the opportunity for a new medical device, there must be a clinical need for the device, meaning there is an unmet need in the designated product use case. In the case of PVD, prevalence of the disease and the current diagnosis process will be evaluated to demonstrate that there is a clinical need for devices to improve the PVD diagnosis process.

3.1 Prevalence

Clinical need depends on prevalence of PVD because if improvements in PVD diagnosis could benefit a large number of people, then there is greater incentive to pursue the project. PVD is a widespread disease, affecting 200 million people worldwide as well as over 8.5 million Americans [7] . For such a common disease, we would expect a more thorough and accessible diagnosis process. However, PVD is underdiagnosed due to reasons including lack of symptoms in early stages as well as issues with the current diagnosis process. To put this in perspective, an estimated 30% of the adult U.S. population has PVD, but two-thirds of those cases are asymptomatic [8].

With such a large portion of cases consisting of asymptomatic patients, diagnosis can be challenging. Often times, symptoms are the only reason patients are recommended for an ABI, meaning many PVD cases progress unknowingly. Therefore, when patients eventually become symptomatic, there is already significant damage to the arteries. Undiagnosed PVD can lead to severe complications and impact quality of life as the disease progresses. Without intervention, PVD can result in strokes, heart attacks, and other life-threatening vascular complications. Additionally, there is a high mortality associated with PVD, as seen in one study that found the five-year crude death rate among patients diagnosed with PVD to be 33.2% [9]. Therefore, given the high prevalence of PVD in our population as well as the consequences that come with lack of diagnosis, there is a clinical need for improvement in the diagnosis process.

3.2 Issues with Current Diagnosis Process

The current diagnosis process has shortcomings that contribute to PVD underdiagnosis. By investigating the said shortcomings, we can identify both a clinical need for an improved diagnosis process as well as specific opportunities for improvement.

Clinical screening, the first step in the PVD diagnosis process, is a quick and easy way to determine if a patient is at risk for PVD. It involves questioning the patient on both presence of symptoms and risk factors. While this can be useful in determining if further action is needed, it is not sufficient alone for a diagnosis [10]. On the other end of the spectrum, angiographies provide a clear diagnosis while also showing extent of disease progression that can be useful in determining treatment options. However, since angiographies are lengthy and invasive procedures, it is not suitable for every at-risk patient. This leaves us in the middle of the options with ABI.

ABI has been used for preliminary PVD screening, but is underutilized because it is a relatively time-consuming test that requires technical expertise to conduct. The total time for an ABI test to be completed can vary depending on factors like the practitioner's technique, set up time, and patient rest time. In general, the test is said to take 10-20 minutes, excluding rest time for the patient prior to the test [11]. One study on ABI time reported an average time of 5 minutes for the test, with a range of 3-11 minutes, but this was a small study of only one provider and did not include set up and patient prep time [3]. Nevertheless, knowing that the actual test time can be sub 5 minutes, indicates that set up time is a large barrier to use of ABI in practice.

Additionally, ABI is not an effective test for patients with noncompressible arteries, such as diabetics. Inflatable cuff blood pressure methods do not provide an accurate measurement on noncompressible arteries, so since ABI tests use inflatable cuffs, they are not ideal for these patients [12]. The current alternative is a Toe-Brachial Index, which is similar to ABI but uses the toe instead of ankle artery because toe veins are less susceptible to vascular stiffening [1]. However, toe-brachial index has not been proven to provide equal accuracy in PVD diagnosis when compared to ABI [13], [14]. Therefore, there is an open issue surrounding PVD screening for diabetic patients. Diabetics are an at-risk group for PVD, which points towards a clinical need for a PVD diagnostic tool that is better suited for vascular stiffening.

Issues with ABI in practice open up the design space for a device to fill the same role. There is a clinical need for a device that screens for PVD with similar accuracy and sensitivity when compared to ABI but is quicker and easier to use. Developing such a device would be working towards the goal of making PVD screening and diagnosis more accessible, thus improving outcomes for PVD patients by catching the disease as early as possible.

4. Prior Art

During this stage of researching the possibility of a device for screening and diagnosis of PVD, prior art must be evaluated. Looking at current devices on the market that fill the same product space, we can have a better understanding of opportunities for innovation. Similarly, evaluating available publications on technology related to the device research shows what has been researched but less commercialized.

4.1 Current Devices: ABI

This project seeks to fill the same space as ABI in the PVD diagnostic process: a non-invasive screening to predict PVD before moving a patient on to angiography. Therefore, most prior art research consisted of existing ABI devices. First, the inflatable cuff and doppler method for ABI is the most common ABI test in practice.

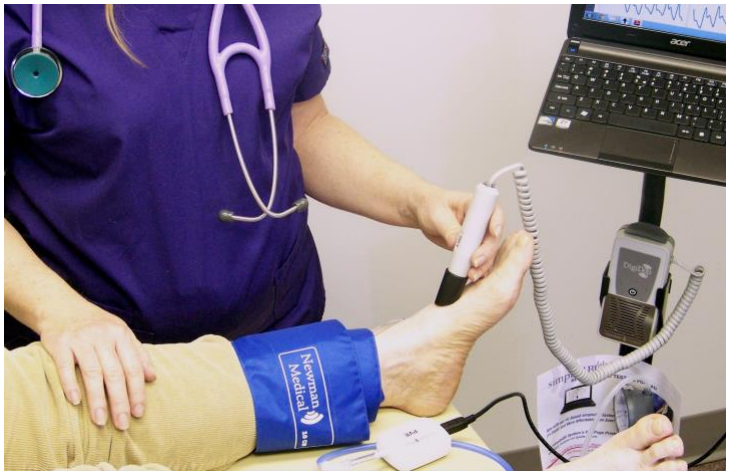

Figure 4.1: An inflatable blood pressure cuff and handheld doppler being used for conducting an ABI test. Newman Medical is the manufacturer of the equipment used in the picture. [15]

During a manual ABI that uses an inflatable cuff and doppler ultrasound, any combination of the two required tools will be sufficient. However, many medical device companies will sell inflatable cuffs and handheld dopplers as a bundled device. Some ABI devices are all encompassing with cuffs, dopplers, and results, but still require manual running of the test. For example, the VISTA AVS Vascular ABI device shown below creates a manual ABI module.

Figure 4.2: VISTA AVS Vascular ABI cart showing the inflatable cuffs and handheld doppler.[16]

The ABI device shown is one of many options. Other common sellers of manual ABI components and/or devices include Medtronic and Becton Dickinson.

4.2 Current Devices: Digital ABI

Improvement on ABI tests has been attempted by digital ABI devices. These devices automate the ABI process and eliminate some of the need for technical expertise. On the market, there are digital ABI devices that used the traditional inflatable cuff blood pressure measurements to give the ABI result. The premise of these devices is similar, there are usually 4 cuffs connected to a monitor, as a central hub. These cuffs inflate and collect blood pressure measurements all at the same time. The measurements are then processed by the monitor and then displayed as ABI, which the provider can then interpret as needed.

Smart-ABI, shown below, is a digital ABI in clinical trials in the US that uses Bluetooth connection to inflate three cuffs (both legs and one arm) to collect blood pressure measurements that translate to an ABI reading [17].

Figure 4.3: Smart-ABI device. [17]

Additionally, the device uses volume plethysmography to serves as a measurement of blood flow recovery in the artery. Volume plethysmography is a technique that involves flashing infrared light through an artery and then noting how the blood volume affects amount of light reflected back [18]. That amount of light is then presented as volumetric blood flow. This metric provides additional information about vascular health beyond blood pressure, and thus this device has the potential to provide greater accuracy beyond standard ABI.

Test time is a critical metric when evaluating digital ABI devices, since a lower test time is more likely to lead to wider use of a device. The Slovenian digital ABI device, MESI ABPI, posts the fastest test time of all digital ABI devices at one minute excluding setup time [19]. MESI ABPI is a central hub with 3 cuffs attached, as shown below.

Figure 4.4: MESI ABPI device. [19]

Each cuff inflates and deflates simultaneously to get blood pressure measurements in only one minute. The ABI results are then displayed on the monitor. The automation of the cuff inflation/deflation and measurements reduces potential for human error, thus improving accuracy of the ABI results. Additionally, the device is sold on a cart, which makes it easily portable around hospitals and offices. Overall, MESI ABI appears to be an efficient and appealing digital ABI device due to its low test time. A study validating the speed and accuracy of MESI ABPI found it to give slightly higher measurements when compared to standard doppler ABI, but still proved to be an effective screening method for PVD [20]. MESI ABPI was approved by the FDA as of December 2020, meaning it is now the fastest ABI option available in the US [21].

Moving beyond standard blood pressure measurements, the ABI device QuantaFlo^{TM} (formerly FlowChec^{TM}), manufactured by Semler Scientific Inc, shows alternatives to traditional ABI. QuantaFlo is marketed as a digital ABI but does not explicitly use blood pressure measurements like manual ABI or other digital ABI devices. Instead, QuantaFlo^{TM} uses LEDs in a pulse oximetry style clamp to detect blood flow, the process known as blood volume plethysmography [22]. This is similar to Smart-ABI, but QuantaFlo^{TM} is a cuffless device.

Figure 4.5: QuantaFlo™ sensor connected to a laptop while the software processes the measurements to produce an ABI. [23]

The blood flow measurements are then compared at the fingers and toes to create an ABI style ratio. In the study conducted by Semler Scientific Inc, QuantaFlo™ was shown to be an effective tool for detection of PVD when compared to the standard doppler ABI method [22]. Since this technology diverged from other ABI methods, it was again validated against angiography and was demonstrated to have both high sensitivity and accuracy when predicting PVD [24]. The test time for QuantaFlo™ is around 5 minutes, which is similar manual ABI test, but has less set up time, thus making QuantaFlo™ a relatively fast exam [23]. When considering both manual ABI and digital ABI, QuantaFlo™ appears to have the most potential to fill the role of an easily accessible and convenient PVD screening tool. The Semler Scientific study was conducted in primary care, which is the ideal setting when considering the goal of detecting PVD as early as possible.

4.3 Current Devices: Continuous Non-Invasive Blood Pressure Monitoring

Outside of the PVD diagnosis space, there are devices striving for better blood pressure monitoring. Specifically, there is a clinical need for continuous blood pressure monitoring in order to get more accurate patient data. Dynocardia is a funded startup working to develop a continuous non-invasive blood pressure monitoring device. This device is worn on the wrist like a watch, so that patients' data is seen over longer periods of time and thus not skewed by

external factors. Dynocardia uses its patented technology known as ViTrack™ to generate blood pressure readings from spaciotemporal force data collected by an optic sensor [25]. The sensor is worn on the wrist, as shown below.

Figure 4.6: Dynocardia's wearable sensor with ViTrack™ technology. [25]

Dynocardia's founder, Mohan Thanikachalam MD, believes that ViTrack™ could be applied to other blood pressure reading scenarios other than continuous monitoring [26]. For instance, since the sensor would theoretically work on any part of the body, readings could be taken at the wrist and ankle to produce an ABI measurement. Additionally, this type of optic sensing is less affected by the artery stiffening that reduces accuracy of diabetic patients manual ABI measurements, which makes the technology an ideal candidate for expansion into use for PVD.

4.4 Publications

In addition to current devices, there is also relevant prior art information to be extracted from research and publications. Outside of the medical device space, the concept of biomarkers for PVD screening has been explored. One study explored the possibility of using a combination of various biomarkers, or measurable substances and/or indicators of disease, as a screening tool for PVD [27]. This study evaluated the combination of β(2)-microglobulin, cystatin C, high-sensitivity C-reactive protein, and glucose in their presence's ability to predict PVD. Results

showed that this panel of biomarkers was effective at predicting PVD when used along with clinical screening for risk factors in the primary care setting [27].

While the biomarker method of screening for PVD is an effective approach in diagnosis terms, it would not fit the desired goals for this project. Use of biomarkers required patients to have blood drawn and tested, which while it is not particularly invasive compared to angiography, it is extremely time consuming. Therefore, with the exception of diabetic patients, a manual ABI test would still be a more efficient screening tool in practice.

5. User Needs

In early-stage research of a product, user needs are critical for evaluating different design paths. Dr. Mitch Cahan at Mount Auburn Hospital helped shape the following needs.

User needs is led by the requirement for a device that has accuracy similar to or better than ABI in terms of screening for PVD. The goal of this device is to fit in the same space ABI current occupies as a screening tool, meaning predictive accuracy for PVD diagnosis. Part of this user need means the device must take similar measurements to ABI throughout the body. This would include the typical one arm and both legs necessary for ABI.

The most critical user need as well as design specification is test setup and run time totaling under 5 minutes. One of the primary issues with current ABI, and also a reason it is not used as widely as necessary, is the time-consuming nature of the manual procedure. This problem has been attempted to improve upon by digital ABI devices, but no devices appear to have come close to the desired time constraint except the Slovenian MESI ABPI mentioned under prior art. Additionally, ABI requires a patient to lie at rest prior to the test, which acts as another barrier to achieving a fast test time. A sub 5-minute time length is a requirement because in order to achieve the actual goal of an accessible screening device, the test must be able to fit in during the limited time that providers actually have with patients, especially for general practitioners.

Similar to time requirements, affordability is necessary for accessibility. The goal for this requirement would be a device that can be purchased by a majority of both hospitals and private practices regardless of specialty. Even if a device fit time constraint and ease of use, the device would not be widely implemented in offices and hospitals if it was outside an affordable price range.

Other necessary user needs include the device being both portable and easy to clean between patients. In order to be an accessible device, a single to few device(s) must be able to serve entire private practices, hospitals, and groups. These user needs must be taken into account when evaluating potential technologies that could improve upon ABI and the general PVD diagnosis process.

6. Potential Solutions: Modified Digital ABI

Based on the prior art section, it is clear that digital ABI has been explored by various companies and holds a lot of potential. Digital ABI in principle solves various issues with ABI like reducing manual error and eliminating need for technical expertise that goes along with the doppler ABI method. However, there are still open issues among the digital ABI devices. Length of set up and test time remain the largest obstacle, since the 5-minute time frame has been identified as a critical user need. Additionally, many of the digital ABI devices identified use inflatable cuffs, which is known to be an inaccurate method for diabetic patients.

Furthermore, if this project was pursued, one option would be to design an improved digital ABI that attempts to address the current unmet needs. The founder of Dynocardia, the non-invasive continuous blood pressure monitoring device discussed in prior art, believes that their technology could be expanded into a digital ABI. This would involve syncing multiple of the wearable devices to yield an ABI measurement in a timely manner but is a feasible application of their ViTrack^{TM} technology. There is also opportunity to explore other cuffless non-invasive blood pressure monitoring technologies that involve optic sensors as seen in QuantaFlo^{TM}.

7. Potential Solutions: Pulse Oximetry

Given difficulties with ABI and other blood pressure measurements, there is also potential for creating a simplified screening that fills a similar role to ABI, but without blood pressure. When screening for PVD, the general need is to compare blood flow metrics in the upper body to the lower body. Blood pressure is the metric traditionally used, and while it is the most heavily researched metric in relation to PVD, it is not the only option. Pulse oximetry, a common technology used to measure blood oxygen levels, serves as a possibility for PVD screening.

7.1 Pulse Oximetry Background

Pulse oximetry is used to measure blood oxygen levels, which is a measurement out of 100% that represents how much of the hemoglobin in a patient's blood is saturated with oxygen. Ideally, we have 100% blood oxygen saturation, but abnormal levels are considered to be anything below 95% [28]. Blood oxygen level is already considered a vital sign, and is taken at the finger in both primary care and hospital settings [29]. Pulse oximetry is used to measure blood oxygen levels by using LEDs to flash an area of tissue, and then the quantity of light that is transmitted through the area is interpreted as oxygen saturation based on how much light hemoglobin absorbs at the specific wavelength [29].

Pulse oximetry is an imperfect method; there are issues with skin texture/color as well as inaccurate readings based on activity [30]. However, pulse oximetry is still widely used because it is a highly efficient non-invasive method that provides readings almost instantly, taking only seconds to produce a value. Keeping in mind that the goal of this project to improve the PVD diagnostic process seeks to create a device that would be used widely in many different care settings, blood oxygen saturation is an appealing blood metric.

7.2 Pulse Oximetry and PVD

Based on the prediction that poor blood flow due to blockages in the lower limb arteries could lead to lower oxygen saturation in the blood, there have been studies exploring a possible linkage between blood oxygen levels and PVD. One such study concluded that comparing blood oxygen saturation of the toe and finger actually has a higher sensitivity than ABI when it comes to predicting PVD in diabetic patients [31]. This is a fascinating result because it solves both the issue of time and inaccuracy with diabetic patients that can be a barrier to using ABI. QuantaFlo^{TM} already utilizes a similar optic sensor method to measure blood flow and yield an ABI, but there is a possibility that pulse oximetry could simplify this process to speed up total test time significantly.

Using pulse oximetry as a PVD screening method involves comparing blood oxygen saturation at the finger and at the toe. If toe saturation is less than finger saturation by more than 2%, then this is considered a sign of PVD [32]. In a study that compared sensitivity and specificity of pulse oximetry compared to ABI for screening asymptomatic patients for PVD, pulse oximetry was found to be on par with ABI [32].

To explore pulse oximetry, a Wellue Bluetooth Pulse Oximeter was used to take various blood oxygen level measurements. The Wellue Pulse Oximeter is a commercial device for at home monitoring of blood oxygen levels [33]. The purpose of these measurements was to complete preliminary prototyping by seeing how fast pulse oximeters give readings and explore a commercially available device's ability to take readings on toes in addition to fingers. It is also important to note that this experimentation with the Wellue Pulse Oximeter was not intended for recording blood oxygen levels, but rather exclusively an exploration of test time and ease of use. For the finger, the pulse oximeter was placed on the index finger, as shown below.

Figure 7.1: Pulse oximeter placed on index finger.

Based on 20 measurements taken, the average time to get results on the index finger was 6.2 ± 1.1 seconds. The pulse oximeter was then placed on the second toe to investigate how the device preforms on different parts of the body.

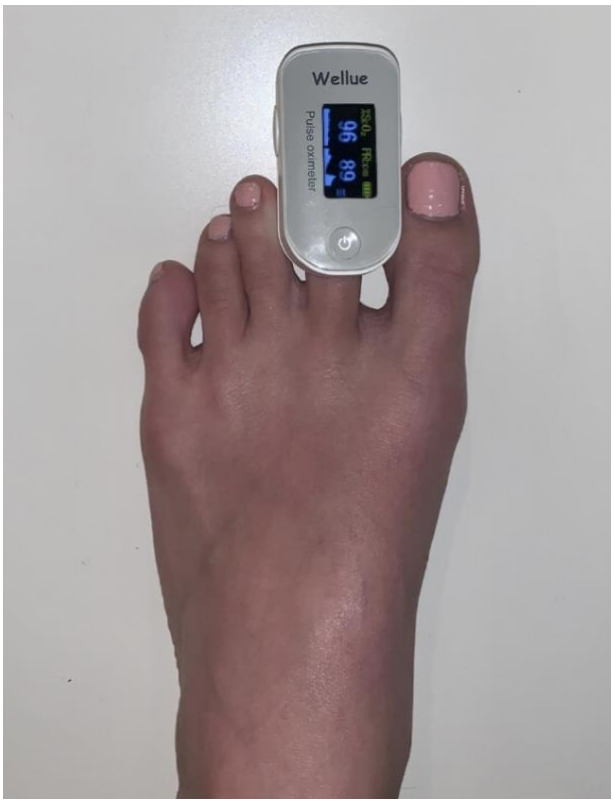

Figure 7.2: Pulse oximeter placed on second toe.

When taken on the toe, the average time to get results was 18.3 ± 2.9 seconds. This disparity indicates that pulse oximeters, at least on the commercial end might be calibrated exclusively for fingers. Under the assumption that medical grade pulse oximeters offer higher quality sensors, it is likely that such pulse oximeters could be better suited for use on toes in addition to fingers. Even if toe and finger measurements could not be taken synchronously, the speed of pulse oximetry places it at a fraction of the time it takes to compete an ABI, both manually and digitally. Additionally, exploration with the Wellue Pulse Oximeter demonstrated that these devices are generally very easy to use and require virtually no technical expertise.

7.3 Pulse Oximeter PVD Device

If this project were continued, a pulse oximetry based PVD device would be a prime possibility to explore. Amount and breadth of studies validating pulse oximetry as a screening tool for PVD are still lacking compared to ABI, but there is still potential to utilize this as an option. Pulse

oximetry has a huge advantage of providing results on the order of seconds as well as already being widely manufactured and used. We can envision a digital ABI-like device that incorporates pulse oximeters into a format that will display the toe/finger percentage ratio as a PVD indicator. This could take the form of other digital ABIs with a central hub and display screen that pulse oximeters are connected to. Alternatively, with many Bluetooth pulse oximeters already on the market, this could easily be incorporated into a phone, tablet, or computer app that serves for calculating ratios and displaying results.

When considering a pulse oximetry based PVD device, it is important to acknowledge limitations of such a device. Blood oxygen saturation is a less researched metric in regard to PVD so there is need for more validated studies that employ this method. Additionally, it is important to remember known obstacles with pulse oximetry, like issues with skin tone that arise with optic sensors. Nevertheless, if these obstacles are explored and understood, then there is still opportunity to use pulse oximetry for PVD screening.

8. Comparing Potential Solutions

For evaluating the possibilities within the digital ABI space and pulse oximetry, a Pugh chart will be used to compare specific attributes. This analysis will help determine what options could be worth pursing in a continuation of this project. In the scope of this project, limited options are evaluated and are explained as followed:

1. Digital ABI w/ Inflatable cuffs (baseline). This type of digital ABI will be used as the baseline; consider this to be a device like Smart-ABI or MESI ABPI.
2. Modified Digital ABI. This is the case of partnering with Dynocardia or exploring other cuffless non-invasive blood pressure measuring techniques
3. Pulse Oximetry. This is the case of exploring a pulse oximetry based device.

The following metrics will be considered:

A. Total test time: a critical user need since low test time would make the device more widely used in primary care.

B. Ease of use: a user need that would reduce need for technical expertise in this stage of the diagnosis process.

C. Accuracy, a user need that requires the device to have similar accuracy to manual ABI in screening for PVD.

D. Cost, a user need that determines how accessible this device would be in practice.

	Total Test Time	**Ease of Use**	**Accuracy**	**Cost**	**Total**
Digital ABI w/ Inflatable Cuffs (baseline)	0	0	0	0	0
Modified Digital ABI	+1	+1	+1	-1	2
Pulse Oximetry	+2	+1	-1	+1	3

Table 6.1: Pugh chart for potential solutions

Explanations for Pugh chart scores are offered below:

A. Total Test Time:

1. Modified Digital ABI: A modified digital ABI that utilizes cuffless blood pressure measurements would likely be faster than the baseline digital ABI since it would not require the inflation/deflation of cuffs. This would likely be able to achieve a test time on the order of minutes.
2. Pulse Oximetry: Pulse oximetry offers measurements almost instantly, meaning this option has the potential to create a total test time on the order of seconds, including set up time. Pulse oximetry also has to potential to eliminate pre-test rest time for the patient, which could also be an advantage.

B. Ease of Use:

1. Modified Digital ABI: A cuffless method would likely be easier to use than the baseline digital ABI due to a simplified patient set up process.

2. Pulse Oximetry: Pulse oximetry is already widely used and has the advantage of being very simple. Therefore, a device using pulse oximetry would likely be easier to use than the baseline digital ABI, further eliminating the need for technical expertise.

C. Accuracy:

1. Modified Digital ABI: Cuffless blood pressure measurements have to potential to provide greater accuracy, as seen in the case of ViTrack^{TM}. Thus, modifications and exploring different blood pressure technologies could provide greater accuracy than the baseline digital ABI.
2. Pulse Oximetry: Pulse oximetry has not been extensively researched in association with PVD, and also has been shown to have reduced accuracy depending on skin color and texture. Therefore, it has the potential to be less accurate than the baseline digital ABI.

D. Cost:

1. Modified Digital ABI: Cuffless blood pressure measurements rely on optic sensors that tend to be more expensive than the established inflatable cuff and doppler technology. Therefore, a modified digital ABI has the potential to have a higher cost than the baseline digital ABI.
2. Pulse Oximetry: Pulse oximetry devices are widely accessible and affordable, so this option would likely come at a lower cost to buyers than the baseline digital ABI.

In summary, pulse oximetry appears to be the best option for continuing this project based on the metrics considered and research available. Pulse oximetry has the potential to create a device that can be used in primary care and hospital settings by physicians as well as nurses. This technology offers the huge advantage of providing almost instant measurements. When considering the goal of creating a device that would increase PVD screening, a fast and easy to use device could achieve this, as long as accuracy remains similar to ABI. Pulse oximetry is not the gold standard, like angiography, but it would streamline the diagnosis process and thus have the intended effect of reducing undiagnosed cases of PVD.

9. Conclusion

Based on prevalence of PVD as well as underdiagnosis, there is an established clinical need for a device that will streamline PVD diagnosis process and increase number of patients that are able to receive an early diagnosis. Within the current diagnosis process, ABI is used as the metric to fill the gap between clinical examination and angiography, so the clinical need lies in need for an improved screening tool that serves similarly to ABI. In prior art, various ABI tests were considered. QuantaFlo^{TM} appears to be the best device currently on the market that hits most of the user needs and design goals identified by this project. While QuantaFlo^{TM} itself appears to be relatively efficient device for use in both primary care and hospital settings, ABI is still overlooked for patients that are asymptomatic. The tendency for PVD to be overlooked in asymptomatic patients leads to the critical user need of a sub 5-minute total set up and test time.

With the user needs in mind, there is room in the clinical setting for a new screening tool for PVD. Based on the background research in the PVD and ABI design space, there are feasible design options both in modifying the digital ABI concept as well as exploring pulse oximetry as a simple and significantly faster possibility.

9.1 Limitations

This project was focused on exploring prior art and clinical need for background purposes if the project was pursued further. However, given the number of ABI devices on the market, not all devices were covered under prior art. Additionally, the pulse oximetry exploration was limited since full and thorough experimentation was outside the scope of this project.

The problem this project aimed to solve also involves convincing providers to screen for PVD on a regular basis outside symptomatic and high-risk groups. This requirement is an obstacle, even if an ideal device is created because support from the medical community is critical. For instance, if a pulse oximetry based device was to have a quick, easy, and accurate test, there would still need to be a shift in practice to incorporate such a device on a large scale.

9.2 Recommendations

Based on the background research and prior art discussed throughout this project, the recommendation for continuation would be to pursue pulse oximetry as well as a modified digital ABI with cuffless blood pressure measurements. The comparison done via Pugh chart puts pulse

oximetry at a greater potential, but there is still more research to be done into both options. Next steps for pulse oximetry would include a full experiment validating pulse oximetry as a metric for PVD screening and then incorporating pulse oximetry into a device that provides a ratio and PVD indicator. For modifying digital ABI, next steps would include pursuit of non-invasive cuffless blood pressure devices from both a research route and a partnership route. In general, this project is worth continuing given the extensive underdiagnosis of PVD. A more efficient and accessible PVD diagnosis process has the potential to impact millions of patients worldwide.

References

[1] Gul, F., and Janzer, S. F., 2021, "Peripheral Vascular Disease," *StatPearls*, StatPearls Publishing, Treasure Island (FL).

[2] "Peripheral Vascular Disease" [Online]. Available: https://www.hopkinsmedicine.org/health/conditions-and-diseases/peripheral-vascular-disease. [Accessed: 27-Apr-2021].

[3] Pearson, T., Kukulka, G., and Ur Rahman, Z., 2009, "Ankle Brachial Index Measurement in Primary Care Setting: How Long Does It Take?," South Med J, **102**(11), pp. 1106–1110.

[4] Tummala, S., and Scherbel, D., 2018, "Clinical Assessment of Peripheral Arterial Disease in the Office: What Do the Guidelines Say?," Semin Intervent Radiol, **35**(5), pp. 365–377.

[5] "Ankle Brachial Index," Stanford Medicine 25 [Online]. Available: https://stanfordmedicine25.stanford.edu/the25/ankle-brachial-index.html. [Accessed: 27-Apr-2021].

[6] "Peripheral Angiogram," www.heart.org [Online]. Available: https://www.heart.org/en/health-topics/peripheral-artery-disease/symptoms-and-diagnosis-of-pad/peripheral-angiogram. [Accessed: 27-Apr-2021].

[7] "Peripheral Artery Disease," www.heart.org [Online]. Available: https://www.heart.org/en/health-topics/peripheral-artery-disease. [Accessed: 30-Apr-2021].

[8] Federman, D. G., Trent, J. T., Froelich, C. W., Demirovic, J., and Kirsner, R. S., 1998, "Epidemiology of Peripheral Vascular Disease: A Predictor of Systemic Vascular Disease," Ostomy Wound Manage, **44**(5), pp. 58–62, 64, 66 passim.

[9] Caro, J., Migliaccio-Walle, K., Ishak, K. J., and Proskorovsky, I., 2005, "The Morbidity and Mortality Following a Diagnosis of Peripheral Arterial Disease: Long-Term Follow-up of a Large Database," BMC Cardiovasc Disord, **5**, p. 14.

[10] Khan, N. A., Rahim, S. A., Anand, S. S., Simel, D. L., and Panju, A., 2006, "Does the Clinical Examination Predict Lower Extremity Peripheral Arterial Disease?," JAMA, **295**(5), pp. 536–546.

[11] "Ankle-Brachial Index (ABI)," Cleveland Clinic [Online]. Available: https://my.clevelandclinic.org/health/diagnostics/17840-ankle-brachial-index-abi. [Accessed: 28-Apr-2021].

[12] Aerden, D., Massaad, D., von Kemp, K., van Tussenbroek, F., Debing, E., Keymeulen, B., and Van den Brande, P., 2011, "The Ankle--Brachial Index and the Diabetic Foot: A Troublesome Marriage," Ann Vasc Surg, **25**(6), pp. 770–777.

[13] Høyer, C., Sandermann, J., and Petersen, L. J., 2013, "The Toe-Brachial Index in the Diagnosis of Peripheral Arterial Disease," J Vasc Surg, **58**(1), pp. 231–238.

[14] Stoekenbroek, R. M., Ubbink, D. T., Reekers, J. A., and Koelemay, M. J. W., 2015, "Hide and Seek: Does the Toe-Brachial Index Allow for Earlier Recognition of Peripheral Arterial Disease in Diabetic Patients?," Eur J Vasc Endovasc Surg, **49**(2), pp. 192–198.

[15] "Newman Medical ABI 300 Basic ABI Testing : Newman Medical ABI300 : Medical Equipment | ABI Machines & PVR Equipment" [Online]. Available: https://discountcardiology.com/Newman-Medical-ABI-300-Basic-ABI-Testing.html. [Accessed: 27-Apr-2021].

[16] "New ABI Machine - New Vista AVS Vascular ABI Machine," MedPlus Equipment Services.

[17] "Smart ABI Series," Peripheral Artery Disease [Online]. Available: https://www.smartabi.com/. [Accessed: 28-Apr-2021].

[18] Montemayor, E., and Aziz, M. B., 2021, "Arterial Doppler Imaging, ABI, and Plethysmography," StatPearls.
[19] "MESI ABPI MD," MESI – Simplifying Diagnostics [Online]. Available: https://www.mesimedical.com/mesi-abpi-md/. [Accessed: 26-Apr-2021].
[20] Špan, M., Geršak, G., Millasseau, S. C., Meža, M., and Košir, A., 2016, "Detection of Peripheral Arterial Disease with an Improved Automated Device: Comparison of a New Oscillometric Device and the Standard Doppler Method," Vasc Health Risk Manag, **12**, pp. 305–311.
[21] Ltd, M., "New Technology Advancement by MESI in Detecting Peripheral-Arterial Disease to Benefit US Patients" [Online]. Available: https://www.prnewswire.com/news-releases/new-technology-advancement-by-mesi-in-detecting-peripheral-arterial-disease-to-benefit-us-patients-301252916.html. [Accessed: 28-Apr-2021].
[22] Diage, T. R., Johnson, G., and Ravipati, G., 2013, "Digital Ankle-Brachial Index Technology Used in Primary Care Settings to Detect Flow Obstruction: A Population Based Registry Study," BMC Research Notes, **6**(1), p. 404.
[23] "QuantaFlo," Semler Scientific [Online]. Available: https://www.semlerscientific.com/quantaflo/. [Accessed: 28-Apr-2021].
[24] Gajanana, D., Raikar, M. G., Ram, P., Bhalla, V., Figueredo, V., Janzer, S., and George, J. C., 2019, "Validation of Digital Ankle-Brachial Index as a Screening Tool in Symptomatic Patients with Peripheral Arterial Disease," Cardiovasc Revasc Med, **20**(3), pp. 207–209.
[25] "Dynocardia," Dynocardia [Online]. Available: https://www.dynocardia.care. [Accessed: 26-Apr-2021].
[26] Thanikachalam, M., 2021, "Conversation with Founder of Dynocardia."
[27] Hiatt, W. R., Zakharyan, A., Fung, E. T., Crutcher, G., Smith, A., Stanford, C., and Cooke, J., 2012, "A Validated Biomarker Panel to Identify Peripheral Artery Disease," Vasc Med, **17**(6), pp. 386–393.
[28] American Thoracic Society and American College of Chest Physicians, 2003, "ATS/ACCP Statement on Cardiopulmonary Exercise Testing," Am J Respir Crit Care Med, **167**(2), pp. 211–277.
[29] Torp, K., Modi, P., and Simon, L., 2021, "Pulse Oximetry," StatPearls.
[30] Health, C. for D. and R., 2021, "Pulse Oximeter Accuracy and Limitations: FDA Safety Communication," FDA.
[31] Siao, R. M., So, M. J., and Gomez, M. H., 2018, "Pulse Oximetry as a Screening Test for Hemodynamically Significant Lower Extremity Peripheral Artery Disease in Adults with Type 2 Diabetes Mellitus," J ASEAN Fed Endocr Soc, **33**(2), pp. 130–136.
[32] Kumar, M. S., Lohiya, A., Ramesh, V., Behera, P., Palepu, S., and Rizwan, S. A., 2016, "Sensitivity and Specificity of Pulse Oximetry and Ankle-Brachial Index for Screening Asymptomatic Peripheral Vascular Diseases in Type 2 Diabetes Mellitus," J Assoc Physicians India, **64**(8), pp. 38–43.
[33] "FS20F Bluetooth Finger Oximeter," Wellue Health. [Online]. Available: https://getwellue.com/pages/fs20f-bluetooth-finger-oximeter. [Accessed: 10-May-2021].