Reutilization of Pulse Pressure and Tonometry Equipment

BME 200/300
University of Wisconsin-Madison
Department of Biomedical Engineering
December, 2016
Team Members:
Naren Chaudhry - *Team Leader*
Yiqun Ma - Co*mmunicator*
Cristian Naxi - *BSAC*
Ian Baumgart - *BPAG*
Callie Mataczynski - *BWIG*

Advisor: Dr. Willis Tompkins
Client: Dr. Naomi Chesler

ABSTRACT

System vascular impedance is a mathematically derived spectrum of data that indicates opposition to pulsatile blood flow. Impedance cannot be directly measured. Rather, it is calculated using data from pulsatile waveforms and blood volume flow waveforms. Three years ago, Dr. Nancy Sweitzer conducted research on impedance to blood flow using tonometry and blood flow equipment. The owner of the leftover equipment, Dr. Naomi Chesler, organized our team to reassemble the instruments with the ultimate goal of measuring impedance data in healthy individuals. In the process of reassembly, an inventory was determined of which devices function, which devices have missing or incomplete parts, and which instruments can be reutilized for further use in future research. These instruments primarily use the data acquisition software *NIHem* to collect and analyze data. A procedure for measuring systemic vascular impedance using *NIHem* was also found.

Contents

1 INTRODUCTION

1.1 Motivation

Ventricular failure is the number one cause of death in people with cardiovascular disease, and it can be prevented with early screening and diagnosis[1,2]. An important biomarker for overall cardiovascular health is systemic vascular impedance, or the opposition to pulsatile blood flow[3]. Systemic vascular impedance cannot be measured directly; rather, it is calculated using pulsatile waveforms via tonometry and blood volume flow waveforms via echocardiography. Traditionally speaking, vascular impedance is measured through an invasive procedure which is both costly and risky and not typically performed in humans [4]. A system that measures systemic vascular impedance in a noninvasive manner would be cost-effective and beneficial to the health care systems, insurance companies, and patients. The main focus of this project is to incorporate pulse pressure and tonometry equipment into a system that accurately measures systemic vascular impedance, as well as other biomarkers, in a noninvasive manner.

The medical instruments that were integrated into a system were provided by the client, Dr. Naomi Chesler. Dr. Chesler, a professor and active researcher at the University of Wisconsin-Madison, has requested an identification, assessment, and integration of medical instruments leftover from a former professor and researcher, Dr. Nancy Sweitzer. The instruments were used in past research conducted by Dr. Sweitzer but have been unexploited since her departure in 2014 [5]. The usage history of the instruments were analyzed via Dr. Sweitzer’s literature that was published during her time at UW-Madison. The conditions of the instruments have been unknown until an inventory of the components was performed. Some instruments are missing so that a working system that accurately measures systemic vascular impedance is not possible. A diagram depicting the functions and integration of the different components was created despite missing medical instruments.

1.2 Problem Statement

There are medical instruments in Dr. Chesler's lab which need to be identified, reconditioned, and assembled into a working system that noninvasively assesses systemic vascular impedance by measuring the pulse pressure with tonometry and blood flow with echocardiography. In addition, a diagram needs to be created depicting their functions and connectivity. The system needs to be assembled to do so with healthy volunteers [5].

2 BACKGROUND

Knowledge of the anatomy and physiology of the heart and vascular system is required in order to interpret the data gathered from the tonometry pulse pressure equipment. Understanding of the relevant information begins with the biology of the heart. For the purposes of this project, the left ventricle is responsible for the measured pulse pressure and impedance data. This is because the left ventricle pumps blood into the body and arteries [6]. The right ventricle on the other hand, pumps the unoxygenated blood to the lungs where gas exchange can occur [6]. For this reason, blood that exits the left ventricle is pumped through the systemic vascular system [6].

Since systemic vascular data is easier to gather than pulmonary data (measurements of pulmonary data require tampering with the organs in the chest cavity), doctors and scientists have created ways to gauge biomarkers for cardiovascular health simply by measuring systemic cardiovascular data [7]. An important measure of cardiovascular health is vascular impedance which is defined as the ratio of the blood pressure waveform and the local blood flow waveforms

[8]. However, these measurements are not easy to obtain noninvasively. Usually, pressure waveforms are replaced with distension (changes in diameter of the vessels) so as to make the calculation easier [7].

Understanding impedance requires a more in-depth understanding of the biomechanical properties blood vessels and how they relate to the mechanic properties of blood flow. One can begin to understand impedance by making an analogy between the cardiovascular system and an electrical circuit, an assumption made in the Windkessel model [source involving the circuits]. However, the major distinction between these two systems is that cardiovascular impedance is opposition to oscillatory blood flow whereas the resistance in an electrical circuit is opposition to non-oscillatory blood flow [9]. This makes sense since the heart ejects blood periodically, causing corresponding periodic changes in pulse pressure at a certain point in the vessel.

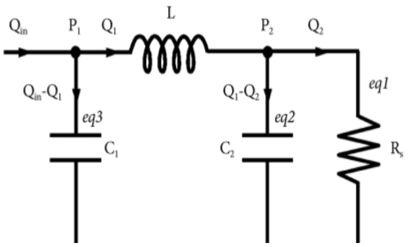
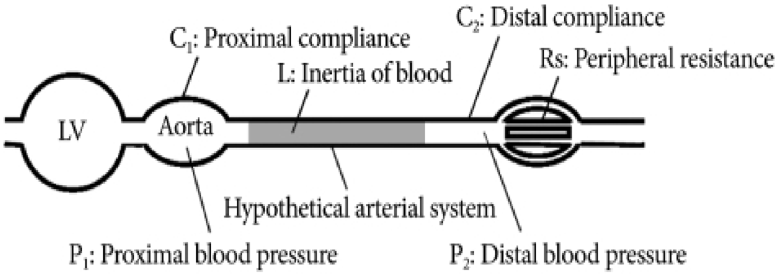
Characteristic impedance specifically, is related to the arterial stiffness of the vessel [9]. There is data to support that the stiffer an arterial wall is, the higher the amplitude of reflection of the pulse pressure is sent back to the heart [9]. This in turn increases the work that the heart has to do to eject the ventricular blood. It can be assumed that the higher characteristic impedance of a vessel is, the more work the vessel forces the heart to do [9]. Clinicians can use impedance to gather data about patient-specific heart load and make more accurate diagnoses [9].

The equation relating characteristic impedance is simple enough:

$$Z = \frac{\rho * F}{A},$$

where ρ= blood density, F = The propagation speed of the pulse (different from blood flow), and A = the cross sectional area of the vessel.

In order to simplify calculations of impedance, the Windkessel model for vascular impedance can be used, which makes an analogy between the cardiovascular system and an electrical circuit. Below in **Table 1**, the compliance values of the vessels are treated as capacitors, the blood pressure values are treated as branching circuits, the inertia of the blood is treated as an inductor (this makes sense since the lighter the mass of an object, the more inclined the object will be to move when acted upon by a force), and the peripheral resistance provided by the vessels is treated as a resistor.

<table>
<tr><th colspan="2">Table 1</th></tr>
<tr><td>Electrical Circuit</td><td>Cardiovascular System</td></tr>
<tr><td>
</td><td>
</td></tr>
</table>

An important distinction to make here is the difference between vascular impedance and vascular resistance. Vascular resistance is a single value that conveys the instantaneous resistance to blood flow whereas vascular impedance is reported as a ratio of two functions [10]. Impedance is reported as a spectrum with frequencies on the x-axis and the corresponding modulus ratios associated with each frequency value. On the right in *Figure: 1* is an example of the way vascular impedance is reported. Modulus is defined as the amplitude of the harmonic. A harmonic is a mathematically derived sinusoidal wave taken from the pulsatile waveform [10]. The harmonics are multiples that represent increasing heart rate [11].

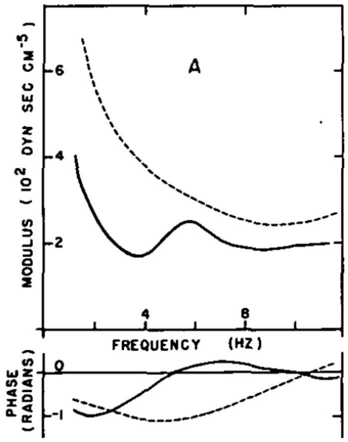


Figure 1. Example of impedance spectrum

Knowing the above information, research was performed to assess different components in regards to impedance. Relevant to our work is Nancy K. Sweitzer M.D, Phd. Sweitzer who is currently working as chief of the cardiology department at the University of Arizona College of Medicine - Tucson. Three years ago Dr. Sweitzer conducted several experiments using the pulse pressure and tonometric instruments the team must reutilize. Two of these studies include studying left ventricular responses to acute changes in late systolic pressure augmentation, and effects of the HeartMate II [12] left ventricular assist device as observed by serial echocardiography. A short summary of the instrument use in each of these studies gives information needed to further understand instrument function and may give the team ideas for conduction of future experiments.

When studying the left ventricular responses to acute changes in late systolic pressure augmentation in 2013, Sweitzer used the *cuff inflator* to obtain a base systolic and diastolic blood pressure. Using these readings, the calibration of the tonometric wave functions were performed. The transducer was then used to measure arterial tonometry from the brachial, radial, femoral, and carotid arteries. An electrocardiogram (*Acuson Sequoia)* was then used to measure the mitral flow, mitral relaxation, left ventricular out flow. Results were then digitized via CD-ROM and sent to a cardiovascular engineering lab for analysis [11]. In summary, the semi-automated computer-controlled cuff calibrated the system and the transducer and electrocardiogram collected experimental data. Together, these instruments produced digitized results for analysis and figures such as *Figure 2* above.

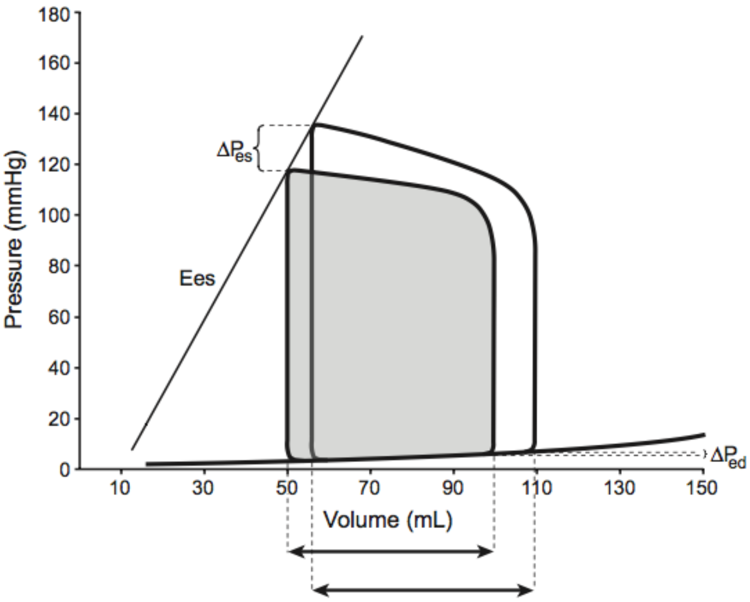


Figure 2. Shows an example of a graph that may be synthesized with the tonometric equipment [5].

When studying the effects of the HeartMate II in 2013, Sweitzer, Chapman, and Allana used serial echocardiography. Along with the instruments used when studying left ventricular responses to changes in systolic pressure augmentation, they used an echocardiography system called *NIHem* [2]. In the research methods and results, the explanation of the function of the *NIhem* device is brief, but includes measuring based off of the Doppler readings. This same technology was used, but not mentioned in the left ventricular response article [14]. In summary, the *NIHem* along with the Acuson Sequoia are used in real studies to measure ventricle size, ejection fraction, aortic valve thickening, and tricuspid regurgitation.

Dr. Naomi Chesler has a BS in general engineering as well as an MS in mechanical engineering, a PhD in medical engineering and a post-doctoral fellowship with Georgia Tech and Emory University. At UW-Madison, Dr. Chesler has been heavily involved with research in vascular biomechanics and hemodynamics.

3 DEVELOPMENT PROCESS

3.1 Methods

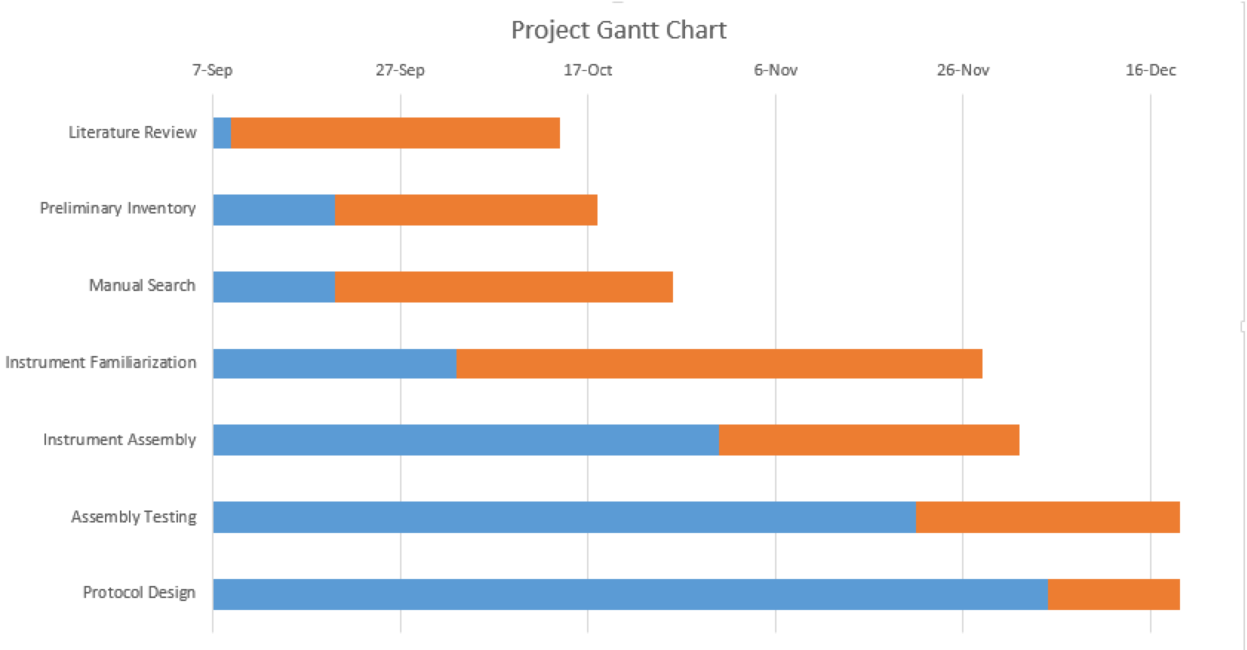


Figure 3. Project Gantt chart

3.1.1 Organizing and Preliminary Inventory

At the beginning of the project, the team was presented with all the instruments, cables, and sensors that left behind by Dr. Sweitzer. The team started off sorting the machines, untangling cables, and then organized the machines on a cart for future use. The team also started an inventory with any information we were able to find from each machine, including manufacturer, part, preliminary description, serial number, and notes, in which information such as missing parts was included. This information is found in Appendix 8.4.

3.1.2 Literature Review

Review of current literature was a lengthy process that took between 6-8 weeks because systemic vascular impedance is a relatively ambiguous and unused measurement. Many papers the team found inaccurately described impedance as vascular resistance, a possibility that Dr. Chesler predicted at the beginning of the semester. With Dr. Chesler helping clarify certain aspects of impedance, the team continued to revise the findings of impedance throughout the semester.

3.1.3 Manual Search

Many of the documents given to the team, including the data acquisition protocols that Dr. Sweitzer used, were not useful at the beginning of the semester because the team had not yet reassembled the machines. The team started searching for manuals for each machine using the information available. The search, for the most part, included emailing and calling manufacturers and looking at protocols from old research articles published by Dr. Sweitzer herself or other specialists in the field.

3.1.4 Instrument Assembly

During the literature review and manual search, the team started experimenting with the machines by somewhat randomly connecting cables and sensors (many of the discoveries about how the machines worked were made by trial and error). The machines were organized into three separate systems (discussed in section 4.2), according to their functions. The client had doubts about whether or not the *NIHem* Data Acquisition Tower was actually an ECHO machine. These doubts were confirmed in early November.

3.1.5 Assembly Testing

Assembly testing included trying to power on the machines and testing their functions. With the power source connected, the *NIHem* DAQ Tower was able to boot on. However, the *NIHem* DAQ Tower the computer was password protected, and the team could not find the password for about two weeks. Eventually the client provided the team with a correct password. Another obstacle was that the *NIHem* DAQ Docking Station would not power on, even with the power source correctly connected. Team member Callie Mataczynski took the power source home and her father, Mr. Kevin Mataczynski, an electrical engineer, examined the power source and found that the transformer was broken. The team ordered a new transformer with the help of the client, but did not have time to install and test it before writing this report.

3.1.6 Protocol Design

After learning how the assembled systems work, the team wrote a protocol for using the instruments so that the client can use the protocol to direct her research.

3.2 Obstacles

1. At the beginning of the project, the team was presented with many machines and tangled cords. It was hard to determine the connectivity of each cord and machine.
2. The *NIHem* Data Acquisition Tower is password protected. The team was not able to find documentation of the password at first.
3. The *NIHem* Data Acquisition Docking Station did not power on.
4. For an extended period of time the team mistakenly considered the *NIHem* DAQ Tower to be an ECHO machine, which works as a Doppler blood flowmeter. The client had doubts about whether or not the *NIHem* DAQ Tower was actually an ECHO machine. These doubts were confirmed in early November.

4 RESULTS

4.1 Inventory

The team took an inventory of every component received from Dr. Chesler and was put into a table that included the component's suspected use and its attributed instrument. This was an early goal of the team to catalogue every piece of the ensemble so that missing components could be discovered quickly. It also served to familiarize the team with the technical components used in hemodynamic analysis. The inventory was updated throughout the project duration. An up-to-date version of the inventory is included in Appendix 8.4.

4.2 Functions

In order to discover how impedance could be calculated from these instruments, the team first needed to understand the many functions offered by each instrument. By reading manuals and other clues left in Dr. Sweitzer's lab notes, the team found many physiological measurements that the instruments can acquire. Each of these measurements was researched to understand the importance and the mechanism by which each can be tested. The measurements that can be acquired by instrument functions are listed below.

Electrocardiogram (EKG)

Measures the electrical rhythm of the heart using four electrical leads placed on the skin. One lead is the ground and the other three detect electrical signals on the skin produced by the heart. From these signals P, QRS, and T waves can then be generated [15].

Single Lead Arterial Tonometer

A single lead tonometer is applied to an artery at a certain pressure to deform the artery.. It then measures the pressure due to the arterial expansion, which directly correlates to the blood pressure within the artery [16]. This means it's an acceptable representation of the pulsatile pressure waveform given calibration from sphygmomanometric measurements.

Oscillometric Blood Pressure

A blood pressure cuff inflates, completely occluding blood flow through the artery. The pressure of the cuff then begins to deflate. At a certain point, blood flows through the artery again. At this point sounds can be heard through the microphone indicating pressure waves overcoming cuff pressure (Korotkoff sounds). The pressure reading will also oscillate corresponding to the pulsatile pressure, the amplitude of which can be taken as the mean arterial blood pressure [17].

Photoplethysmogram (PPG)

Measures the change in volume of a vascular bed due to pulsatile blood flow using a blood oximeter. The oximeter transduces light across a vascular bed. The blood in those vessels absorb light, and therefore the transmitted light is directly related to the amount of blood in the bed. The PPG waveform varies not only with cardiac rhythms, but also respiratory and nervous activity. Nonetheless, valuable indications can be extracted from PPG waveforms [12].

Electromagnetic Blood Flow

Using an electromagnet, a magnetic field is established around an exposed blood vessel. Blood flow induces a voltage which is then sensed by stationary leads on each side of the blood vessel. Blood flow and velocity are then measured as the change in magnitude of the field due to charged particles flowing through the vessel [18]. This is an invasive procedure, as the meter probe needs to be applied directly around the vessel.

Auscultatory Blood Pressure

Using a cuff and stethoscope, the systolic and diastolic blood pressures in a vessel can be measured by relieving cuff pressure from above expected systolic pressure to below diastolic pressure and listening for Korotkoff sounds [17].

Doppler Ultrasound

A transducer sends ultrasonic waves into arteries which reflect off of red blood cells. The reflected waves are then sensed by the transducer and blood flow wave is measured. The velocity of the flow wave can be taken as

$$u = \frac{a\,|fs - fo|}{2\,cos(\theta)\,fo}$$

where u is the velocity of blood flow, a is the speed of sound, fo and fs are transmitted and received frequencies, respectively, and θ is the angle of incidence [16].

4.3 Instruments

Once the functions of each instrument were understood, the team organized the instruments that could work in conjunction into systems. The systems are shown in the block diagrams below in *Figure 4*.

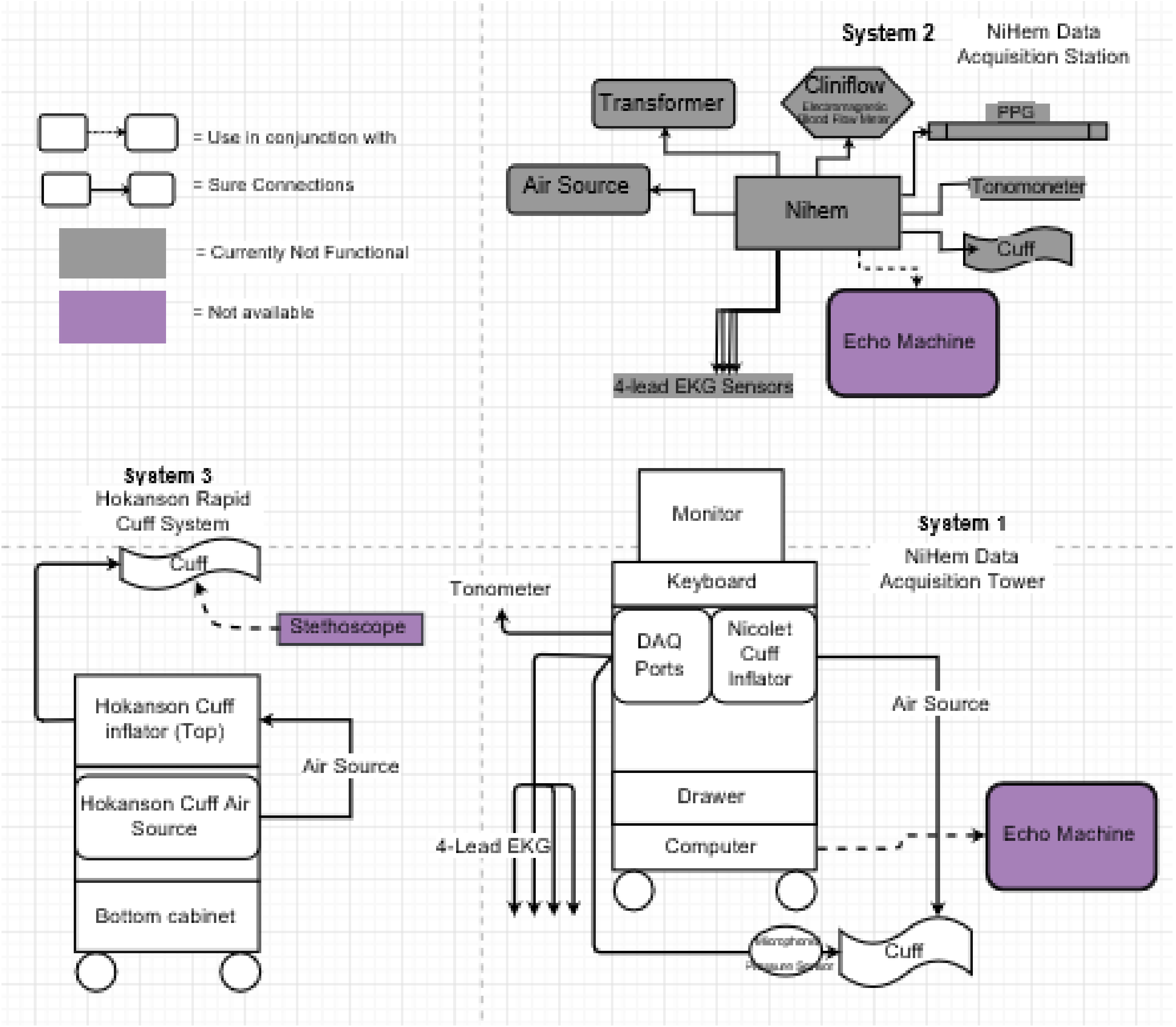


Figure 4. Block Diagram of the instruments

4.2.1 System 1 *NIHem* DAQ Tower

- 4-lead EKG
- Single Lead Arterial Tonometer
- Blood Pressure Cuff + Microphone - oscillometric blood pressure
- Doppler Ultrasound for Doppler flow wave

4.2.2 System 2 *NIHem* DAQ Docking Station

- 4-lead EKG
- Single Lead Arterial Tonometer
- Photoplethysmogram (PPG)
- Blood Pressure cuff + microphone - oscillometric blood pressure
- Carolina Medical Cliniflow II - electromagnetic flowmeter
- Doppler Ultrasound

4.2.3 System 3 Hokanson Rapid Cuff System

- Hokanson Rapid Cuff Inflator
- Hokanson Air Source
- Stethoscope - auscultatory blood pressure

4.4 Calculation of Impedance

The non-invasive procedure for the calculation of systemic vascular impedance (aortic input impedance) was found in a 1999 paper comparing the efficacy of the non-invasive procedure to the traditional invasive one [19]. The procedure requires: tonometric pulse pressure waveforms from right brachial and right common carotid arteries, sphygmomanometric pressure from the right brachial artery, EKG, pulsatile flow waveform from the left ventricular outflow tract (LVOT) gathered by Doppler ultrasound. The calculation of systemic vascular impedance can then be approximated as:

$$Z_{in}(n)=M_p(n)/M_f(n)\ ;\ \phi_z(n)=\phi_p(n)-\phi_f(n)$$

Where M_p and M_f are the modulus of the pressure and flow waveforms, respectively, at harmonic n in the frequency domain.

An additional non-invasive procedure for the characteristic impedance, that is the impedance of any vessel in a local area, was found in a 2016 paper [16]. This calculation requires: tonometric pulse pressure waveform, the applanation pressure of the tonometer, and a pulsatile flow waveform gathered by Doppler ultrasound from adjacent regions of the vessel. Using these measurements, characteristic impedance can be calculated as:

$$Z_c=1/A\cdot(dP/du)$$

where A is the area of the vessel and dP/du denotes the change in pressure (P) with respect to the change in flow (u).

5 DISCUSSION

5.1 Cliniflow and Doppler Echocardiogram with Respect to Impedance Calculations

An important calculation the team considers in respects to impedance is the measurement of blood flow and velocity. To gather this set of information, there are two machines within the systems that do so; namely, the Cliniflow (electromagnetic blood flowmeter) and the Doppler echocardiograph. At the ending point of this task, the team does not have the cliniflow working. The cliniflow also has ethical considerations outlined below in section 5.2. The Doppler echocardiograph on the other hand measures flow non-invasively. The team was unable to get results from the Doppler machine, however, because the Doppler's acquisition device (the *NIHem*) was not working within the slotted time.

5.2 Ethical Considerations

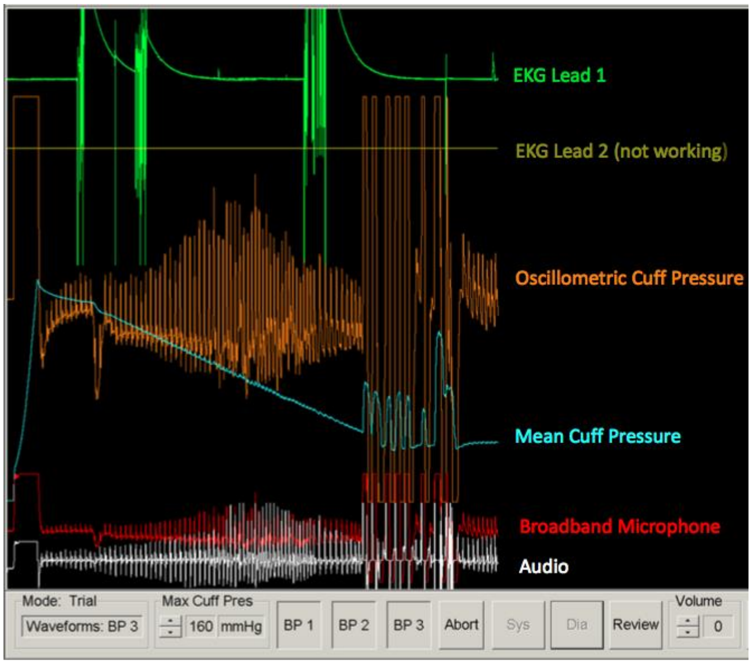
When collecting data for Impedance calculations, specifically blood flow, the level of invasiveness needs to be considered for its ethical ramifications. To obtain blood flow a Doppler Echocardiography or an Electromagnetic Blood Flowmeter (EMF) could be used as explained in 5.1.

A Doppler Echocardiography uses a noninvasive procedure; only involving patients to remove clothing and jewelry and lie down in a supine position. A transducer is then placed on arteries throughout the body. The patient is able to resume normal activity after the procedure. There are no ethical ramifications to consider in this procedure, unlike the EMF.

Measuring blood flow through an EMF involves placing a probe around an exposed artery. Surgery is required in order to expose an artery. Involving anesthesia, incision, and recovery, such a surgery poses a risk on patients health and is an ethical consideration that cannot be overcome by the team; meaning, the team will not look towards the Cliniflow to measure blood flow.

5.3 Potential Sources of Error When Measuring With Nicolet Machines

A source of error the team found occurred when collecting blood pressure measurements from the Nicolet Cuff Sensor. In *Figure 5* below, one can see that there is a lot of noise in the latter part of the graph. During this collection time, there was brachial muscle contractions by the subject; thus leading to inaccurate results and the noise seen on the graph. When conducting graphs in the future, explicit directions to hold still during the test must be given.



Mode: Trial

Waveforms: BP 3

Max Cuff Pres 160 mmHg

Volume 0

Figure 5. Graph of Data Collected from the Nicolet Cuff Sensor and Cuff Inflator

6 CONCLUSIONS

6.1 Conclusion

Dr. Chesler tasked our team with reutilizing biomedical equipment in order to measure system vascular impedance and with creating a schematic that can accurately and neatly summarize the connectivity and function of each instrument. In the process, the team successfully assembled two functional systems, System 1 and System 3 (shown in the schematic in section 4.2, *Figure 4*). With the systems assembled, the team is able to noninvasively take simultaneous EKG, pulse pressure, and sphygmomanometric data, with the exception of one faulty EKG lead in System 1. The client is now aware of the capabilities of the instruments, as well as what instruments are missing. For example, System 1 is missing an ECHO Doppler

Ultrasound machine for blood flow measurement, and System 3 is missing a stethoscope for blood pressure measurement. Also, the team produced a user protocol for the client that guides the use of the machines (section 8.2 Instrument Guide).

6.2 Future Work

There is still much work to do on this project before it can be used by Dr. Chesler for her research. As indicated in the instrument guide (Appendix 8.2) and inventory (Appendix 8.4), some of the instruments are still missing parts or need parts replaced. Specifically, the *NIHem* DAQ Station air source needs to be diagnosed, and the *NIHem* DAQ Tower's EKG leads should be replaced. Additionally, Cardiovascular Engineering Inc. has been contacted by the team to procure a manual for the *NIHem* DAQ Tower system, but contact must be maintained with the company in order to assure its arrival. Once the noted instruments are fixed completely, the accuracy of each measurement mode must be assessed by cross checking acquired data with verified instruments. Additionally, the Doppler Ultrasound system will have to be acquired by the lab or team to facilitate the impedance measurement. The viability of the procedures for measuring impedance must then be assessed. From our understanding of the instruments, both impedance measurements reported could be acquired, but functionally there could be a misunderstanding or logistic problem that disallows for impedance procedure. If the procedure is possible, it would then be important to verify that the impedance values are reasonable and accurate. Once these things are established, biomarker research can commence using the instruments. It is the team's understanding, however, that Dr. Chesler will be using a newer, more compact system in her lab for impedance measurement. As Dr. Yen suggested in our poster presentation, a more compact software package could even be designed to assess impedance without the need for the bulky equipment the team was given.

7 REFERENCES

1. U.S. Department of Health & Human Services, "Deaths, percent of total deaths, and death rates for the 15 leading causes of death in 5-year age groups, by race and sex: United States, 1999-2014", Federal Register, 2016.
2. N. Chesler, "VTB-Research", Vtb.bme.wisc.edu, 2016. [Online]. Available: http://vtb.bme.wisc.edu/research.html. [Accessed: 18- Oct- 2016].
3. C. Vlachopoulos, P. Xaplanteris, V. Aboyans, M. Brodmann, R. Cífková, F. Cosentino, M. De Carlo, A. Gallino, U. Landmesser, S. Laurent, J. Lekakis, D. Mikhailidis, K. Naka, A. Protogerou, D. Rizzoni, A. Schmidt-Trucksäss, L. Van Bortel, T. Weber, A. Yamashina, R. Zimlichman, P. Boutouyrie, J. Cockcroft, M. O'Rourke, J. Park, G. Schillaci, H. Sillesen and R. Townsend, "The role of vascular biomarkers for primary and secondary prevention. A position paper from the European Society of Cardiology Working Group on peripheral circulation", *Atherosclerosis*, vol. 241, no. 2, pp. 507-532, 2015.
4. F. Londoño, P. Segers, P. Shiva-Kumar, S. Peddireddy and J. Chirinos, "Sublingual nitroglycerin in patients with heart failure and preserved ejection fraction: Impact on central and regional carotid and radial input impedance and hemodynamics", Artery Research, vol. 8, no. 4, p. 147, 2014.
5. N. Chaudhry, I. Baumgart, Y. Ma, C. Mataczynski and C. Naxi, "Project Design Specification: Impedance/Tonomety System", 2016.
6. “Anatomy of the Heart - Texas Heart Institute Heart Information Center", *Texasheart.org*, 2016. [Online]. Available: http://www.texasheart.org/HIC/Anatomy/anatomy2.cfm. [Accessed: 19- Oct-2016].
7. "Magnetic Flow Meters", *Omega.com*, 2016. [Online]. Available: http://www.omega.com/prodinfo/magmeter.html. [Accessed: 19- Oct- 2016].
8. P. Brands, A. Hoeks, M. Rutten and R. Reneman, "A noninvasive method to estimate arterial impedance by means of assessment of local diameter change and the local center-line blood flow velocity using ultrasound", *Ultrasound in Medicine & Biology*, vol. 22, no. 7, pp. 895-905, 1996.
9. N. Sweitzer, S. Hetzel, J. Skalski, M. Velez, K. Eggleston and G. Mitchell, "Left Ventricular Responses to Acute Changes in Late Systolic Pressure Augmentation in Older Adults", *American Journal of Hypertension*, vol. 26, no. 7, pp. 866-871, 2013.
10. W. Milnor, "Arterial impedance as ventricular afterload", *Circulation Research*, vol. 36, no. 5, pp. 565-570, 1975.
11. N. Chesler, "Meeting with Ian Baumgart", 2016.
12. A. Alian and K. Shelley, "Photoplethysmography", ScienceDirect.com, 2016. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1521689614000755. [Accessed: 14-Dec- 2016].
13. C. Chapman, S. Allana, N. Sweitzer, T. Kohmoto, M. Murray, D. Murray, M. Johnson and P. Rahko, "Effects of the HeartMate II Left Ventricular Assist Device as Observed by Serial Echocardiography", *Echocardiography*, vol. 30, no. 5, pp. 513-520, 2013.
14. Chirinos, J.A. J. of Cardiovasc. Trans. Res. (2012) 5: 243. doi:10.1007/s12265-012-9359-6
15. "Electrocardiogram - NHLBI, NIH", Nhlbi.nih.gov, 2016. [Online]. Available: https://www.nhlbi.nih.gov/health/health-topics/topics/ekg/. [Accessed: 14- Dec- 2016].

16. Y. Kato et al., “Noninvasive simultaneous measurement of blood pressure and blood flow velocity for hemodynamic analysis,” 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Orlando, FL, 2016, pp. 2570-2573. doi: 10.1109/EMBC.2016.7591255
17. Y. Genç, Ş. Altunkan, O. Klnç and E. Altunkan, "Comparative study on auscultatory and oscillometric methods of ambulatory blood pressure measurements in adult patients", Blood Pressure Monitoring, vol. 13, no. 1, pp. 29-35, 2008.
18. Carolina Medical Technical Staff, Operator's Handbook for the Cliniflow II, Model FM701D, Carolina Medical Electronics, Inc. 1981
19. R. Kelly and D. Fitchett, "Noninvasive determination of aortic input impedance and external left ventricular power output: A validation and repeatability study of a new technique", Journal of the American College of Cardiology, vol. 20, no. 4, pp. 952-963, 1992.

8 APPENDIX

8.1 Product Design Specification

Function

The primary goal of this project is to reutilize a system of instruments previously used for research, but have since been unused and their procedures forgotten. These instruments can probe multiple aspects of the cardiovascular system and were used to research the efficacy of cardiovascular biomarkers as metrics of cardiovascular health. A secondary goal is to subsequently develop a protocol to use these instruments to measure impedance and other cardiovascular metrics. The instruments collectively determine pulsatile pressure for systemic vascular impedance only (pulmonary impedance requires a more invasive procedure). The instruments have to produce an accurate reading of the impedance to systemic blood flow.

Client Requirements

The client, Professor Chesler, wants the disused equipment from Dr. Nancy Sweitzer’s experiments to be assessed and reutilized for use in her research. Dr. Chesler has asked us to investigate how the machines are able to measure systemic vascular impedance (or aortic input impedance). Assessment of the machines includes:

- An inventory of the components of each device and the devices themselves
- A manual outlining the integration of the components and how they operate
- An assessment of the accuracy of data the devices collect

A manual was provided that describes the function and set-up for one of the instruments. Any equipment provided must have a surface or surfaces that can be wiped down easily.

Design Requirements

1. Physical and Operational Characteristics

A. Performance Requirements

The instruments will be involved with measure impedance of the systemic vascular system. Based on literature research on Nancy Sweitzer, described later in this document, as well as independent research, the team will be able to determine the frequency of device use and the loading/unloading patterns.

B. Safety

Until it is determined how to safely use each instrument by finding and reviewing each device's instruction manual, the team will use utmost precaution when handling each device. Gloves will be worn and all electromagnetic sensitive equipment (e.g. pacemakers) will be kept away from radiological equipment such as the Doppler ultrasound until exact dangers can be assessed in instruction manuals.

C. Accuracy and Reliability

There are not yet available sample data for the instruments. The team will try to obtain sample data and communicate with the client for an acceptable range of error. The system to be designed will be strictly for screening purposes only, and will not serve as a diagnostic device. Therefore, slightly larger error margins will be tolerated.

D. Life in Service

This system must be able to withstand testing and data collection 8 hours a day anywhere from 1-7 days per week. There is no distance this system needs to travel at the present time. This system has been in use already for an unknown amount of time.

E. Shelf Life

The shelf life conditions include a lab setting. While in storage dust and dirt may collect. The batteries of this device may eventually corrode, however the amount of time of this occurring is unknown. Note, the batteries, wiring, and circuitry to some components of this system may already be damaged.

F. Operating Environment

The system must be able to handle lab conditions. This includes standard room temperature, pressure, and humidity. It also must endure sanitation by means of spray and cloth or sanitation wipes.

G. Ergonomics

The system must be easy to operate, requiring no strain or discomfort. The instruments will be assembled on carts so that all necessary buttons, switches, instruments, etc. are easily within reach from a standing position and do not require bending or heavy lifting to access.

H. Size

The intended size of the device will be/ should be the same as outlined in the blueprints of the original device. Based on observation of the devices, most of the instruments are large enough to require carts to be transported. Once an inventory of the lab is complete, more information will be provided in this category.

I. Weight

The devices are heavy enough to require carts to transport. Modern ECHO instruments are typically portable and require little maintenance(1). However, close examination of the ECHO instrument in the lab revealed that it required multiple separate components, all of which were loaded on a cart. Information on the identity of the other devices wasn’t provided by the client.

J. Materials

All the parts for the instruments either already exist or need to be replaced with the original model. Therefore we do not need to determine whether a material can be used in the design, as long as the existing parts work or the replacement parts are the same as the original ones.

2. Production Characteristics

A. Target Project Cost

The entire system reassembly should not cost no more than the price of replacement parts. Dr. Chesler has not set a budget, but it is the objective of the project to repair rather than replace as many components as possible. Some components will inevitably need to be replaced, which should be the only cost associated with the project.

3. Miscellaneous

A. Standards and Specifications

For this project U.S. regulations regarding electrical equipment standards as well as medical equipment standards will need to be considered. The electrical equipment standards that will be followed fall under Occupational Safety and Health Administration (OSHA) regulations Subpart S(2). Regarding medical equipment regulation, the project is subject to the U.S. Food and Drug Administration's (FDA) Code of Federal Regulation (CFR) Title 21 Subchapters H(3) and J(4). Each instrument in the assembly will be verified against recall and obsolescence. The course of this project will unlikely require any modifications to any of the instruments, which would require much more in-depth evaluation of these standards. Regulations for human subject testing are also to be considered when developing a protocol for using these instruments. CFR Title 45 Part 46(5) and 690(6) and must be approved by an Institutional Review Board before studies may commence. Patient information must be stored securely vis a vis HIPAA Privacy Rule and Security Rule delineated in CFR Title 45 Parts 160(7) and 164(8).

B. Patient Related Concerns

The device will need to meet the standard requirements for sterility before each test vis a vis CFR(3,4). The comfort of the patient during potential testing is also important, but patient testing, but patient procedures are outlined in one of Dr. Sweitzer's research publications noted below. If there is human testing within this project, the collected data will need to be stored in a secure database that comply with HIPAA regulations regarding patient privacy(7,8).

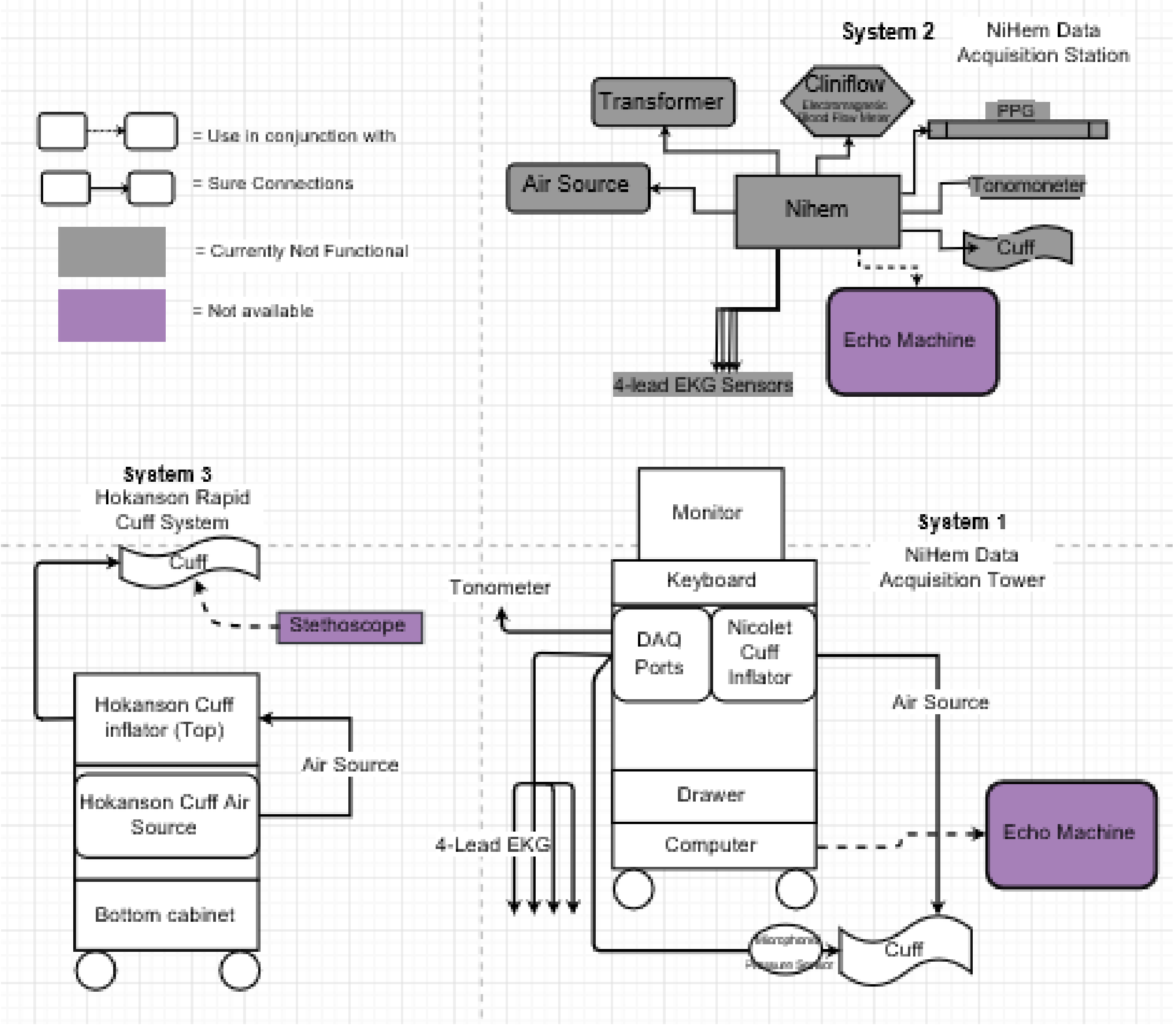
C. Background

Previous research with these instruments had been conducted by Nancy Sweitzer, M.D., who left the University of Wisconsin in 2014. A review of her publications(9,10,11) has revealed some information about the methods used by Dr. Sweitzer. One particularly enlightening publication(9) aims to determine a causative relationship between late systolic aortic pressure augmentation, measured by central augmentation index (AI), and myocardial diastolic performance, measured by lateral annular mitral velocity. In *Methods,* the procedure includes measuring blood pressure using a cuff apparatus, measuring arterial tonometric waveforms using a custom transducer, possibly one of the instruments in Dr. Chesler's lab, as well as using a Doppler electrocardiogram to measure mitral inflow. AI and lateral annular mitral velocity can be calculated using these three measurements as described in *Data/statistical Analysis*. The conclusions from the study determine that AI is not a strong determinant for poor heart health and that other metrics should be explored. Though this article does not provide immediate direction for the protocol design, it does indicate which instruments were used in Dr. Sweitzer's research.

References

1. "Siemens Acuson CV70 Cardio-Vascular ultrasound machine," Sale Medical. [Online]. Available:http://www.sale-medical.com/products/Siemens-Acuson-CV70-Cardio%252dVascular-Ultrasound-Machine.html. Accessed: Sep. 24, 2016.
2. Electrical, 1910 OSHA §1910.301-399 2016.
3. Medical Devices, 21 C.F.R. §21.800-898 2016.
4. Radiological Health, 21 C.F.R. §21.1000-1050 2016.
5. Protection of Human Subjects, 45 C.F.R. §46.101-505 2016.
6. The Common Rule for the Protection of Human Subjects, 45 C.F.R. §690.101-124 2016.
7. General Administrative Requirements, 45 C.F.R. §160.101-552 2016.
8. Security and Privacy, 45 C.F.R. §164.102-534 2016.
9. Sweitzer, Nancy K. et al., "Left Ventricular Responses to Acute Changes in Late Systolic Pressure Augmentation in Older Adults," American Journal of Hypertension, 26(7) 866-871, March 2013. DOI: 10.1093/ajh/hpt043
10. Givertz, Michael M. et al., “Acute Decompensated Heart Failure: Update on New and Emerging Evidence and Directions for Future Research,” *Journal of Cardiac Failure*, 19(6) 371-389, June 2013. http://dx.doi.org.ezproxy.library.wisc.edu/10.1016/j.cardfail.2013.04.002
11. Sweitzer, Nancy K. et al., “Comparison of Clinical Features and Outcomes of Patients Hospitalized With Heart Failure and Normal Ejection Fraction (≥55%) Versus Those With Mildly Reduced (40% to 55%) and Moderately to Severely Reduced (<40%) Fractions,” *The American Journal of Cardiology*, 101(8) 1151-1156, April 2008. http://dx.doi.org.ezproxy.library.wisc.edu/10.1016/j.amjcard.2007.12.014

8.2 Instrument Guide



System Diagram

1. System 1 *NIHem* Data Acquisition Tower

1.1 Setup

- Plug in and switch on the instruments (two switches behind the tower, one on computer)
- Connect EKG lead matrix to the leftmost port on the front of the left box
- Connect the tonometer (small black probe with white pad) to the middle port on the left box
- Connect the cuff microphone to the right port on the left box
- Connect the cuff air catheter to the top left port on the right box
- See *NIHem* manual pp. 3

1.2 Measurement Capabilities

1.2.1 Oscillometric Blood Pressure with EKG

- Procedure
    - See *NIHem* Operator’s Manual pp. 4
    - See *NIHem* User Notes pp. 1
- Equipment
    - BP cuff + microphone
    - Blue EKG leads

1.2.2 Tonometry

- Procedure
    - See *NIHem* Operator’s Manual pp. 8
    - See *NIHem* User Notes pp. 5
- Equipment
    - Low profile tonometers with large port adapters

1.2.3 Transthoracic Echocardiogram

- Procedure
    - See *NIHem* Operator’s Manual pp. 10
    - See *NIHem* User Notes pp. 28
- Equipment
    - Ultrasound system

1.2.4 Doppler Echocardiogram

- Procedure
    - See *NIHem* Operator’s Manual pp. 11
    - See *NIHem* User Notes pp. 28
- Equipment
    - Ultrasound system

1.2.5 Transit Distances

- Procedure
    - See *NIHem* Operator’s Manual pp. 12
    - See *NIHem* User Notes pp. 24
- Equipment
    - Tape measure

1.2.6 Brachial Reactivity

- Procedure
    - See *NIHem* Brachial Reactivity Acquisition pp. 39
- Equipment
    - Ultrasound system

1.3 Notes

The trace labelled "lead II" from the EKG does not respond to lead stimulation. This still needs full diagnosis. The 3-ring bound "*NIHem* Manual, User Notes" was not written for this system, but many of the protocols are applicable to the DAQ Tower as well as the DAQ Station. Notable functional differences are that the Tower provides additional Brachial Reactivity measurement, but does not include PPG or invasive measurement capabilities. Brachial Reactivity protocols are found in the manilla folder. This instrument should only be used in a research setting and is not clinically viable (as per the sticker on the tower).

System 2 *NIHem* Data Acquisition Station

2.1 Setup

- Plug in *NIHem* docking station through the transformer (grey metal box)
- Dock the Dell laptop on the *NIHem* docking station
- Connect all leads to the labelled ports
- See *NIHem* manual pp. 3

2.2 Measurement Capabilities

2.2.1 Oscillometric Blood Pressure with EKG

- Protocol
    - See *NIHem* Operator's Manual pp. 4
    - See *NIHem* User Notes pp. 1
- Equipment
    - Blood pressure cuff + microphone
    - *NIHem* air source
    - Black EKG leads

2.2.2 Tonometry

- Protocol
    - See *NIHem* Operator’s Manual pp. 8
    - See *NIHem* User Notes pp. 5
- Equipment
    - Low profile tonometer with small port adapter

2.2.3 Photoplethysmogram

- Protocol
    - See *NIHem* Operator’s Manual pp. 9
    - See Hokanson Rapid Cuff Inflator Manual pp. 4
- Equipment
    - Blood oximeter strip
    - System 3

2.2.4 Transthoracic Echocardiogram

- Protocol
    - See *NIHem* Operator’s Manual pp. 10
    - See *NIHem* User Notes pp. 28
- Equipment
    - Ultrasound system

2.2.5 Doppler Echocardiogram

- Protocol
    - See *NIHem* Operator’s Manual pp. 11
    - See *NIHem* User Notes pp. 28
- Equipment
    - Ultrasound system

2.2.6 Transit Distances

- Protocol
    - See *NIHem* Operator’s Manual pp. 12
    - See *NIHem* User Notes pp. 24
- Equipment
    - Tape measure

2.2.7 Invasive Blood Pressure

- Procedure
    - See Invasive Calibration Procedure

- Equipment
    - Millar BP catheter
    - Tableside Invasive *NIHem* box

2.2.8 Invasive Blood Flow

- Procedure
    - See Invasive Calibration Procedure
- Equipment
    - Carolina Medical Cliniflow II

2.3 Notes

The system has never been turned on because the transformer (grey metal box) needed a new component (purchased). The air source this system is also broken and needs a full diagnosis. The 3-ring bound manual entitled "*NIHem* Manual, User Notes" corresponds specifically to this system. This instrument should only be used in a research setting and is not clinically viable (as per the *NIHem* manual).

System 3 Hokanson Rapid Cuff System

3.1 Setup

- Plug in both machines using the grey power cords
- Connect the air outlet on the bottom machine (air source) to the air inlet to the top machine (rapid cuff inflator) using the black plastic hose
- Connect grey cuff hose to air outlet on top machine (rapid cuff inflator)
- Connect a cuff and the plastic plug or two cuffs to the y-joint of the grey cuff hose
- Connect foot switch to the back of the rapid cuff inflator
- Turn on the switches on both machines
- See Rapid Cuff Inflator Manual pp. 2

3.2 Measurement Capabilities

3.2.1 Auscultatory Blood Pressure

- Procedure
    - See Hokanson Rapid Cuff Inflator Manual pp. 4
- Equipment
    - Stethoscope
    - Cuff

3.2.2 Plethysmogram

- Procedure
    - See *NIHem* Operator's Manual pp. 9
    - See Hokanson Rapid Cuff Inflator Manual pp. 4
- Equipment
    - Cuff
    - System 2
    - Strain gauge plethysmograph

3.3 Notes

A stethoscope is not provided that would be required to measure auscultatory blood pressure. The Rapid Cuff Inflator manual suggests using a strain gauge plethysmograph (not provided) for plethysmogram data acquisition, but the blood oximeter strip from System 2 could be used instead.

Measurements

1. Aortic Input Impedance

This procedure was found in the 1999 paper by Kelly, R. and Fitchett, D. 1999 that compared the efficacy of a novel noninvasive measurement of impedance against the invasive method. The calculation can be acquired using either System 1 or System 2. This list should not be used as a procedure, but rather a guideline for understanding how impedance can be calculated using the instruments above.

1. Acquire tonometric pulse wave recording of the right carotid artery with simultaneous EKG acquisition
2. Acquire tonometric pulse wave recording of the right brachial artery with simultaneous EKG acquisition
3. Acquire oscillometric blood pressure of the right brachial artery with simultaneous EKG acquisition
4. Average all brachial pulse waves and carotid pulse waves using EKG R peak as reference to find average waves for each artery
5. Assign peak and trough values of brachial pulse wave as systolic and diastolic pressures based on oscillometric blood pressure measurements
6. Integrate calibrated brachial pulse wave to find mean brachial pressure
7. Calibrate carotid pulse wave to brachial diastolic and mean pressure values - this will be used as the approximation of aortic pulse pressure wave

8. Acquire flow wave of left ventricular outflow tract (LVOT) using Doppler echocardiogram
9. Similarly average the LVOT flow waves
10. Align pressure and flow waves by shifting the foot of the pressure wave to onset of aortic flow
11. Convert pressure and flow waves to a Fourier series
12. Impedance at each harmonic can be taken as the modulus of the pressure divided by the modulus of the flow

2. Characteristic Impedance of Systemic Artery

This procedure was found in the 2016 paper by Kato, Y. et al. [2] that proposed a method to calculate characteristic impedance of an artery using simultaneous pressure and flow measurements. It is not confirmed that a single *NIHem* system can simultaneously record the two waveforms, but by using the *NIHem* station and *NIHem* tower in conjunction, the procedure should be possible.

1. Affix the low profile tonometer on the artery of interest and record applanation pressure. Optimal applanation pressure is expounded in the paper.
2. Affix the Doppler ultrasound probe just proximal to the tonometer
3. Simultaneously acquire pulse pressure and flow waveforms
4. Average each waveform without phase correction
5. Characteristic impedance can be taken as the change in pressure with respect to change in flow (dP/du) divided by the cross sectional area of the artery (which can be derived from the Doppler data)

<u>References</u>

1. R. Kelly and D. Fitchett, "Noninvasive determination of aortic input impedance and external left ventricular power output: A validation and repeatability study of a new technique", *Journal of the American College of Cardiology*, vol. 20, no. 4, pp. 952-963, 1992.
2. Y. Kato *et al*., “Noninvasive simultaneous measurement of blood pressure and blood flow velocity for hemodynamic analysis,” *2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, Orlando, FL, 2016, pp. 2570-2573. doi: 10.1109/EMBC.2016.7591255

8.3 Instrument Visual Aides

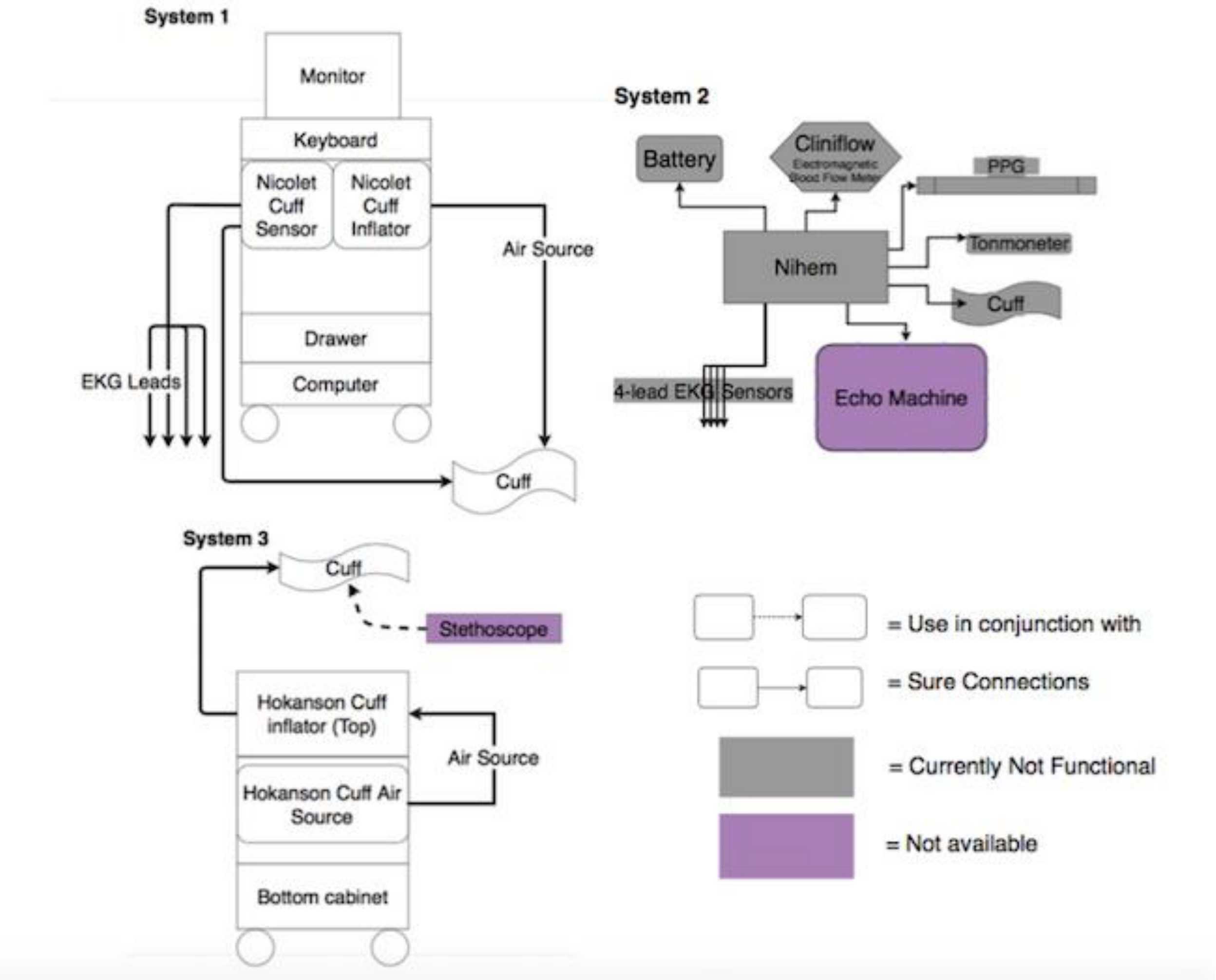


Figure 8.3.1. *NIHem* Data Acquisition Tower diagram

Figure 8.3.2. *NIHem* data acquisition tower

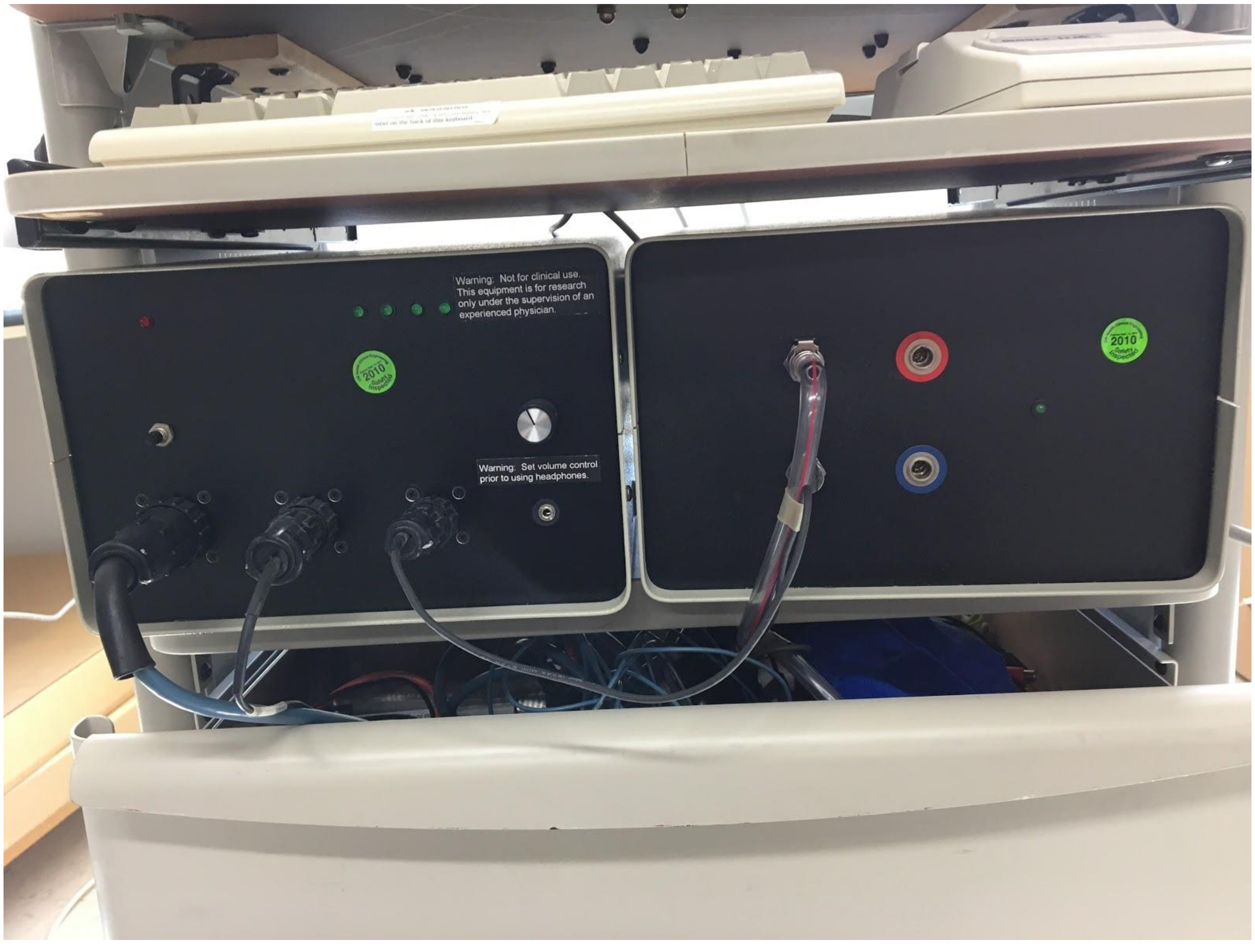


Figure 8.3.3. *NIHem* DAQ Tower components

Figure 8.3.4 Cliniflow II Blood Flowmeter

Figure 8.3.5. Rapid Cuff Inflator

8.4 Inventory

Manufacturer	Part	Description	Serial Number	Associated Machine	Notes
Hokanson	Rapid cuff inflator	Grey machine on top of black cart	8180623		manual in drawer of black cart
Hokanson	Cuff Inflator Air Source	Grey machine on lower shelf of black cart	9290613		
Cardiovascular Engineering	NiHem DAQ Station	Black docking station for a laptop with lots of labelled inputs			Missing Dell laptop needed for interface with the system
Cardiovascular Engineering	NiHem DAQ Tower	Tower cart with instruments, computer, and monitor on top			user: administrator ; pass: nihem
Carolina Medical Electronics Inc.	Cliniflow II	Model FM701D Electromagnetic Blood Flowmeter	004801A		Manual found
Cardiovascular Engineering Inc.	Invasive Tableside component	Black box with pressure input ports		NIHem DAQ Station	
	NiHem power transformer	grey metal box		NIHem DAQ Station	Transformer blown, Callie has replaced
Etronics	NiHem air source	grey metal box with fan exhaust		NIHem DAQ Station	Broken - needs full diagnosis
	Calibration chamber	clear plastic case with wires		NIHem DAQ Station	Protocol for calibration in NIHem binder
	Output hose	Gray tube with blue Y connector		Rapid cuff inflator	
	Black power cords (2)			Rapid cuff inflator	
	Low profile tonometers with small port plug (2)			NiHem DAQ Station	
	Low profile tonometers with large port plug (2)			NiHem DAQ Tower	
	Pulse oximeter strip			NiHem DAQ Station	
	Cuff with open hose			Rapid cuff inflator	
	Cuff with port adapter + mike			NiHem DAQ Station	
	Blue EKG leads			NiHem DAQ Tower	
	Black EKG leads			NiHem DAQ Station	
	Grey ultrasound transducer			Ultrasound machine	Ultrasound machine not currently available
	Bag of misc. A/V adapters				
	Tape measure	in drawer of black Hokanson cart		NiHem DAQ Tower/Station	
	Stopwatch	in drawer of black Hokanson cart		Rapid cuff inflator	