ABSTRACT

DEVELOPMENT OF AN fMRI COMPATIBLE LOWER BODY NEGATIVE PRESSURE SYSTEM

by
Pratap Singh Kunwar

The lower body negative pressure (LBNP) system provides a controlled, measured orthostatic stress to the cardiovascular system, which can be used with a magnetic resonance imaging (MRI) machine to study cardiovascular and cerebrovascular responses to graded LBNP. In the past, even though functional MRI (fMRI) was considered as one of the best modalities with which to measure small metabolic changes in the brain, it has not been used with an LBNP system to measure cerebrovascular changes. This was due to the lack of an fMRI compatible LBNP system.

In this project, an fMRI compatible LBNP system was first constructed without using any ferromagnetic materials. The LBNP system was then tested to verify its compatibility with an MRI system. Concurrently, a software program was also developed for data acquisition and analysis. Using the developed software, an electrocardiogram (ECG) and measurements of blood pressure, heart rate, chamber pressure and blood flow in the brain were collected at 3 minutes each of 0, -10, -20, -30, -40 and -50 mm Hg lower body suction to confirm the accuracy and the reliability of the developed system. The measured heart rate increased and changes of blood flow in the brain decreased with the graded LBNP. The results of this pilot study support the literature. It has been demonstrated that this newly developed LBNP system is fMRI compatible, accurate, safe to use, reliable and can be used to study cardiovascular and cerebrovascular responses to graded LBNP.

DEVELOPMENT OF AN fMRI COMPATIBLE LOWER BODY NEGATIVE PRESSURE SYSTEM

by
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DEVELOPMENT OF fMRI COMPATIBLE LOWER BODY NEGATIVE PRESSURE SYSTEM

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To my family and friends, who with their love and support have encouraged me through out my graduate studies.

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CHAPTER 1

INTRODUCTION

1.1 Objective

The lower body negative pressure (LBNP) exerts a controlled amount of negative pressure to the lower body in a stepwise fashion, which allows one to study a physiological interaction between the intensity of LBNP and lower body venous blood pooling and its effect on cardiac function. The functional Magnetic Resonance Imaging (fMRI) methodology is considered to be the best modality to measure changes in cerebral blood and metabolism non invasively with the high spatial and temporal resolution in the brain, but this technique has not been used with an LBNP system to measure cerebrovascular changes due to lack of an fMRI compatible LBNP system.

The objective of this thesis was to develop a fMRI compatible LBNP system. The fMRI compatible LBNP system can be used with an MRI machine to study cardiovascular and cerebral responses to graded lower body negative pressure.

A software program was developed using the Laboratory Virtual Instrument Engineering Workbench (LabVIEW) program for data acquisition and analysis [19]. When designing the MRI compatible LBNP system, MRI safety and compatibility of the device and its operation in the magnetic field was considered very carefully and verified.

The hardware component recorded two physiological signals -- Electrocardiogram (ECG) and Blood Pressure (BP) -- from the surface of the body and provided signal conditioning to make the signal suitable for recording. Blood pressure included systolic, diastolic, and mean arterial pressure (MAP). The hardware component also measured the

pressure inside the chamber using a pressure gauge.

The fMRI compatible LBNP system was constructed without using any ferromagnetic materials and then was tested for MRI compatibility. After fMRI compatibility was verified, the pilot experiment was conducted primarily to see whether the developed fMRI compatible system follows the general principle of the LBNP system which is as more blood is pooled towards the leg due to graded negative pressure, the blood flow towards the brain decreases and the heart rate increases to maintain the normal rhythm of the heart. Blood pressure, electrocardiogram (ECG), heart rate, chamber pressure and blood flow in the brain were collected to confirm the accuracy and the reliability of the developed system.

1.2 Background Information

1.2.1 Lower Body Negative Pressure

Several methods [5] have been considered in the past to investigate cardiovascular and cerebrovalscular responses to graded lower body negative pressure. The tilt table is one method (as shown in Figure 1.1) that has been used to evaluate how the human body regulates blood pressure in response to some very simple stresses. This method utilizes gravity to provide a challenge to the cardiovascular system.

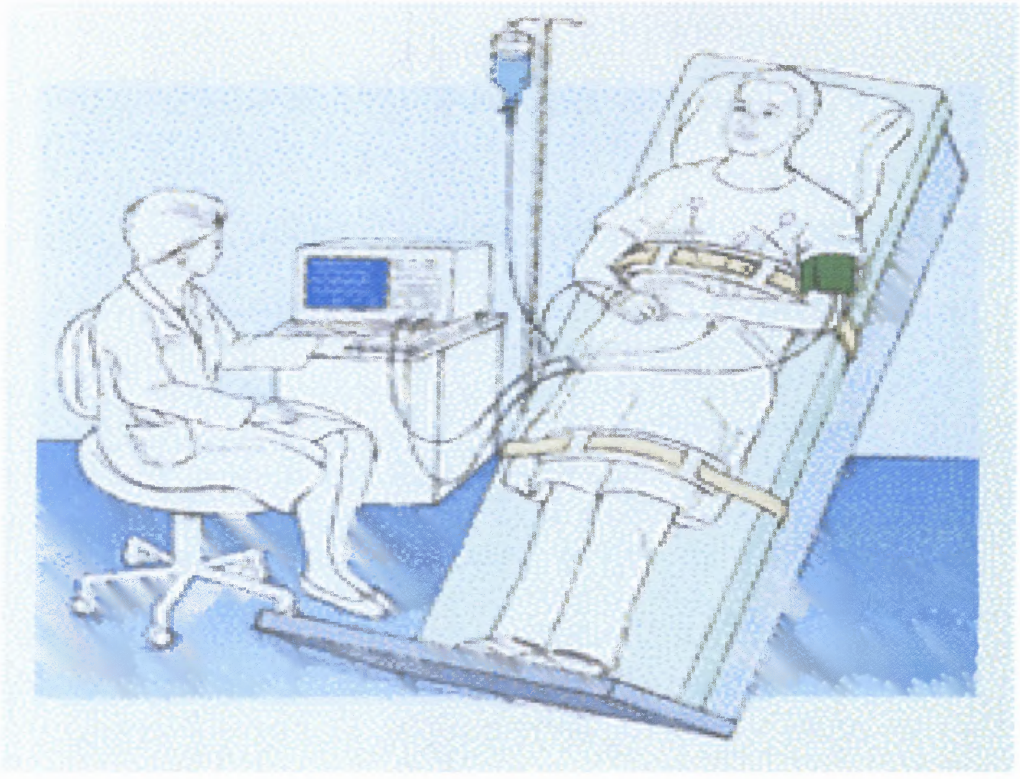

Figure 1.1 Tilt table.

The subject is instructed to lie down on a tilt table. A blood pressure cuff is placed on the arm and the ECG electrodes on the chest allow the doctor to monitor heart rhythm. Safety straps are applied across the chest and legs. The subject begins by lying supine and then after a baseline period they are tilted so that the head is almost upright (60 to 80 degrees). The subject is continuously monitored in the tilted position for up to 45 minutes and then returned to a flat position. The key to this procedure is that the subject does not use their leg muscles thus does not activate muscle contraction to aid the venous return of blood to the upper body. Gravity will then act to pool the blood in the lower body. The cardiovascular system's response to this challenge can then be analyzed. A major study [5] by the Johns Hopkins University demonstrated that the tilt table is not a useful tool for diagnosing heart pathologies in patients. It found no difference in sensitivity to tilt

between heart patients with heart disease and healthy control subjects. In contrast, the LBNP is a more controlled way of testing for cardiovascular problems because it uses suction on the lower limbs to produce a measurable stress. More importantly, the LBNP testing is much less stressful for the patient. Because of the advantages that LBNP provides over other standard techniques (e.g. stand tests, head-up tilt), it is a popular choice among physiologists who investigate the effects of fluid shifts on physiological functioning.

The LBNP has been used in physiological research since the late 1800s and became popular in the 1960s in the aerospace community as a method of physiologically simulating the effects of reentry and high-G stresses on the body [30]. Lower body negative pressure is the application of sub atmospheric pressure to the lower portion of the body. The lower portion of the body includes everything below the iliac crests. LBNP pulls more blood to the lower parts of the body from the heart as shown in Figure 1.2, thereby promoting a transient positive fluid balance resulting in an increase in vascular fluid. In healthy patients cessation of the LBNP quickly leads to return of the blood to normal circulation [28].

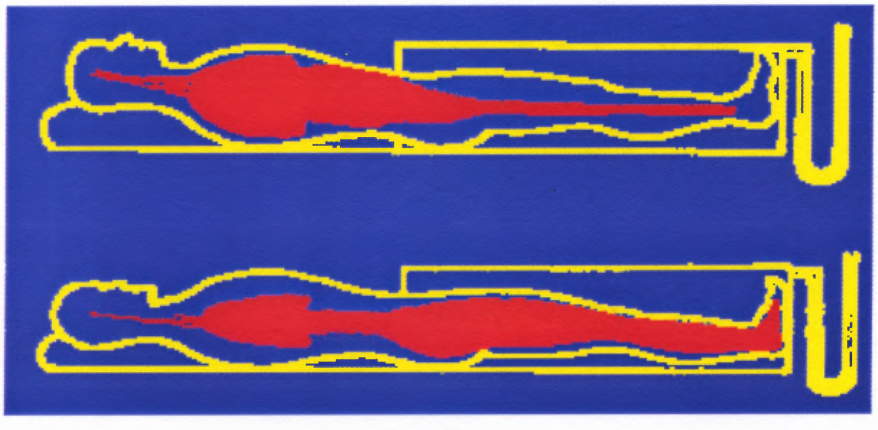

Figure 1.2 Blood flow changes in human body due to applied LBNP.

The non fMRI compatible LBNP device as shown in Figure 1.3 can be made of any materials that will withstand the pressure difference generated. The container, which encloses the lower portion of the body, can be made of wood, metal, or plastic. Windows or entry ports are often built into the device for access to the subject once they are placed inside. Some sort of support can prevent movement of the subject within the device once LBNP is applied. These restraints allow the subject to remain at rest rather than exert muscular forces that interfere with pooling of venous blood.

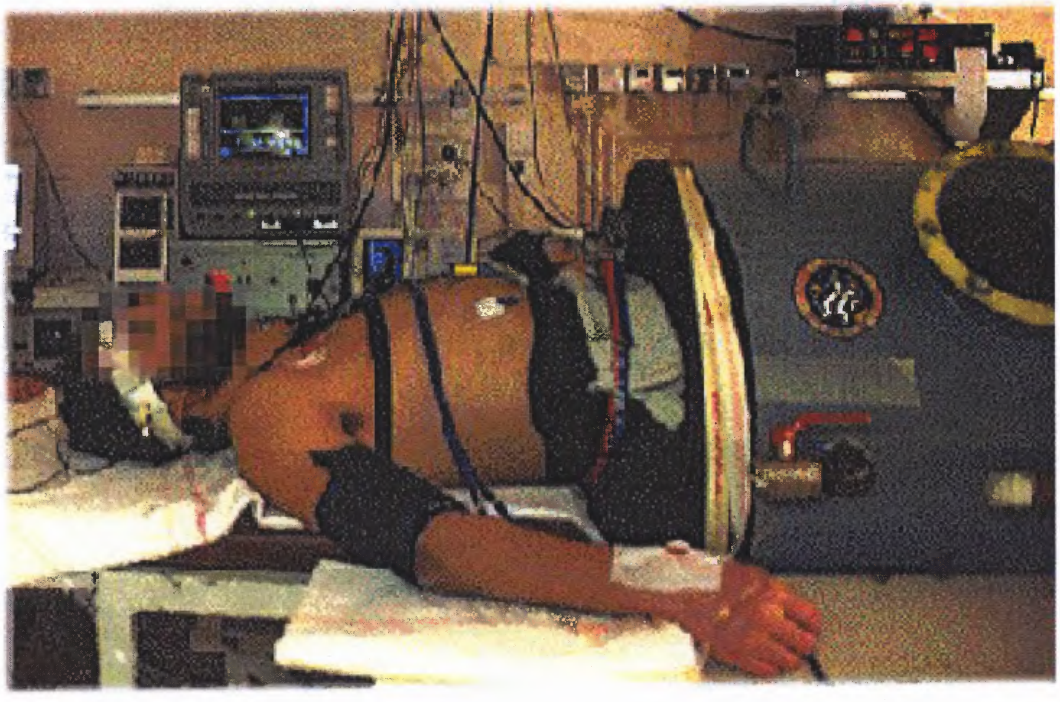

Figure 1.3 LBNP system [11].

An important aspect of the LBNP technique is the seal around the iliac crest portion of the abdomen. It must fit the particular shape of the subject and provide a seal for the development of negative pressure. Subatmospheric pressure is generated by a vacuum motor from a commercial or household vacuum cleaner. The level of negative pressure in the LBNP device can be monitored by pressure transducers located in the

LBNP device. The level of negative pressures covers a wide range, from -5 mm Hg to -100 mmHg and the duration of negative pressure can be from minutes to hours.

The LBNP system has been used in resting subjects and in exercising subjects. LBNP has also been used in animal studies in which rats were anesthetized or tranquilized. Recently, Investigators have used an LBNP device to generate positive pressures rather than negative pressures. The positive pressure translocates blood from the lower body to the thorax. LBNP has been used extensively over the last twenty-five years in investigations studying blood pressure. Because LBNP can lower both central venous pressure and arterial pressure, it is a good technique that elicits cardiovascular reflexes for blood pressure control [30].

1.2.2 Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) is a procedure that uses MRI to measure the quick, tiny metabolic changes that take place in an active part of the human brain. This technique not only allows one to look closely at the anatomy of the brain, but can also aid in determining precisely which part of the brain is handling critical functions such as thought, speech, movement, and sensation [21].

The most commonly used fMRI technique called BOLD fMRI (Blood-Oxygen-Level-dependent fMRI) is based on the differing magnetic properties of the oxygenated (diamagnetic) and deoxygenated (paramagnetic) blood. When an area of the brain becomes metabolically active, oxygen delivery to this site increases. The resulting oxygenated blood has different magnetic properties from deoxygenated blood. The BOLD fMRI is a relative technique in that it must compare images taken during one mental state versus another to create a functional image. The BOLD fMRI paradigms

generally have several periods of rest alternating with several periods of activation. It has been used extensively to indicate the anatomical site of neuronal activation in response to specific task demands. In this pilot experiment, the BOLD fMRI (Blood-Oxygen-Level-dependent fMRI) technique was used to measure cerebral blood flow in response to graded negative pressure [32].

Magnetic Resonance Imaging Signal Formations: Magnetic Resonance Imaging (MRI) uses radio waves (electromagnetic waves with radio frequency) and a strong magnetic field to provide clear and detailed pictures of internal organs and tissues of the human body [16]. The MRI is based on the physics of Nuclear Magnetic Resonance (NMR), a technique used by scientists to obtain microscopic chemical and physical information about molecules. The technique was called magnetic resonance imaging rather than nuclear magnetic resonance imaging (NMRI) because of the negative connotations associated with the word nuclear in the late 1970s [31].

The human body is primarily fat and water. Fat and water have many hydrogen atoms, which make the human body approximately 63% hydrogen atoms [20]. Hydrogen nuclei have an NMR signal. For these reasons, the magnetic resonance imaging primarily images the NMR signal from the hydrogen nuclei. The proton nuclei of hydrogen atom possesses a small magnetic moment when placed within a magnetic field; a torque will be exerted upon them, resulting in a slight energetic advantage of one orientation. These atoms in the human body react to the magnetic field by lining up with the field in an up or down direction. The machine then bathes a part of body in radio waves which are also harmless. These waves cause some of the hydrogen atoms to change the direction they are pointing. Finally, the radio waves are turned off. This allows the hydrogen atoms that

changed direction to return into alignment with the magnetic field. When they do, they give off energy, which can be detected. The MRI machine measures how long it took the hydrogen atoms to return to their previous alignment. This time is different for different types of tissue, especially if the strength of the magnetic field is also changed for each region. A computer can draw a picture based on the different 'return times' of hydrogen atoms in various places in the tissues, supplying a different shade or color for each region where the time was different. Diseased tissue in particular will show a different return time for the hydrogen atoms than the healthy tissue around it and will stand out in the image.

In an MRI experiment, the object to be imaged is placed in a large, static magnetic field. A superconducting magnet commonly supplies the magnetic field. Without an external magnetic field, a group of protons assumes a random orientation of magnetic moments, producing an overall magnetic moment of zero. Under the influence of an applied external magnetic field, B0, the protons assume a nonrandom alignment in two possible orientations: parallel and anti parallel to the magnetic field. A slightly greater number of protons exist in the parallel direction, resulting in a measurable sample magnetic moment in the direction of magnetic field, B0, as shown in Figure 1.4.

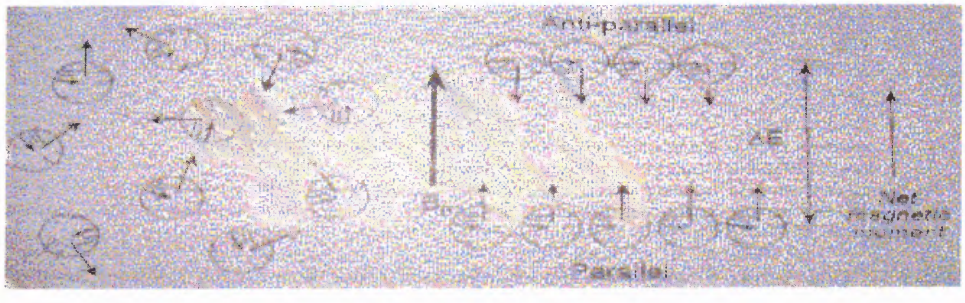

Figure 1.4 Simplified distributions of free protons without and with an external magnetic field [16].

The frequency of the precession is directly proportional to the strength of the magnetic field and is defined by the Larmor Equation:

$$\omega_{\phi} = \gamma B_{\phi} \tag{1.1}$$

where: ω_{ϕ} is the precession angular frequency (Hz), γ is the gyromagnetic ratio (a property of the material) and B_o is the external magnetic field strength (Tesla)

Because of this resonance phenomenon, if an oscillating magnetic field at this resonance frequency is applied to the object, then the spins will absorb energy and become excited. The oscillating magnetic field is called a radio frequency (RF) field. This process, known as excitation, results in the magnetization being partially or completely tipped into the plane perpendicular to main magnetic field. Once excited, the magnetization precesses around the static magnetic field at its resonant frequency given in equation (1.1), above. A coil placed near to the object can detect this precessing magnetization as shown in Figure 1.5.

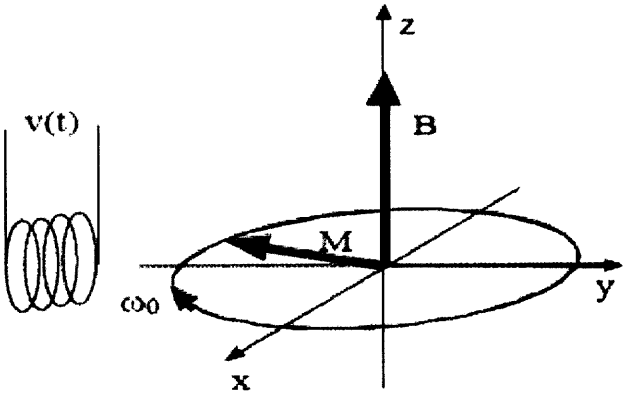

Figure 1.5 Excited magnetization precessing around the static magnetic field thus inducing a voltage, v(t), in a nearby coil [21].

Following excitation, the magnetization returns to its equilibrium state according to an exponential decay processes. The magnetization precessing in the plane perpendicular to the static field, decays exponentially with the time constant T2. The mechanism underlying this decay term is the incoherent (and unrecoverable) phase dispersal of the signal due to interactions between nuclear spins. In the presence of an inhomogeneous magnetic field, spins will have differing precessing rates induced by this inhomogeneity also causing phase dispersal and more rapid signal decay [21].

The decay of magnetization including both T2 (spin-spin interactions) and magnetic field inhomogeneity is given a time constant called T2. Finally, the magnetization returns to its equilibrium state, aligned to the main magnetic field with time constant, T1. Much of MRI is based on exploiting differences in these parameters to develop image contrast between different tissues.

The MRI unit used in this pilot experiment had field strength of 3 Tesla (Advanced Imaging Center at the University of Medicine and Dentistry of New Jersey in collaboration with Rutgers University of New Jersey), which is 75,000 times stronger than earth's average field strength of $4 * 10^{-5}$ Tesla. This field is so strong that no ferromagnetic material is allowed anywhere near the machine; the magnet would cause anything metallic to fly across the room towards the machine, possibly injuring someone [33].

1.2.3 Blood Pressure

Blood pressure (BP) is the pressure of the blood flowing through blood vessels against the vessel walls. It depends on blood flow (how much blood is pumped by the heart) and the resistance of blood vessels to blood flow [22]. If the pressure is high, the heart must work much harder to maintain adequate blood flow to the body. Blood pressure is continually changing depending on activity, temperature, diet, emotional state, posture, physical state, and medication use. Blood pressure readings are usually given as two numbers: for example, 110 over 70 (written as 110/70). The first number is the systolic BP reading and the second the diastolic blood pressure. Systolic BP represents the maximum pressure exerted when the heart contracts. It begins with the opening of the aortic valve and the rapid ejection of blood into the aorta. This is followed by "run-off" of blood from the proximal aorta to the peripheral arteries. On the arterial pressure waveform, this appears as a sharp rise in pressure followed by a decline in pressure. The diastolic pressure represents the pressure in the arteries when the heart is at rest. Mean arterial pressure (MAP) represents the average pressure within the arterial system. Since diastole typically lasts approximately two thirds of the entire cardiac cycle, the mean arterial pressure value is closer to the diastolic value than to the systolic value.

Mean arterial pressure is defined as the sum of diastolic pressure plus one third of the pulse pressure. It can also be mathematically calculated as

$$MAP = 1/3 \text{ (systolic+2* diastolic)} \tag{1.2}$$

1.2.4 Electrocardiogram

An electrocardiogram (ECG) is a graphical representation of the electrical activity of the heart plotted along a time axis [15]. It is a measurement that is recorded at the surface of the skin and is generated by electrical currents from the cardiac muscle action potentials that causes the contraction of the heart. A typical electrocardiogram as shown in Figure 1.6 consists of a regular sequence of waves, the P, QRS, and T waves. Each of these waves is generated by specific events in the cardiac cycle. The P wave is generated by the contraction of the atria. The QRS complex is the contraction of the ventricles and the T wave is generated by the relaxation of the ventricles. The amplitude of each of these components depends on the orientation of the heart within the individual and the position of the leads (electrodes) used to record the ECG.

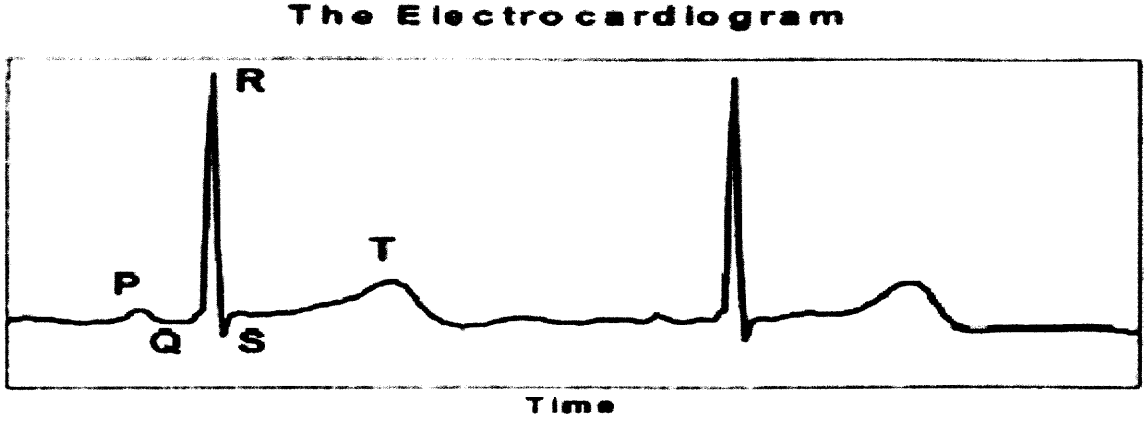

Figure 1.6 Characteristic of ECG.

Using a pair of surface electrodes and a ground electrode, the measurements of the ECG signal are obtained. The differential voltage signal can be measured on the surface of the skin. The locations of the two electrodes differ depending on the desired emphasis on the signal. Because of the size of the QRS complex, if one is only interested in heart rate, then almost any position of the two electrodes will be sufficient to detect it.

Since the QRS complex is the easiest component of the ECG wave to detect, it is used as the calculation point for the determination of the heart rate.

1.2.5 Heart Rate

Heart rate is the number of heart beats per unit time, usually expressed in beats per minute. The heart rate is based on the number of contractions of the ventricles (the lower chambers of the heart).

Because the ECG is plotted along a time axis, the linear distance between neighboring peaks of simultaneous heartbeats on an ECG corresponds to the time necessary for a single cardiac cycle (heartbeat). The heart rate can be calculated from the time interval between the R peaks of the ECG as mentioned above in Section 1.2.4.

$$\text{Heart Rate} = 60 \text{ (in sec)} / \text{(R to R interval)} \tag{1.3}$$

Since the blood is pulled towards the legs when the LBNP is applied, the heart rate is expected to increase to maintain a normal rhythm of the heart.

CHAPTER 2

IMPLEMENTATIONS

2.1 General System Overview

This system employs an MRI experimentation room and an MRI control room. The devices such as a blood pressure monitor (DINAMAP PRO 100, GE Electric Company, USA), ECG amplifier (V75-01, Coulbourn Instruments, Allentown, PA), Pressure gauge (DTG, Crystal Engineering, San Luis Obispo, CA), Vacuum Pump (QL60A, Shop Vac Corp., PA, USA) and Rheostat (3PN116B, The superior Electric Corp., CT, USA) in the MRI control room were interfaced with the LBNP chamber in the MRI experimentation room as shown in Figure 2.1 to monitor and record blood pressure, electrocardiogram (ECG), heart rate, chamber pressure and blood flow in the brain during all LBNP protocols. The details of each device are described in Section 2.2.

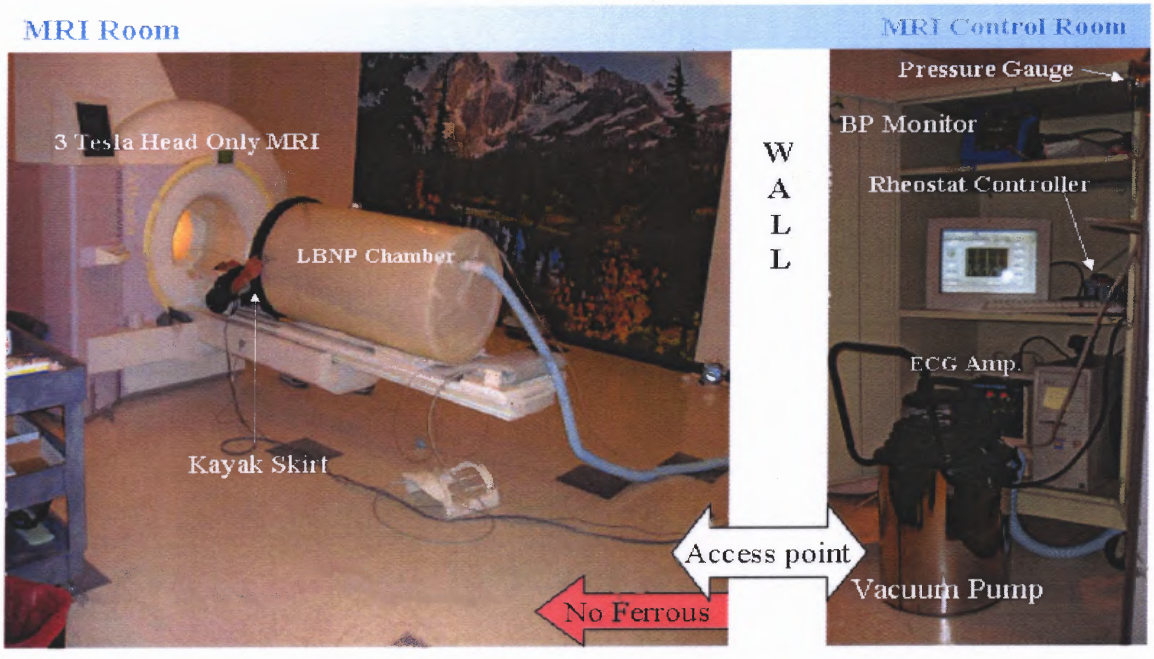

Figure 2.1 System Overview.

2.2 Hardware Descriptions

The main hardware for the fMRI compatible lower body negative pressure are an LBNP Chamber, ECG Amplifier, Blood Pressure Monitor, Pressure Gauge and MRI machine.

2.2.1 LBNP Chamber

The main component of the LBNP system is the LBNP chamber as shown in Figure 2.2 in which the lower body (hips and legs) of the subject is exposed to negative pressures from 0 to -50 mm Hg. If suction is applied to the chamber, this causes the body fluid to move from the chest and upper body to the lower body. This shift of fluid is very similar to the shift of fluid that occurs when people stand upright. In the past, different types of chambers, consisting mostly of metal tanks, have been used as LBNP chambers. However, for this project, since it had to be MRI compatible, the LBNP chamber was constructed without any ferromagnetic materials to able to withstand negative pressure created by the external vacuum [28].

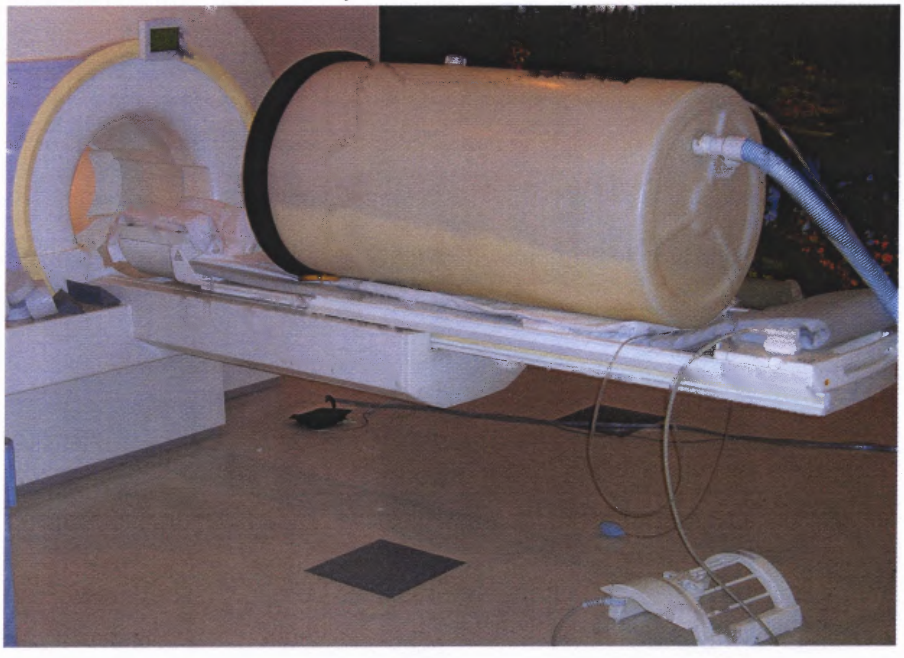

Figure 2.2 Chamber.

During the LBNP building process, different types of non-ferrous materials were used. The materials used in this chamber were plastics, wood, foam, PVC pipe, glue, nylon and rubber.

A cylindrical plastic chamber with dimensions of 50 inches in length and 25 inches in diameter was chosen. The weight of the LBNP chamber with a subject cannot exceed 300 lb because the MRI patient bed cannot hold more than 300 lb. This means that the weight of the chamber has to be as light as possible, around 50 lb for a 250 lb subject. A cylinder was chosen because it has the best strength for it weight. For example, a box would be weak along its sides and would bow inward under stress. Customized foam was put inside the chamber for the subject's comfort and also to rise subject to center of cylinder because a Kayak skirt's opening was in center.

Another important aspect of the LBNP technique was to seal around the iliac crest portion of the abdomen of the subject. It must fit the particular shape of the subject and provide a seal for the development of negative pressure. Customized sizes of Kayak skirts as shown in Figure 2.3 were bought for the subjects. This was chosen because it was made using nylon and synthetic rubber made by the polymerization of chloroprene. The 24 ft plastic tube, ¼ inches diameter, was sealed to the chamber and was used to connect the LBNP chamber in the MRI experimentation room to the pressure gauge in the MRI control room which indicates the pressure inside the chamber in real time.

Figure 2.3 Kayak Skirt.

2.2.2 Pressure Gauge

The pressure gauge (Crystal Engineering, San Luis Obispo, CA 93401), with built up RS 232 interfaces, measures the pressure inside the cylindrical chamber in real time. According to its manual [12], this device is capable of measuring pressure with accuracy in temperatures ranging from 14 degree F to 122 degree F and the pressure can be displayed in up to nine different pressure scales (PSI, kPa, etc.) on an easy to read, full five digit, liquid crystal display. Among the different scales, mm Hg was chosen as standard throughout this project.

Figure 2.4 Pressure Gauge.

This pressure gauge as shown in Figure 2.4 was connected to COM 1 of the computer and a custom LabVIEW program was used to acquire data from the pressure gauge and then store and display the information in the computer. The details of the LabVIEW program to acquire data from the pressure gauge are described in Section 2.3.2.3. This pressure gauge reads the chamber pressure in real time using the 24 ft plastic tube from the control room (outside the MRI room).

Note, 1 atm = $1.01325 \cdot 10^5$ N / m^2 = 14.695 psi (pound square inch) = 760 mmHg.

2.2.3 ECG Amplifier

Amplifiers are an important aspect of modern instrumentation systems to measure biopotentials. They are required to increase signal strength while maintaining high fidelity. The signal that comes out of the human body through ECG electrodes has very low signal strength and therefore needs to be amplified to display and store it in the computer.

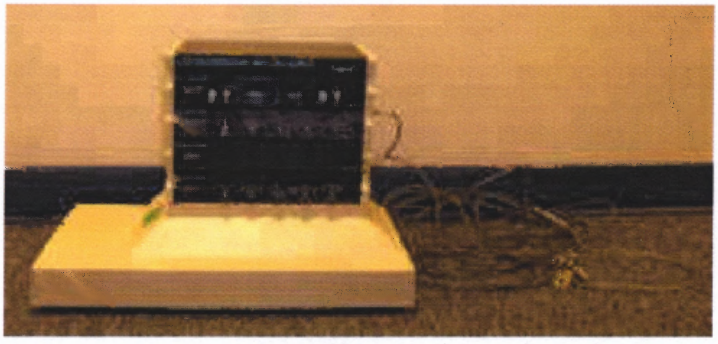

Figure 2.5 ECG amplifier with 24 ft MRI compatible cable.

The essential function of the ECG amplifier as shown in Figure 2.5 was to take a weak electric signal in the form of a voltage from the body and increase its voltage level so that it could be further processed, recorded, or displayed. This ECG amplifier also needed a long MRI compatible cable to reach the subject in the MRI machine; a 24 ft MRI compatible cable was used to connect the ECG amplifier connector and ECG electrodes. The ECG was collected via three disposable ECG electrodes from the body. An ECG amplifier and filter module (V75-01, Coulbourn Instruments, Allentown, PA) received the signal from the electrodes, amplified and sent the signals to the computer [10]. Digitization of these signals was performed by means of an National Instruments data acquisition board (National Instruments, Austin, TX) and a custom LabVIEW

program. The detail of the LabVIEW program for this device are described in Section 2.3.2.1.

2.2.4 Blood Pressure Monitor

This blood pressure monitor device as shown in Figure 2.6 measures blood pressure automatically, non-continuously and it is non invasive. It was manufactured by GE Medical System [8], known as the "Dinamap" line of non-invasive, non-continuous blood pressure monitor. It has display functions that include sytolic, diastolic and mean arterial pressure (MAP).

Figure 2.6 Blood Pressure Monitor, 24 ft hose and plastic cuff connector.

The hose (flexible tube) that came with this device was too short to reach the subject in the MRI room from the BP monitor in the control room, and was therefore replaced with a 24 ft MRI compatible hose, as shown in Figure 2.6. The metal connector at the end of the wire was replaced with a plastic Cuff Connector as shown in Figure 2.6 to make it MRI compatible. User-programmable high and low alarms for systolic, diastolic and MAP are also available in this device. This blood pressure monitor was connected to COM 2 of the computer and the LabVIEW program was used to acquire data from the pressure monitor and then stored and displayed in the computer. The detail

of the LabVIEW program to operate this device and to acquire data from it is described in Section 2.3.2.2. This blood pressure monitor device measures blood pressure in real time using the 24 ft hose from the control room (outside the MRI room).

2.2.5 Vacuum Pump with Rheostat

An external vacuum pump (QL60A, Shop Vac Corp., PA, USA) with Rheostat controller (3PN116B, the superior Electric Corp., CT, USA) as shown in Figure 2.7 was placed in the control room (outside of the MRI room) and was used to develop and maintain negative pressure within the chamber during the experiment. A plastic pipe about 24 ft long and 2 inches in diameter was used to connect the vacuum engine to the LBNP chamber in the MRI room.

Figure 2.7 Vacuum Pump with Rheostat.

2.2.5 MRI Machine

A Siemens 3 Tesla Allgera Head Only MR System (Siemens, USA) as shown in Figure 2.8 was used to take an image of changes in blood flow during graded lower body negative pressure (LBNP). This machine is owned and operated by the Advanced Imaging Center at the University of Medicine and Dentistry of New Jersey in collaboration with Rutgers University of New Jersey.

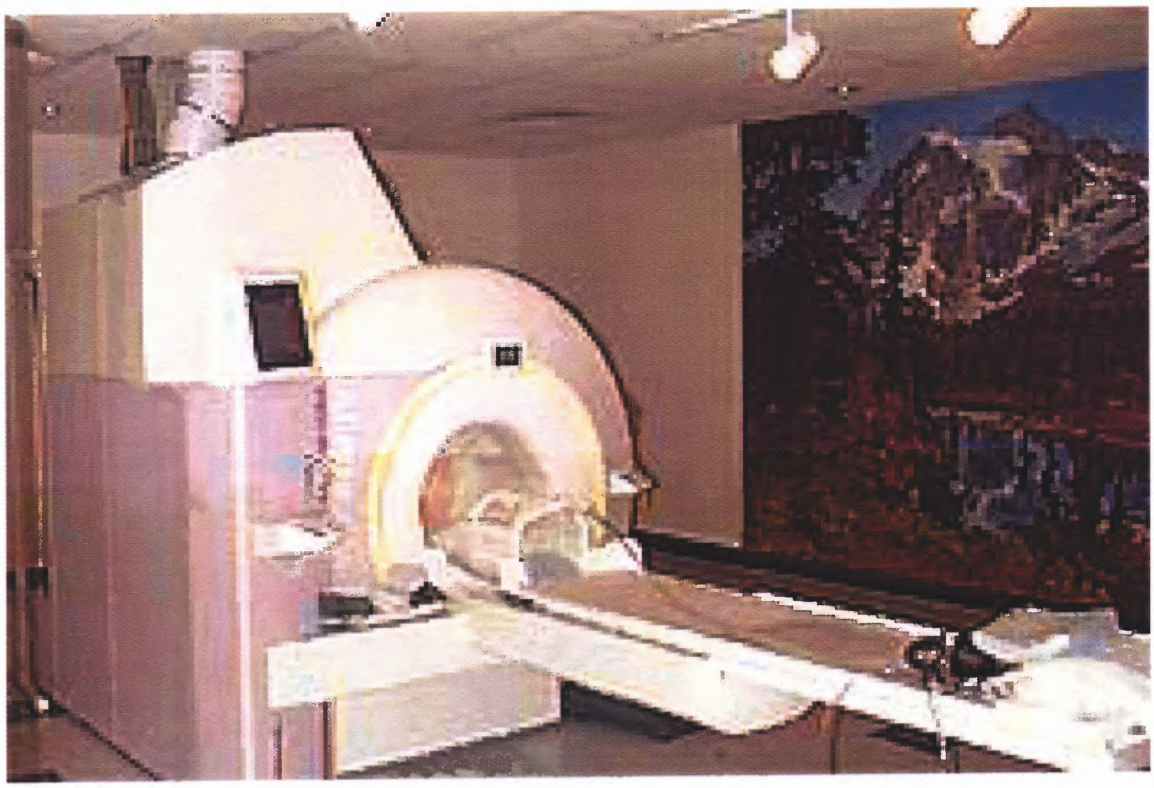

Figure 2.8 MRI machine [32].

The MRI machine is a large, cylindrical (tube-shaped) machine that creates a strong magnetic field around the patient. The details about MRI and fMRI are described in Section 1.2.2.

During the pilot experiment in this project, the fMRI compatible LBNP chamber was placed on the MRI bed as shown in Figure 2.8. More about the fMRI compatible LBNP chamber is described in Section 2.1.1. The MRI bed was adjusted (moved down) so that the bed inside the LBNP chamber would be same level as the MRI machine. Safety straps were applied across the chamber to make sure it would not roll. The LBNP chamber was connected to the vacuum pump in the MRI control room using 24 ft of {2 inches diameter} plastic pipe; a pressure gauge that indicates the pressure inside the chamber during the experiment was connected using 24 ft of {1/4 inches diameter} hose. During the experiment the hips and legs of the subject's body had to be inside the LBNP chamber and at same time the head needed to be in the fMRI scan region inside the cylinder. In this experiment, the subject did not have to perform a number of small tasks such as tapping the thumb of one hand against each of the fingers of that hand, or rubbing a block of sandpaper, or answering simple questions during the experiment. The flow of blood in the brain was changed automatically as the result of the application of graded negative pressure to the lower body of the subject.

The MRI process goes through the following steps,

A magnetic field is created and pulses of radio waves are sent from a scanner to the head of subject.

The radio waves change the nuclei of the atoms in the brain out of their normal position.

As the nuclei realign back into proper position, the nuclei send out radio signals. These signals are received by a computer that analyzes and converts them into an image of the blood flow in the brain being examined.

This image appears on a viewing monitor of a computer in the control room.

2.3 Software Development and Processing

2.3.1 Introduction to LabVIEW

Another major part of this project was to write a program using LabVIEW for data acquisition and analysis. LabVIEW (National Instruments, Austin, TX) is short for Laboratory Virtual Instrument Engineering Workbench, which is a programming environment in which the user can create programs with graphics. In this regard it differs from traditional text based programming languages like C, and Pascal. However, LabVIEW is much more than a language. It is a program development and execution system [19].

The LabVIEW can decrease the time to speed up program considerably as it is specifically designed to take measurements, analyze data, and present results to the user. Because of LabVIEW's graphical nature, it is inherently a data presentation package. Output appears in any desired form. Charts, graphs, and user-defined graphics comprise just a fraction of the available output option. The LabVIEW programs are called virtual instruments (VI's) because their appearance and operation imitate actual instruments. Behind the scenes it is analogous to the main programs, functions and subroutines from popular programming languages like C or BASIC.

The VI has three main parts:

- The front panel: this is the interactive user interface of the VI, so named because it simulates the front panel of a physical instrument. It can contain knobs, push buttons, graphs and other controls that can be inputted by the user.

- The block diagram is the VI's source code constructed in the programming language G. This is the actual executable program. The components are lower level VI's, built in functions, constants and program execution control structures. Front panel objects have corresponding terminals on the block diagram so data can pass from the user to the program and back to the user.

- In order to use the VI as a subroutine in a block diagram of another VI, it must have an icon and a connector. A VI used within another VI is called a sub VI and is analogous to a sub-routine.

2.3.2 Software Design

The main function of the data acquisition program is to collect data from the different components of the system, store the required information and display it to the user. Each one of the three components that we wish to acquire data from requires a different communication method. A user panel is used to display necessary real-time information to the user for each of the acquired data types.

This main software program as shown in Figure 2.9 for this LBNP system can be divided into three parts: acquisition of the ECG signal and processing, acquisition of blood pressure and acquisition of chamber pressure.

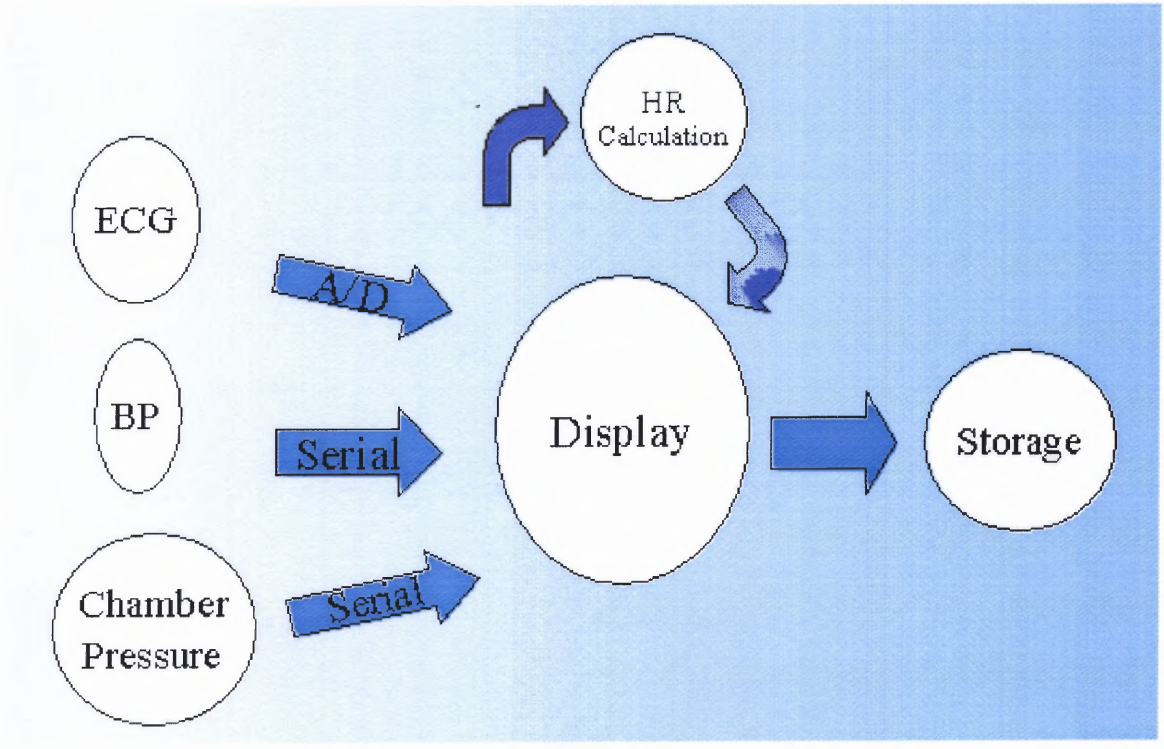

Figure 2.9 Developed software.

2.3.2.1 Acquisition of the ECG and Processing. The beginning of the program is assembled to set the parameters for communications between the software and hardware of the system. The ECG was collected via three disposable electrocardiogram (ECG) electrodes from the body and passed to the computer through an ECG isolated amplifier and analog to digital (A/D) card using a written data acquisition program. The analog output from the amplifier was fed to an analog to digital converter of the computer. In the computer, the analog input was converted to a digital signal at the A/D card. The AI configuration VI allows the programmer to set up channel specifications and buffer size. There was one channel used in the program for the ECG. Buffer size is the storage location where the data are continuously acquired and retrieved. If the rate at which data are retrieved is slower than the rate at which it is acquired, the buffer will fill up which makes LabVIEW overwrite the data. Therefore, the buffer size should be chosen carefully to prevent such problems. For this program, the buffer size was set to 1000 scans and the sampling rate was 250 samples per second. Thus, every second 250 samples were placed in the buffer. The scan rate at which LabVIEW acquires the data from the buffer was set to 1000. The detail of program is shown in Figure 2.10.

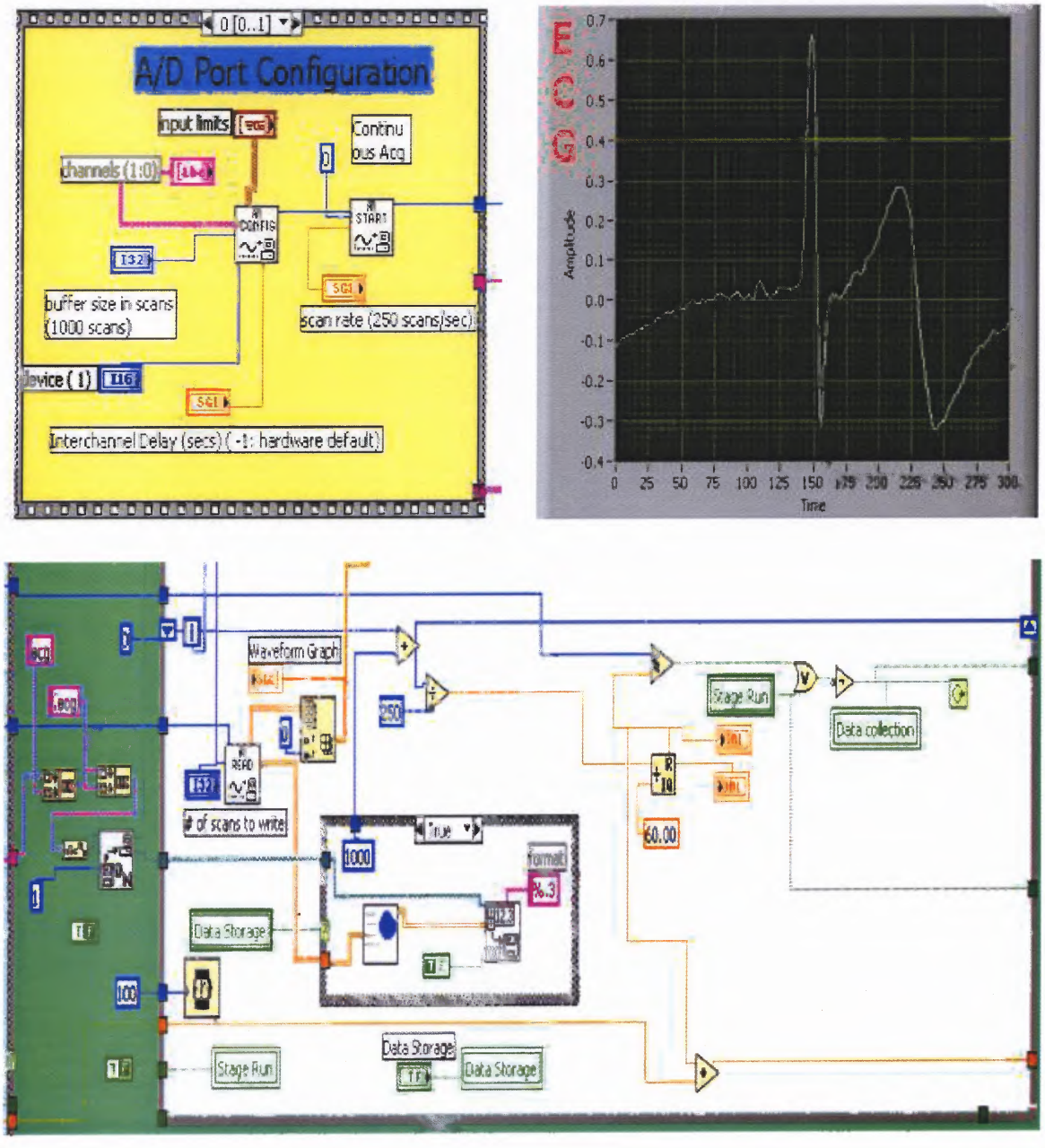

Figure 2.10 Actual diagram and front panel of ECG acquisition.

The next VI in the program is "AI start VI". This VI starts a buffered analog input operation and sets up the sampling rate, which is specified by the programmer. The sampling rate must satisfy the sampling theorem, which states that the sampling rate should be at least twice the highest frequency of the analog signal. Sampling an analog

signal involves taking a sample of the signal at discrete times. The rate at which the signal is sampled is known as the sampling frequency. It is typically expressed in samples per second, or hertz (Hz). The sampling rate chosen for this system is 250 samples per second meaning 250 samples are stored each second. For this program, the highest frequency for the ECG was around 100 Hz and the blood pressure was 50 Hz. Hence, the sampling rate of 250 Hz would be adequate to satisfy the sampling theorem. There was no need to choose a higher sampling rate than 250 samples/sec because it would require more storage capacity and more processing time. Next, the signal was transferred to the "AI Read," where the data were remove from the buffer every 4 seconds via a number of scans to read and the signal was plotted on the front panel. This ECG signal was further processed to calculate instantaneous R-to-R intervals and heart rate.

Calculation of the heart rate and R-to-R interval from ECG signal:

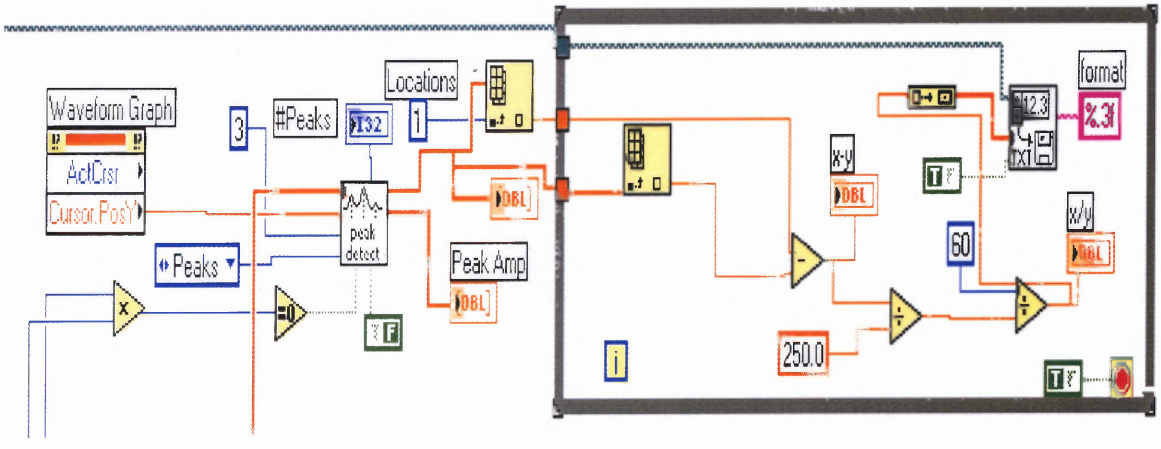

Figure 2.11 Actual diagram of the calculation of the heart rate and R-to-R interval from the ECG.

The ECG was used to calculate an instantaneous heart rate that was measured throughout the protocol. The detail of the LabVIEW program is shown in Figure 2.11. The first processing step for the ECG waveform was to pass the raw signal through the

peak detector. This function scanned the ECG for the QRS complex by using a sliding window to scroll through the waveform to identify localized maxima. The peak detector in the LabVIEW program detects the location of the R wave signal with the help of a threshold line in the ECG graph. The threshold line can be moved up and down by the user to select only the R wave peaks from the rest. The output of the peak wave detector has a column of index of the locations for each of the R waves. The R-to-R interval was the duration of time between each successive R wave as indicated in Figure 2.12. Using the index values from each of the R-waves stored in column 1, the R-to-R interval was calculated in samples between beats. The heart rate, in beats per minute, was calculated using the following formula:

$$\text{Heart Rate} = 60^{*} \text{ (Sample Rate/ R-to-R interval)} \tag{2.3}$$

where the sampling rate was 250 samples per second were as discussed earlier.

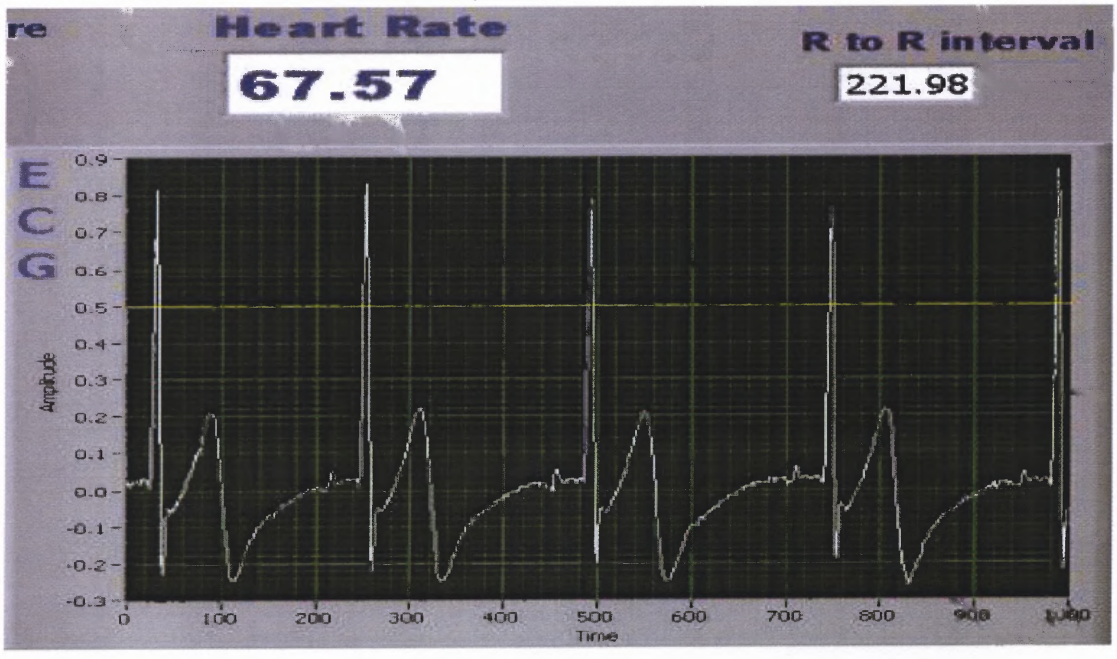

Figure 2.12 Front panel of the ECG graph with a user moveable threshold line.

2.3.2.2 Acquisition of Blood Pressure. Blood pressure data were collected using a blood pressure monitor, which is connected to serial port 1 of the computer.

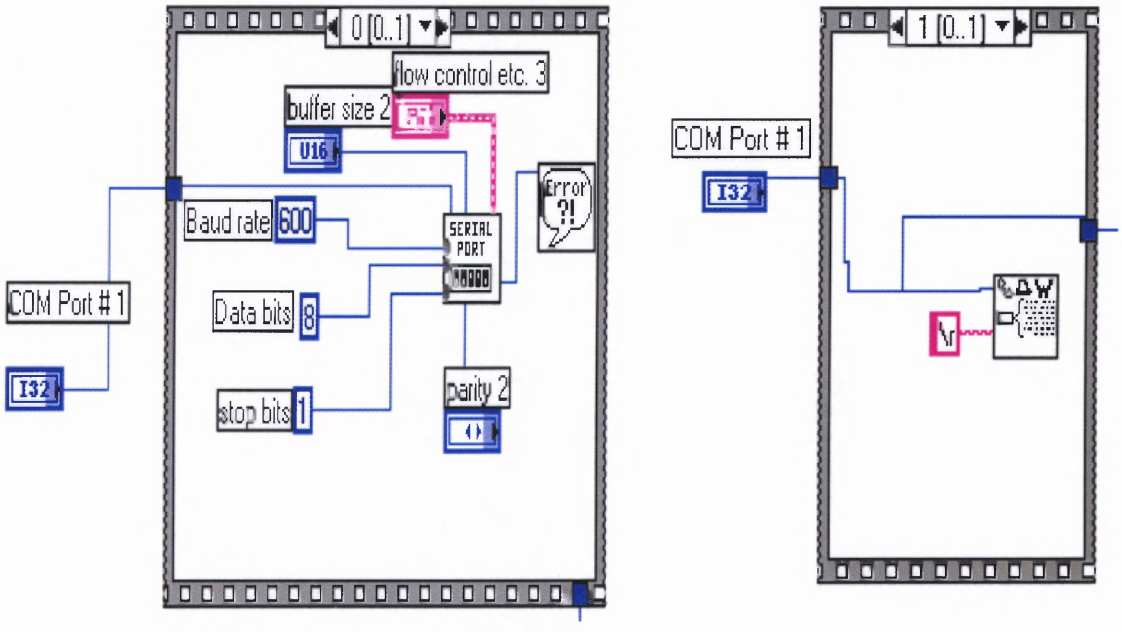

Figure 2.13 Actual diagram of the serial port configuration of blood pressure acquisition.

The baud rate, 600 bits/sec, is the rate of transmission. The "data bits", 8 bits/sec, are the number of bits in the incoming data. The "stop bits" is 1 bit. The parity is 0 for no parity. The "Serial Port Write" writes the data in a string to write to the serial port. The detail of the LabVIEW program is shown in Figure 2.13.

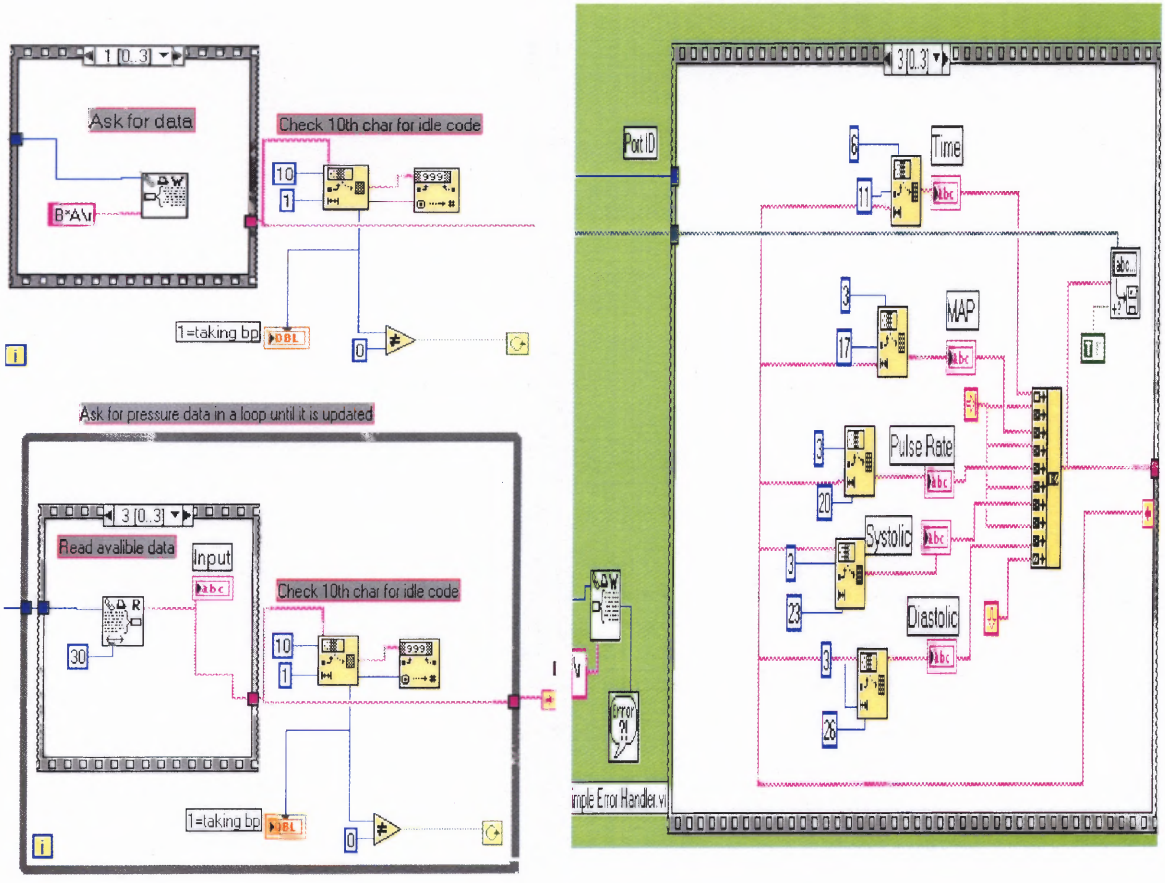

Figure 2.14 Diagram of blood pressure acquisition.

For this particular blood pressure monitor " B*B\r" is the device command to be written to the serial port. This is the code that starts the blood pressure measurement. Again the "Serial Port Write" requests data by sending the command "B*A\r". The "Serial Port Read.vi" reads the available data from the serial port. Then the string subset returns the substring of the input string beginning at the offset and contains the length of the number of characters. It would display and store this as systolic BP, diastolic BP, and MAP. The detail of the LabVIEW program is shown in Figure 2.14.

2.3.2.3. Acquisition of Chamber Pressure. Chamber pressure data were collected using pressure gauge, which was connected to serial port # 2 of the computer. The "serial port vi" initializes the serial port. The baud rate, 9600 bits/sec, is the rate of transmission. The "data bits", 8 bits/sec, is the number of bits in the incoming data. The "stop bits" is 1 bit. The parity is 0 for no parity. The detail of the LabVIEW program is shown in Figure 2.15.

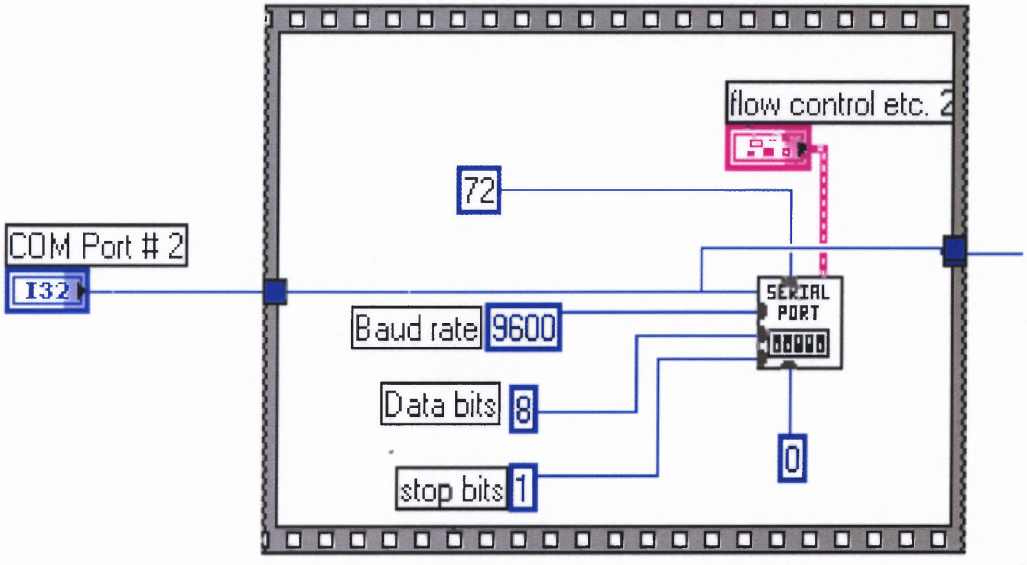

Figure 2.15 Actual diagram of the serial port configurations of chamber pressure.

The "Serial Port Write" writes the data in a string to the serial port. The "string to write" is the data to be written to the serial port. For this particular pressure gauge "?P,U\r" is the device command to be written to the serial port. Next "bytes At serial port.vi" returns in byte count the number of bytes in the input buffer of the serial port 2. The output from this VI is byte count, which is the number of bytes currently queued up

in the serial port buffer, which is input to "Serial Port Read.vi". It reads the number of characters specified by the requested byte count from the serial port 2. This VI returns the bytes read in the string read which was displayed and stored in the computer. The detail of the LabVIEW program is shown in Figure 2.16.

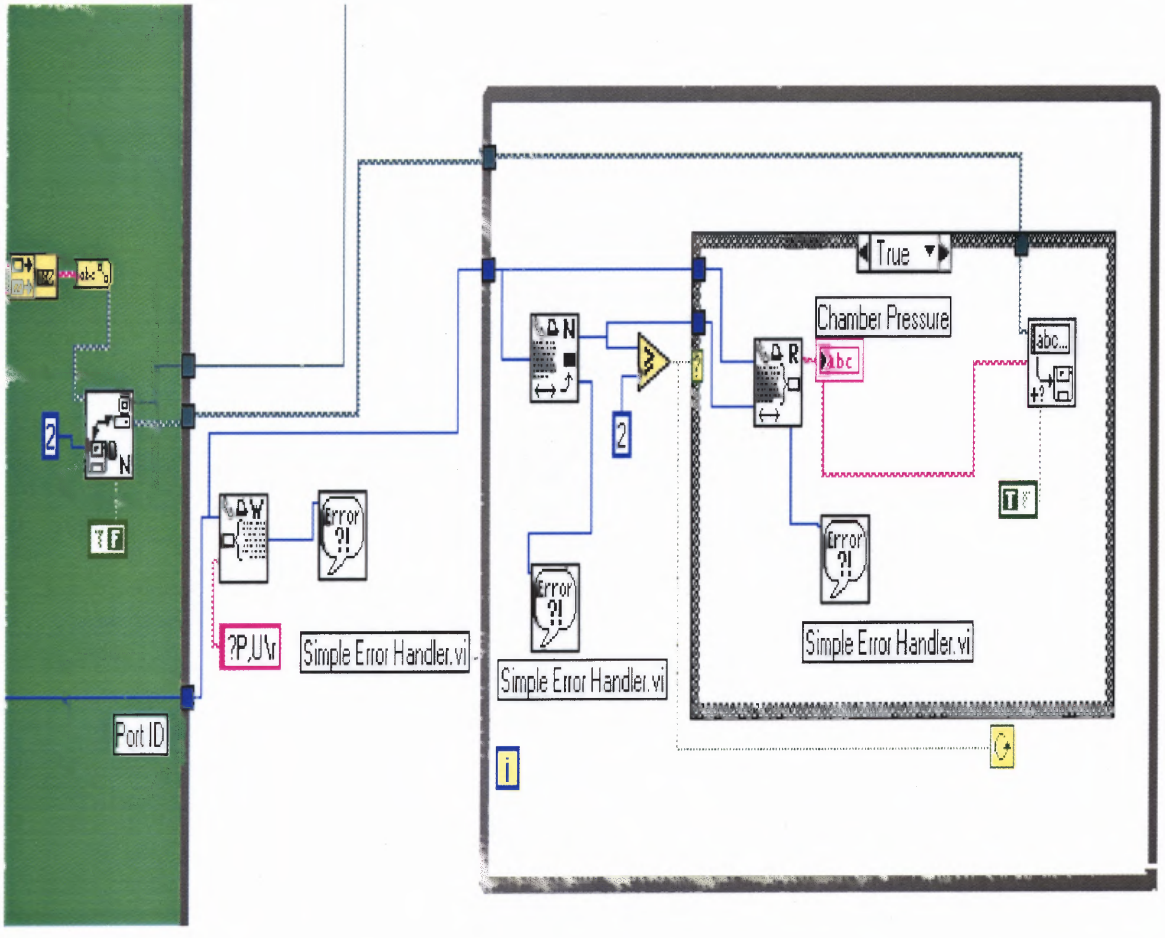

Figure 2.16 Diagram of chamber pressure acquisitions.

Once each individual program worked, they were combined under one main program so that all three acquisitions program could run simultaneously. The user panel of the main software program as shown in Figure 2.17 reads, stores and displays ECG, blood pressure and chamber pressure. It further processes the ECG signal to store and

display the heart rate and R-to-R interval in real time. The duration of each stage, number of stages and data path in software program can easily be changed if needed, shown in Figure 2.18.

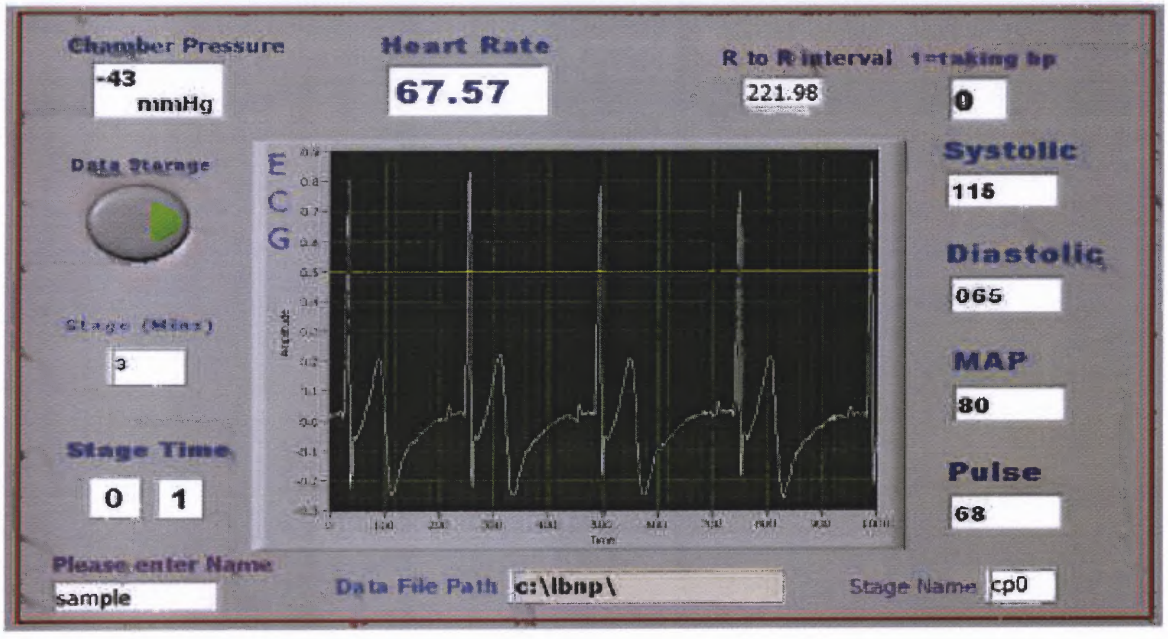

Figure 2.16 User panel of the main program.

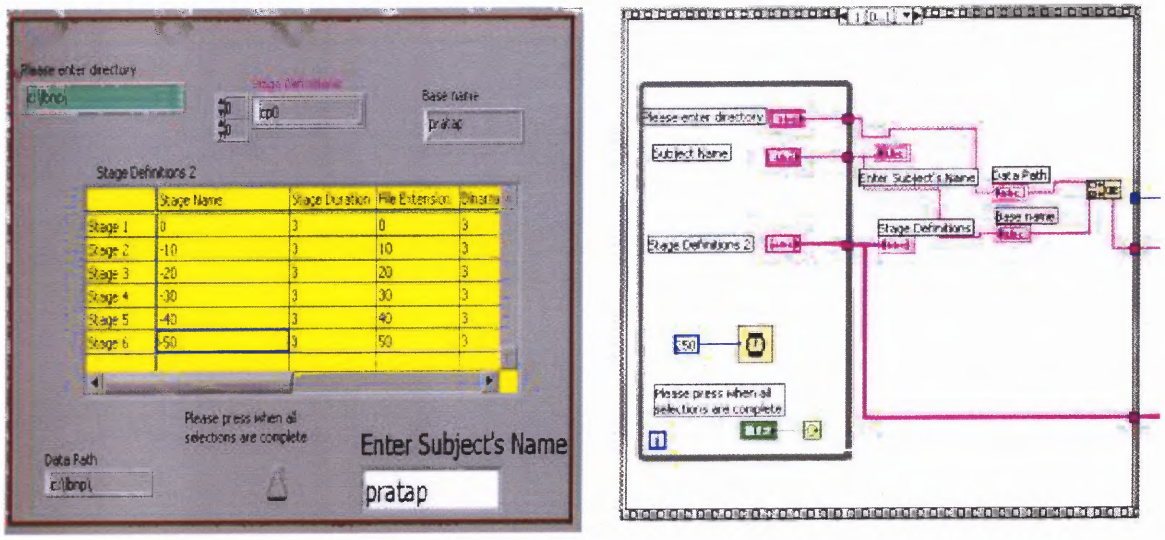

Figure 2.18 Protocol diagram (front panel and block diagram).

CHAPTER 3

SYSTEM VERIFICATION

3.1 System Testing

3.1.1 LBNP Chamber Testing

The LBNP chamber was tested to ensure it could withstand high negative pressures. To do this testing, the chamber was sealed and the negative pressure was increased slowly from 0 mm Hg and onwards using a vacuum pump with a Rheostat. During the initial testing, the plastic chamber started to collapse after –30 mm Hg; therefore some modifications had to be added to make the chamber stronger. Support was placed inside the chamber using PVC pipes and outside using a plastic ring around the chamber as shown in Figure 3.1. With these additions to the chamber, it was able to withstand high negative pressures.

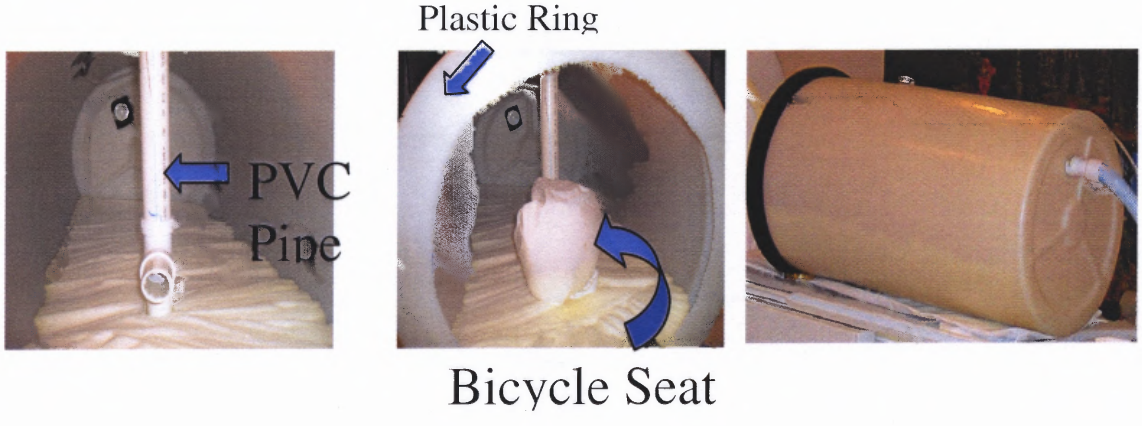

Figure 3.1 Inside the LBNP chamber.

Another important consideration in the chamber was that the pressure observed on the pressure gauge should be present at all positions within the chamber. The hose from the vacuum pump was placed in the middle of the cross-sectional area of the chamber to develop as uniform distribution of negative pressure as possible. The end of the plastic tube from the pressure gauge was put in the middle of the chamber. The pressure was measured at different places (front, back and middle) inside the chamber to detect any variations in the pressure. The following data were recorded as shown in Table 3.1.

Table 3.1 Pressures at Different Places Inside the Chamber

LBNP level (mm Hg)	0	-10	-20	-30	-40	-50
Front (mm Hg)	0.05	-10.50	-20.10	-30.45	-40.25	-50.15
Back (mm Hg)	0.10	-10.60	-20.60	-30.35	-40.10	-50.20
Middle (mm Hg)	0.7	-10.55	-20.30	-30.50	-40.05	-50.05

The variations of pressure inside the chamber are less than 1 %. This error is within the desired specification limits. Another problem encountered during the testing was that the subject was pulled a bit into the chamber once negative pressure was applied. The movement of the subject into the device once LBNP is applied was prevented by fMRI compatible PVC pipe with bicycle seat placed through the chamber as shown in Figure 3.1. This restriction allowed the subject to remain at rest instead of exerting muscular forces that interfere with pooling of venous blood.

3.1.2 Software Testing

Three major parts of the LabVIEW program were used for this system; ECG, blood pressure and the chamber pressure were all measured. The verification process involved checking displays in the device monitor and the user panel to ensure that both readings are the same. Each of these parts was tested separately to make sure that they were functioning correctly. Once these three parts were combined into a single program, it was tested to ensure that it was working simultaneously and properly.

3.1.3 MRI Compatibility Testing

A system is considered "MRI compatible" if it is MRI safe, its use in the MRI environment does not adversely impact the image quality and perform its intended function when used in the MRI environment according to its specifications in a safe and effective manner. The MRI field is so strong that no ferromagnetic material is allowed anywhere near the machine to prevent its being attracted by the magnet. The major challenge of this project was to develop a system that operates safely and reliably in such a strong magnetic field.

A metal detector was used to test all the devices that went to the MRI room to ensure that they are fully MRI compatible. These devices were also checked by putting them close to the MRI coil when the MRI machine was off, to see whether they were attracted to the magnetic coil or not. The test was successful.

3.1.4 LBNP Pilot Experiment

Once the LBNP system was working correctly, it was tested with human subjects before putting it in the MRI machine, to make sure its output would be similar to LBNP experiment results published in journals. Another reason to verify the performance of the LBNP system before putting it in the MRI machine was to ascertain that it would work perfectly before using MRI scanning time which can become costly. An MRI machine costs millions of dollars and scan time is expensive. The MRI machine is also heavily used for clinical purposes which have priority compare to the research purpose. The LBNP system must tested to be sure it is functioning as properly as possible before it is brought into the MRI facility.

Four healthy subjects, with no history of cardiovascular disorder were asked to participate in this pilot experiment and none of them were taking any kind of medication. All of the subjects were asked to take off their shoes before they put their lower body into the chamber. Three ECG electrodes and a blood pressure cuff were placed on the body and arm of the subject respectively. Once the system was ready, the subject was helped to put his/her lower body (legs/hips) into the sealed chamber. Within the chamber, he/she was asked if he/she was feeling comfortable or not. All subjects were asked to maintain normal breathing and to relax. Program protocols were then started to measure the ECG and the blood pressure of the subject at 0 mm Hg for 3 minutes. During that time, the instantaneous heart rate was displayed on the computer and changes were monitored very carefully. After acquiring data for 3 minutes, the program was stopped automatically for the next step (to measure at -10 mm Hg), and then the chamber pressure was changed very slowly to -10 mm Hg using a Rheostat controller. After waiting for a few minutes to

stabilize the biosignal, the program started again to acquire, display and store data for 3 minutes. This procedure was repeated for another 4 steps for -20, -30, -40, and -50 mm Hg. During this protocol, the subject was monitored very carefully and was asked in each stage if he/she was feeling uncomfortable. All the data were saved offline for data analysis, which is described in Section 4.1.

3.1.5 LBNP Pilot Experiment with MRI

Once the LBNP system pilot experiment proceeded without any problem, it was then put into the MRI machine to do the full pilot experiment. This time, fMRI would be used to perform head scans of the subject during graded LBNP. Once the system in the MRI experimentation room and the devices in the control room were ready, one of the subjects who had participated in an LBNP experiment in Section 3.1.4 was asked to participate in this pilot experiment. The reason to have the same subject in both pilot experiments was to compare the results of the two pilot experiments.

The subject was questioned to make sure that he did not have any of these things: a pacemaker inserted, heart valves replaced, metal plates, pins, metal implants, surgical staples, aneurysm clips, permanent eyeliner, bullet wounds, and the subject also was asked to be sure he never had never worked with metal (i.e., a metal grinder).

The subject was asked to remove everything from his body except clothes before he was allowed to go into the MRI room. Three ECG electrodes and a blood pressure cuff were placed on the subject's body and arm, respectively. Once the system was ready, the subject was helped to put his lower body (legs/hips) in the sealed chamber. Once the subject had put his lower body inside the chamber, he was asked if he was feeling comfortable or not. An emergency switch was put in his hand so that he could inform

people in the control room of any discomfort he felt. Then the MRI bed (with LBNP chamber and subject) was moved towards the MRI machine so that his head would be in the right position to scan. The subject was asked to maintain normal breathing and to relax. After waiting a few minutes, the program protocols were started to measure the ECG, blood pressure and blood flow at the brain at 0 mm Hg, for 3 minutes. After acquiring data for 3 minutes, the program was stopped automatically for the next step (to measure at -10 mm Hg), and then chamber pressure was changed very slowly to -10 mm Hg using a Rheostat controller. After waiting for a few minutes to stabilize the biosignal, the program started again to acquire, display and store data for 3 minutes. This procedure was repeated for another 4 steps for -20, -30, -40, and -50 mm Hg. During this protocol, the subject was monitored very carefully, was asked in each stage if he/she was feeling uncomfortable. All the data and MRI scans were saved offline for data analysis, which is described in details in Section 4.2.

3.2 Safety Considerations

Safety is an important issue when designing any device that deals with medical research. When collecting physiological signals, the subject needs to be connected to the amplifier through an electrode. This involves the risk of electric shock since the subject is now part of an electric circuit. To prevent a hazardous condition, an isolation transformer was placed between the electrodes and the amplifier.

Lower Body Negative Pressure (LBNP) testing was done in an incremental manner in small (-10 mm Hg) steps that allowed customization to each subject's tolerance level. Therefore, each subject was not subjected to stress levels of greater magnitude than his/her tolerance level. LBNP exposures are immediately reversible. However, not only is

the stress immediately reversible, but so are the physiological changes. One of the fine points of LBNP is that while fluid (mostly blood) is sequestered in the lower body during the application of negative pressure {thus removing it from the effective circulation} with the cessation of the negative pressure the fluid is immediately "released" back into circulation [16].

Since the technique of MRI is used to image humans, it is important to keep the safety of the subjects as a high priority. Since MRI does not use any form of ionizing radiation, it is considerably safer than x-ray or radio-isotope techniques. However, it is important, especially in a research setting, that the potential hazards of any new developments are carefully considered. Claustrophobia, and other psychological problems, can prevent a subject from being able to enter the scanner, and should be screened for before attempting to scan. It is necessary to check that the subject is fully informed as to the nature of the experiment. Depending on the medical condition of the subject, it may be necessary to monitor them closely during the scanning, and communication is important so that the subject does not feel isolated.

3.3 Data Collection and Processing

As mentioned earlier, the ECG and blood pressure measurements were recorded in a computer throughout the experiment. While acquiring the ECG data, a mathematical procedure (details of the procedure in Section 2.3.2.1) was used to calculate heart rate in real time which was also displayed and recorded. This was a crucial parameter to monitor the condition of the subject and it was also recorded for data analysis. Blood pressure was displayed and stored in terms of systolic, diastolic and MAP. After collection of data at each stage, the next step was to analyze the data which is described in Chapter 4.

CHAPTER 4

RESULTS

4.1 LBNP System Pilot Experiment (without MRI)

All subjects (n=4) completed the entire procedure without any sign of discomfort or any symptoms of presyncope (maximum LBNP tolerance). Off-line data analysis were performed on computer workstations using Excel (Microsoft Corporation, Seattle, USA)

Table 4.1 Parameters Recorded at Each Stage of LBNP

LBNP level (mm Hg)	0	-10	-20	-30	-40	-50
Heart Rate (beats/min)	83 +/- 2	81 +/- 1	84 +/- 2	85 +/- 2	91 +/- 2	96 +/- 2
Systolic BP (mm Hg)	119 +/-4	112 +/- 2	115 +/-3	111 +/- 4	109 +/-3	107 +/- 1
Diastolic BP (mm Hg)	66 +/- 2	64 +/- 2	67 +/- 1	70 +/- 2	67 +/- 4	69 +/- 4
Mean BP (mm Hg)	83+/-2	80 +/- 1	86 +/-2	83 +/- 3	85 +/- 3	83 +/- 2

All of the values are mean +/- S.E.M. of all subjects at each stage.

The mean values of heart rate +/- S.E.M. at different negative pressures clearly shows that heart rate started to increase after –20 mm Hg, are agree with the data published by similar LBNP research [1, 7] as shown in Table 4.2. The heart rate of each subject and mean values +/- S.E.M. during different negative pressures is also plotted in Figure 4.1.

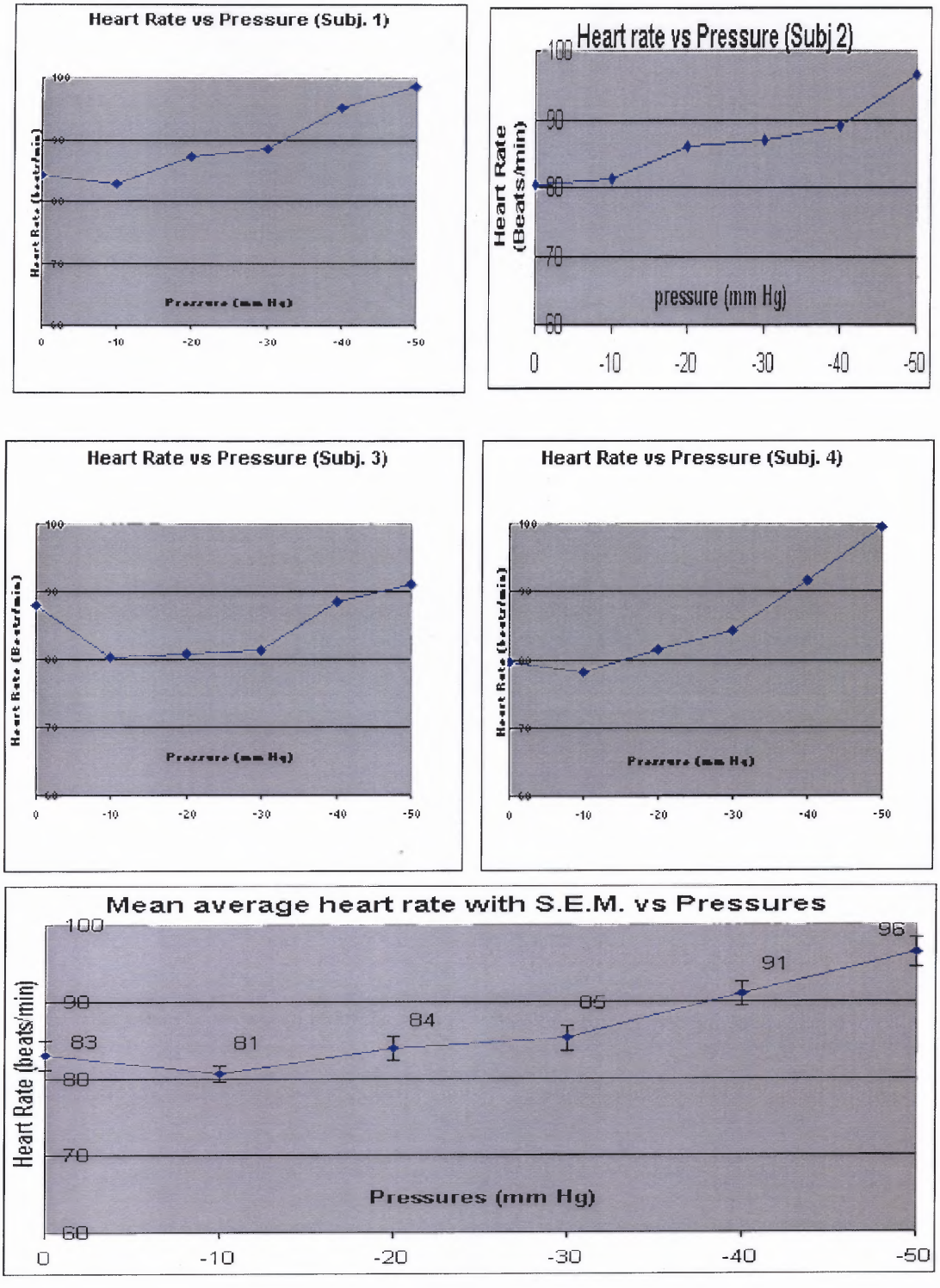

Figure 4.1 Heart Rate vs Negative pressures. The first four graphs show the heart rate vs graded LBNP. The bottom graph is mean values +/- S.E.M, heart rate started to increase after -20 mm Hg.

Table 4.2 Parameters Recorded at Each Stage of LBNP (Table from Published Journal)

Table 1. Hemodynamic parameters recorded at each level of lower body negative pressure

	Lower body negative pressure level (mm Hg)					
	0	−10	−20	−30	−40	−50
Heart rate (bpm)	60±3	59±3	61±3	65±3*	71±4**	83±4**
Systolic BP (mm Hg)	125±3	129±4	128±5	119±4	121±4	120±4
Diastolic BP (mm Hg)	67±3	71±4	71±4	69±2	72±3	77±3**
Mean BP (mm Hg)	86±2	90±4	89±4	86±2	89±2	91±3
$CBFV_{sys}$ (cm s^{-1})	117±7	112±6	112±6	100±6**	96±5**	89±6**
$CBFV_{dias}$ (cm s^{-1})	48±3	45±3	48±3	45±3	45±2	44±3
$CBFV_{mean}$ (cm s^{-1})	71±4	67±3	70±4	63±4**	61±3**	57±3**

BP indicates blood pressure, CFBV, cerebral blood flow velocity, TPR, total peripheral vascular resistance, PRU, peripheral resistance units, CVR, cerebrovascular resistance index. . All values are mean±S.E.M.

The table 4.2 consists of data published in Journal [1]. The mean values of heart rate +/- S.E.M. at different negative pressures clearly shows that heart rate began to increase after –20 mm Hg. The blood flow in the brain started to decrease with graded LBNP. The mean values +/- S.E.M. of Systolic B.P., Diastolic B.P. and MAP are also plotted as shown in Figure 4.2. The mean systolic was decreased significantly and the diastolic increases slightly with the graded LBNP.

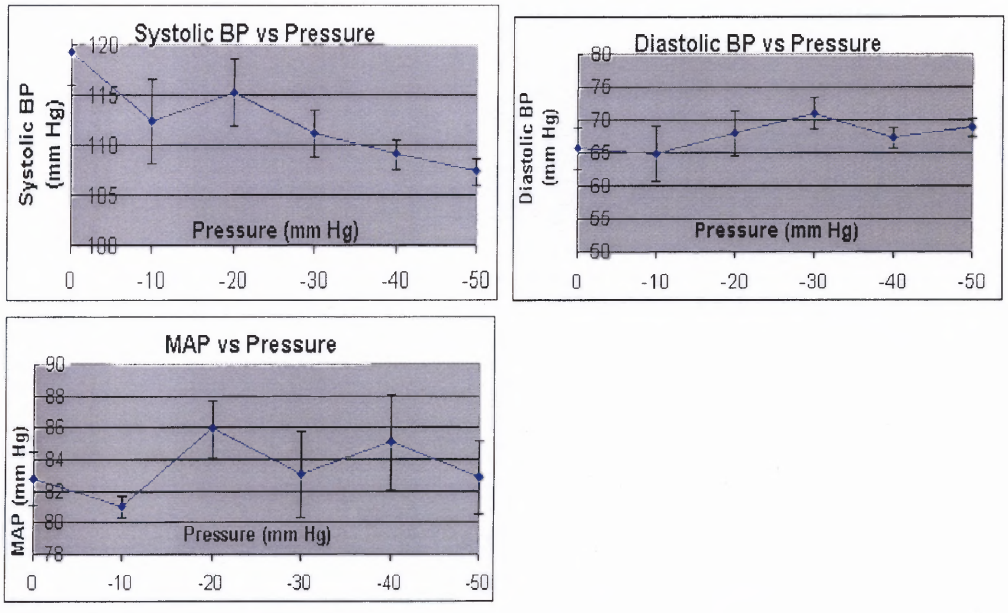

Figure 4.2 Mean values +/- S.E.M (Systolic BP, Diastolic BP and MAP at different negative pressures).

4.2 LBNP System Pilot Experiment in MRI

4.2.1 Cardiovascular Responses

The subject (Subject #2 from Section 4.1) completed the entire procedure without any sign of discomfort or symptoms of any presyncope (maximum LBNP tolerance). The purpose of having the same subject in both pilot experiments was to compare heart rate and blood pressure in the LBNP experiment without MRI and with MRI. These two pilot experiments were not performed one after another, but were conducted in different environments one month after another. As above in the LBNP pilot experiment without MRI (Section 4.1), off-line data analysis was performed on computer workstations with customized data analysis software (Microsoft Excel).

Table 4.3 Parameters Recorded at Each Stage of LBNP {n=1}

LBNP level (mm Hg)	0	-10	-20	-30	-40	-50
Heart Rate (bpm)	69 +/- 0.5	72 +/- 0.75	74 +/- 1	77 +/- 1	81 +/- 0.6	86 +/- 0.3
Systolic (mm Hg)	116 +/- 0.3	121 +/- 0.3	116 +/- 1	117 +/- 1	117 +/- 0.9	120 +/- 0.6
Diastolic (mm Hg)	62 +/- 0.5	63 +/- 0.9	62 +/- 0.3	63 +/- 1	62 +/- 3	67 +/- 1.5
MAP (mm Hg)	89 +/- 0.3	88 +/- 1.3	90 +/- 0.3	92 +/- 1	90 +/- 2	96 +/- 3

All the values are mean +/- S.E.M. of subject at each stage of graded LBNP.

Mean steady-state responses to LBNP (mean values recorded during 3 minutes of each LBNP) are shown in Table 4.3. Systolic B.P. increased slightly but not significantly. The mean values of heart rate +/- S.E.M. at different negative pressures clearly shows that heart rate started to increase from the beginning of LBNP, matched with the data published by similar LBNP research [4, 12] as shown in Table 4.4.

Table 4.4 Parameters Recorded at Each Stage of LBNP (Table from the Published Journal)

Parameters During Increasing Levels of Lower Body Suction

	Control	−10 mm Hg	−20 mm Hg	−30 mm Hg	−40 mm Hg
HR, bpm	65±3.6	68±3.8	75±4.4*	86±5.6*	94±9.1*
SAP, mm Hg	105±3.2	104±3.4	102±2.1	99±1.7	90±3.3*
DAP, mm Hg	67±1.4	67±1.3	68±1.2	68±1.2	63±3.8

HR indicates heart rate; SAP, systolic arterial pressure

All the values are mean +/- S.E.M. of subject at each stage of graded LBNP [4].

Direct comparison of the Subject (same subject) without MRI and with MRI:

Subject 2 (without MRI) **Subject 2 (with MRI)**

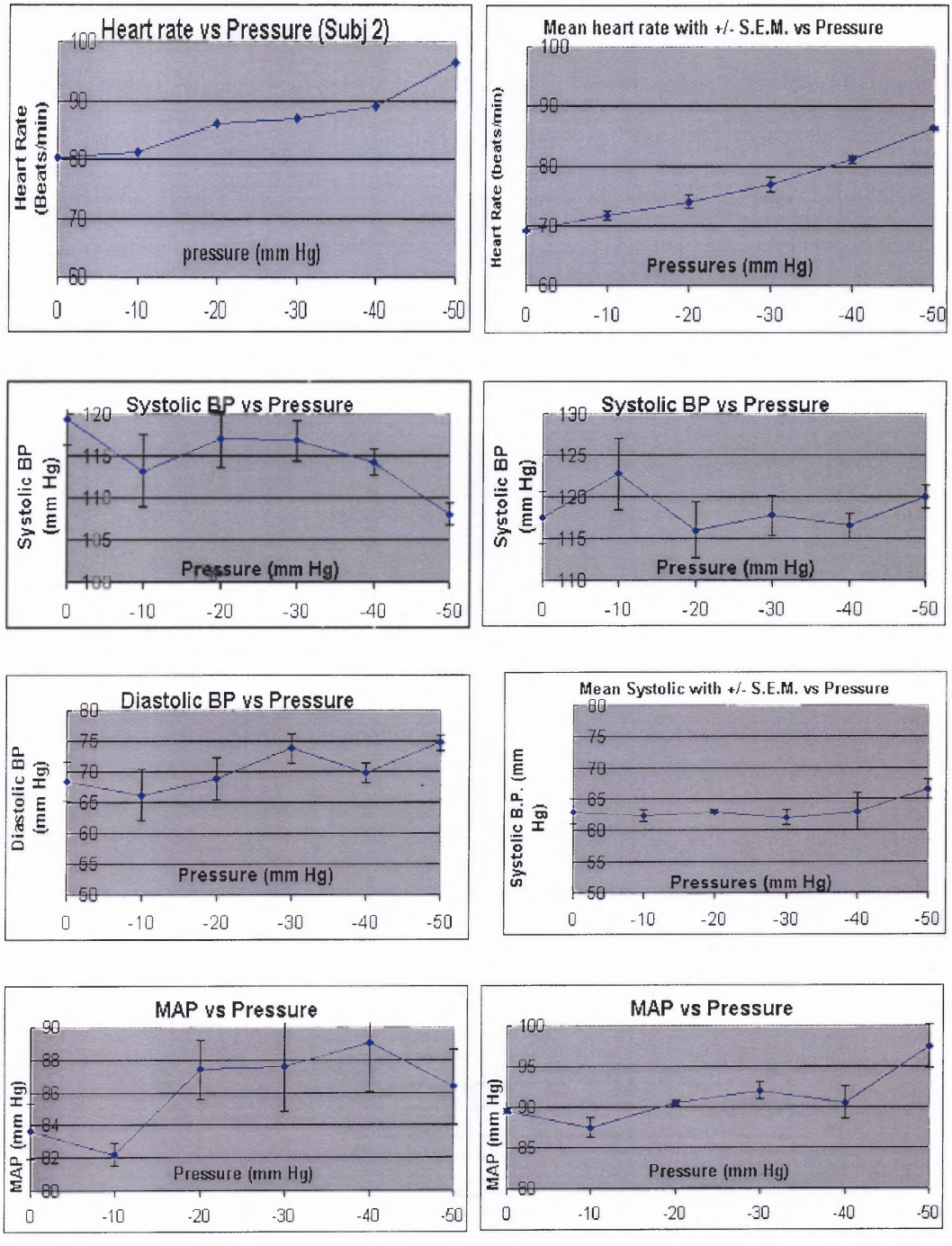

Figure 4.3 Systolic BP, Diastolic BP and MAP vs different negative pressures. The first column is a LBNP pilot experiment {without MRI} and the second column is a LBNP pilot experiment with MRI. The heart rate started to increase from beginning of the graded LBNP in both pilot experiments as shown above.

4.2.2 Cerebrovascular Responses

The fMRI data collected was processed and analyzed using the software called AFNI (Bethesda, MD) to see the changes of blood flow velocity in the brain. AFNI is a set of C programs for processing, analyzing, and displaying functional MRI (FMRI) data - a technique for mapping human brain activity. It runs on Unix+X11+Motif systems, including SGI, Solaris, Linux, and Mac OS X [25]. Time course signal intensity changes were analyzed to detect any temporal patterns in the data.

The anatomical picture that was taken during the pilot experiment using fMRI is as shown in Figure 4.4.

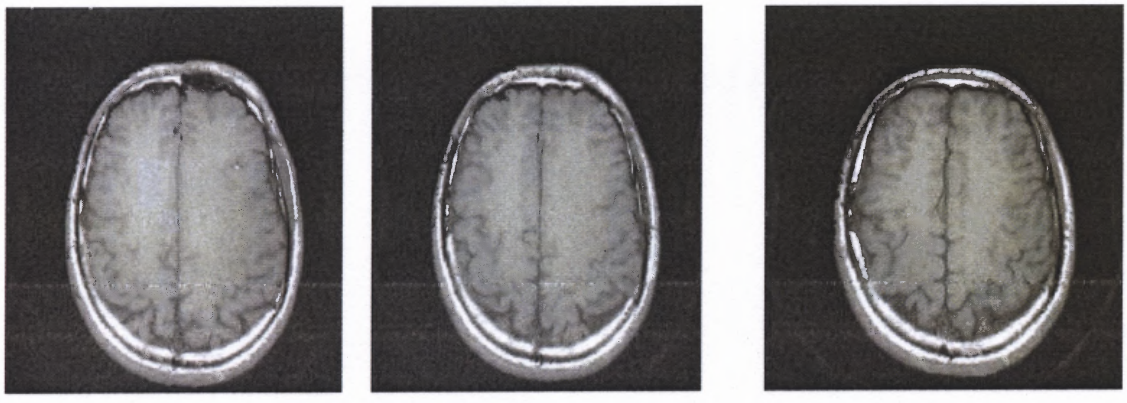

Figure 4.4 Anatomical pictures.

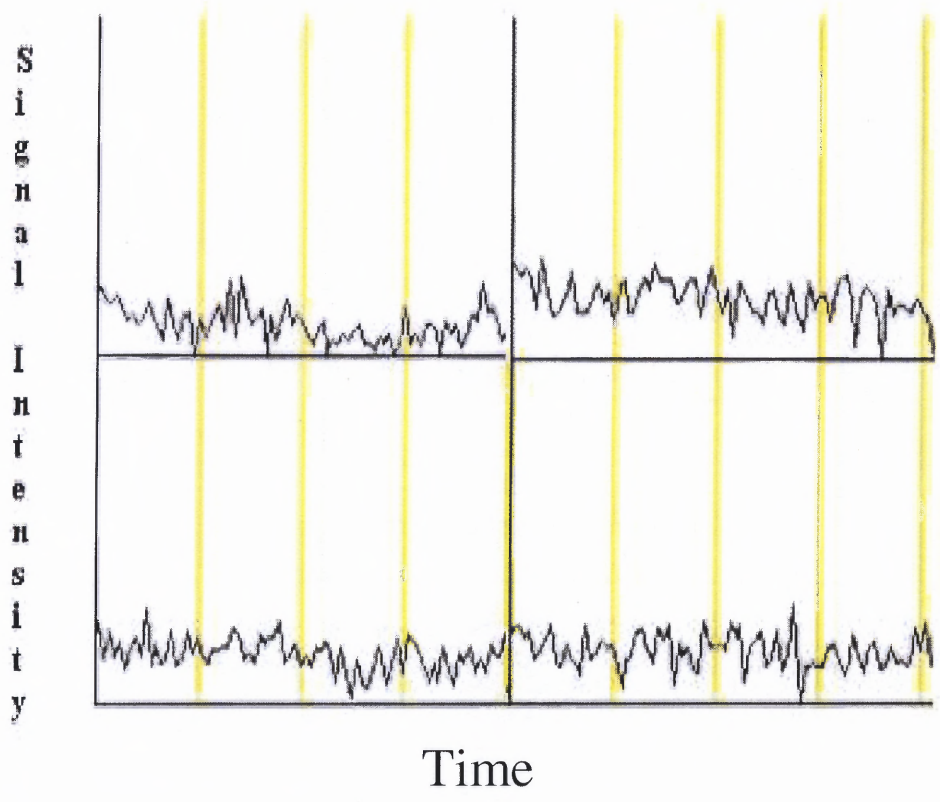

Figure 4.5 The fMRI signal intensity changes from 4(2*2) adjacent voxels during ambient (Room air) pressure is shown.

The graph as shown in Figure 4.5 shows the fMRI signal intensity changes from 4(2*2) adjacent voxels during ambient (Room air). As can be seen no substantial changes in the fMRI intensity was observed.

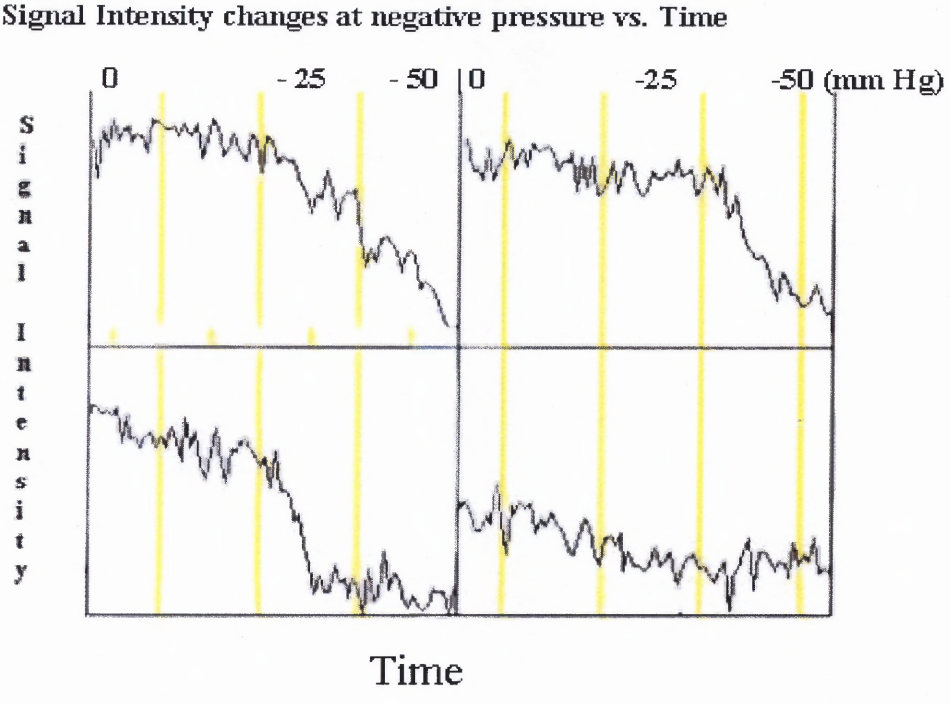

Figure 4.6 The fMRI signal intensity changes during graded LBNP.

The graph as shown in Figure 4.6 shows the fMRI signal intensity changes from 4 representative (2*2) voxels as the chamber pressure was increased in a stepwise fashion from –50 mm Hg to 0 mm Hg uniformly in steps of 10. As can be seen as the LBNP returns to Room Pressure, the cerebral blood flow increases monotonically. This decrease in blood flow in the brain due to graded LBNP supports the LBNP principle that is as more blood is pooled towards the leg due to graded negative pressure the blood flow towards the brain decreases. This result (decrease in blood flow in the brain) supports the data published by similar LBNP research [1,7] using Doppler Sonography instead of fMRI, as shown earlier in Table 4.2.

CHAPTER 5

DISCUSSION

Currently fMRI techniques have not been used to study cardiovascular and cerebrovascular responses to graded negative pressure. A few experiments [1] were carried out recently using the Doppler Sonography which is not considered as an optimum method to study cerebrovascular responses. To use fMRI for this purpose required an fMRI compatible LBNP system. Making an fMRI compatible system was the main goal of this project.

It was a challenging task to make an fMRI compatible LBNP system, as it had to operate safely and reliably in a strong magnetic field. A lot of time in this project was spent doing research, building the system and then testing its function. Sometimes, we had to go back to research when testing failed. The LBNP chamber could not withstand the high negative pressure and we could not find any other fMRI compatible chamber in the market stronger than the one we had, without adding to the chamber weight. Finally, the PVC pipe was bought which was used to give support and strong plastic ring from outside around the chamber. In research, our main task was to investigate how to design, find compatible parts and determine whether it was reasonable priced or not. Most of parts we needed had to be customized for us or we had to customize them ourselves. For the chamber bed, we had to buy a large foam and customize it to fit inside the circular chamber. The long fMRI compatible cable, hose, plastic pipe were bought and made interfaces with devices were designed {ECG amplifier, blood pressure monitor, pressure gauge}. The Kayak skirt also needed to be adjusted fit in our circular chamber without losing any pressure. We used plastics frequently in the connectors, chamber and nails.

Software was another important part of this project; we wanted to allow as much computer control of the machinery as possible, as well as some processing to allow us to see data in real time. Systolic, diastolic and MAP were displayed every 50 seconds through the blood pressure monitor but we wanted to monitor our subjects very closely at each instant. This is the reason why the ECG signal was further processed to have the heart rate display in real time.

This pilot experiment was carried out primarily to determine whether the developed fMRI compatible system could produce results similar to results produced by non-fMRI compatible LBNP systems. In this experiment, LBNP was applied in a graded manner from 0 to –50 mm Hg, to ensure a progression in cardiovascular stress. This methodology is consistent with the LBNP protocols in the literature [1,7] and allows rapid cardiovascular stabilization during each LBNP level. Furthermore, in patients with heart diseases, it might be preferable to apply gradual cardiovascular stress, rather than a sudden stress.

This pilot experiment results followed the general principle of LBNP, as more blood is pooled towards the leg due to graded negative pressure, the blood flow towards the brain decreases and the heart rate increases to maintain the normal rhythm of the heart. Results from this experiment clearly showed that heart rate increases and blood flow in the brain decreased with the LBNP. This pilot experiment gave similar results when the experiment was repeated in a similar environment. All the subjects completed the experiment without any sign of discomfort and the fMRI compatible LBNP system was compatible worked fine with a 3 Tesla MRI machine. The Subject #2 participated in the both LBNP pilot experiments with out MRI and with MRI. The heart rate started to increase from beginning of the graded LBNP in both the pilot experiments as shown in Figure 4.2.

CHAPTER 6

CONCLUSIONS

The main goal of this project was to develop an fMRI compatible lower body negative pressure (LBNP) system and was to write a software protocol that would acquire, display, process, and store data. Based on the goals that were originally set, this project was a successful one. We were able to develop an LBNP system that would work with fMRI and were able to collect ECG and blood pressure data to verify the accuracy of the system.

Through a series of tests, the system was shown to be accurate, reliable and safe. This pilot experiment was called accurate because its result followed the general principle of LBNP which state as more blood is pooled towards the leg due to graded negative pressure, the blood flow towards the brain decreases and the heart rate increases to maintain the normal rhythm of the heart. Results from this experiment clearly showed that heart rate increases and blood flow in the brain decreased with the LBNP. It was called reliable because this pilot experiment gave similar kinds of results when the experiment was repeated in a similar environment. It was called safe because all the subjects completed the experiment without any sign of discomfort and the fMRI compatible LBNP system was compatible with a 3 Tesla MRI machine.

The plotted heart rate and blood flow in the brain against graded lower body negative pressure matched with the results of Table 4.2, data published by similar LBNP research [1,7]. Unlike previous studies, a pilot experiment was performed using fMRI technique to measure blood flow velocity in the brain.

One major improvement of this system would be to replace the Rheostat (manual

vacuum controller) with an automatic controller that is controlled by the LabVIEW program. Presently, the current protocol pauses after each level of recording. The user needs to change the negative pressure by using the Rheostat controller and then has to resume the program for the next pressure level. Such an addition would make experimental process fully computer controlled.

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