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Mock Circulatory System for the Evaluation of Left Ventricular Assist Devices, Endoluminal Prostheses, and Vascular Diseases

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Abstract: A new digital computer mock circulatory system has been developed in order to replicate the physiologic and pathophysiologic characteristics of the human cardiovascular system. The computer performs the acquisition of pressure, flow, and temperature in an open loop system. A computer program has been developed in Labview programing environment to evaluate all these physical parameters. The acquisition system was composed of pressure, flow, and temperature sensors and also signal conditioning modules. In this study, some results of flow, cardiac frequencies, pressures, and temperature were evaluated according to physiologic ventricular states. The results were compared with literature data. In further works, performance investigations will be conducted on a ventricular assist device and endoprosthesis. Also, this device should allow for evaluation of several kinds of vascular diseases.
Key Words: Hemodynamic performance—Mock circulatory system—Pulsatile blood flow—In vitro experiment.

The main components of the circulatory system are the heart, blood, and blood vessels. The circulatory system is composed of two parts: the systemic circulation and the pulmonary circulation in series. In summary, the left ventricle pumps blood into the aorta. The aorta branches into smaller arteries, which in turn branch repeatedly into still smaller vessels and reach all parts of the body. Within the body tissues, the vessels are microscopic capillaries through which gas and nutrient exchange occurs. Blood leaving the tissue capillaries enters converging vessels, the veins, to return to the heart and lungs. The result of the interaction between the heart and the two vessel systems gives magnitude and pattern of the blood pressure and flow.

The Institute Dante Pazzanese of Cardiology and the University of São Paulo are working together in order to develop a digital mock cardiocirculatory loop capable to perform studies in normal and pathologic conditions of the human cardiovascular system. The study has started from the initial concept of Dr. Guerino's analog simulator (1). This kind of equipment has been used in several institutions for the development of cardiovascular devices. Before any in vivo test, some devices and prostheses can be evaluated by in vitro experiments (2,3). In the last decades, mock circulatory systems have been used to evaluate cardiac valves, ventricular assist devices, and also vascular grafts. Those mock systems have been developed according to a device project using technologic advances in order to replicate, as precise as possible, some cardiovascular conditions. The complexity of hemodynamics concerned in the cardiovascular system involves concepts of fluid mechanics. Some

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parameters, such as pressure, flow, temperature, vascular resistance, and compliance, can be reproduced by the use of a mock circulatory system. Pressure, temperature, and flow values could be treated in a signal conditioning system that sends the instantaneous acquired data to a microcomputer to be collected and presented in a virtual instrument panel written in LabView. The in vitro analysis leads to a qualitative and statistical evaluation of the study subject and gives evidences about the device's stability, hydrodynamic performance, assurance, and confidence of the test.

This article describes the conceptual and detailed design, and also the development of a mock circulatory loop system built to evaluate cardiovascular devices and discusses the basic characteristics and features of the instrument.

MATERIALS AND METHODS

Mock circulatory system

In order to relate flow and pressure in a quantitative way, three basic hemodynamic elements were established: resistance, compliance, and inertance (4). The Hagen–Poiseuille equation gives the resistance of a single tube, depending on the tube geometry and the viscosity of the fluid (5). The compliance depends on the ratio of a change in volume and a change in pressure. It is strongly dependent on pressure and it is also affected by the wall tube properties. The fluid inertia is dependent on the liquid density and on the tube geometry.

$$Q = \frac{\pi R^4}{8\mu}\frac{\Delta P}{L} \qquad (1)$$

where Q is the volume flow of an incompressible fluid through a circular tube, R is the internal radius of the tube, P the pressure difference between the two ends, μ the dynamic fluid viscosity, and L is the total length of the tube in the x direction.

The mock loop consists of four components: the pump system, the circulatory system, the test compartment module, and the acquisition and analysis monitoring system.

The pump system arrangement consists of an engine that uses a piston to push a diaphragm, which is fixed inside the chamber, and this device is used to simulate the left ventricle and also, it allows to create an unsteady flow (Fig. 1). A couple of mechanical valves are used to control the fluid inlet and outlet inside the chamber. In addition, there is a reservoir with an electrical resistance and temperature sensor to store the work fluid and keep its temperature in a physiologic level. This reservoir that simulates the veins and left atrium is opened to atmospheric pressure and it is located ahead of the ventricle chamber. The height of the reservoir is used to impose a physiologic atrial pressure to the entrance of the ventricle chamber.

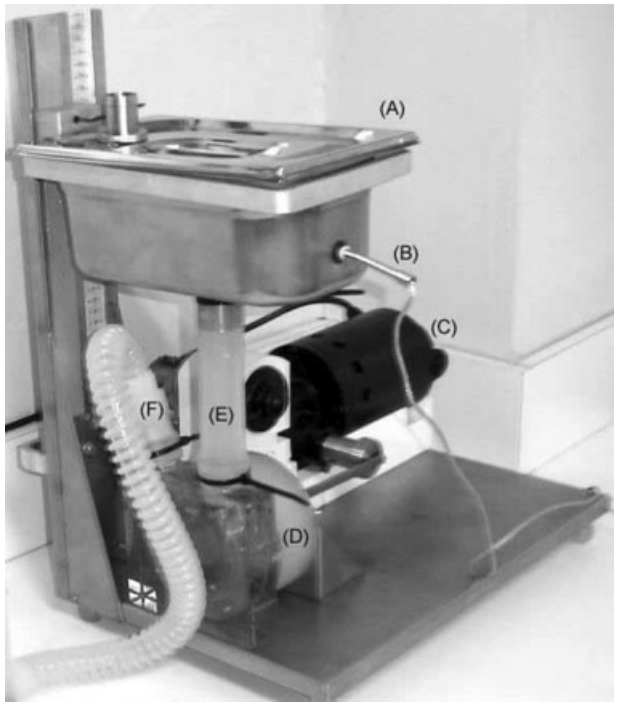

FIG. 1. Photograph of the mock loop showing the (A) reservoir, (B) temperature sensor, (C) pump system, (D) ventricular chamber, (E) inlet, and (F) outlet.

The circulatory system consists of a compliance chamber that represents the vessel wall distensibility and a tourniquet that squeezes a tube segment in order to simulate circulatory system peripheral resistance.

The compliance chamber is made of transparent acrylic walls and there are inlet and outlet connectors. A manually controlled pump placed on top of the chamber allows the management of the volume of compressed air inside the chamber. The variable air volume is a technique for controlling the effective compliance of the system. The air volume inside the chamber is changed according to the fluid volume that passes through the chamber.

A tourniquet that squeezes a tube segment, modifying its internal diameter area, simulates the circulatory system peripheral resistance (Fig. 2). According to Eq. 1, the internal diameter area is a highly relevant variable to the resistance value, and the pressure magnitude is monitored by the transducers.

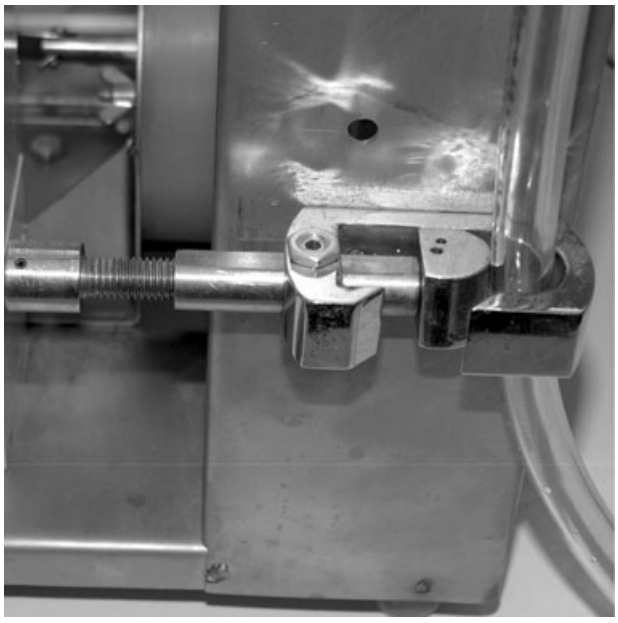

FIG. 2. Circulatory system peripheral resistance.

Both the circulatory resistance and compliance chamber systems are used in order to adjust the sinusoidal wave generated by the pump system to a physiologic wave.

The test compartment module is a device to fix models, like vessel segments, stents, endoprostheses, and artificial hearts, which are under study (Fig. 3). The work fluid should be prepared according to the goal of the experiment and must replicate some properties of the blood (6). If filtered or distilled water is used as the work fluid in an experiment with a natural vessel, it causes edema in the vessel because it is a hypotonic fluid (1) (a hypotonic solution is one in which the concentration of electrolyte is below that in the cells). In this situation, osmotic pressure leads to the migration of water into the cells, in an attempt to equalize the electrolyte concentration inside and outside the cell walls. If the difference in concentration is significant, it can cause the rupture of the cell wall, leading to the death of the cell. Consequently, it is vital that the electrolyte concentration of liquids used during the experiment be matched within the cells.

Blood as a work fluid demands some conditions such as a biocompatible surface to prevent coagulation and controlling mechanical forces to achieve a low hemolysis index (7,8). The velocity has a direct relationship with turbulence and shear stress, which increase blood cell damage. Also, differences in velocity distribution modify the exposure time of the blood cells to stress (9). In addition, vortices prolong the residence time of the blood cells inside the device, which contributes to increase the hemolysis index.

A 37% glycerol : 63% water solution is frequently used in experiments with nonbiologic models, such as vascular prosthesis, ventricular assistant device, and venous filter, in which the viscosity similarity between this solution and plasma is important. However, it is not recommended in experiments with natural vessels because of the principle that, to keep this vessel biologically active, the work fluid must provide some energetic substrate to keep the integrity of the natural vessel's cellular structures (1). In this first experiment to validate the mock system, this solution is chosen because of its similarity with plasma viscosity and density.

The acquisition and analysis monitoring system consists of instrumentation (Fig. 4) and a software module. Instrumentation is composed of a set of transducers (Fig. 5), such as pressure, temperature, and flowmeter, placed at strategic sites of the mock circulatory system to evaluate the model under investigation.

A fluid needs some length to develop the velocity profile after entering the tube or after passing through components as bends, constrictions, etc. The

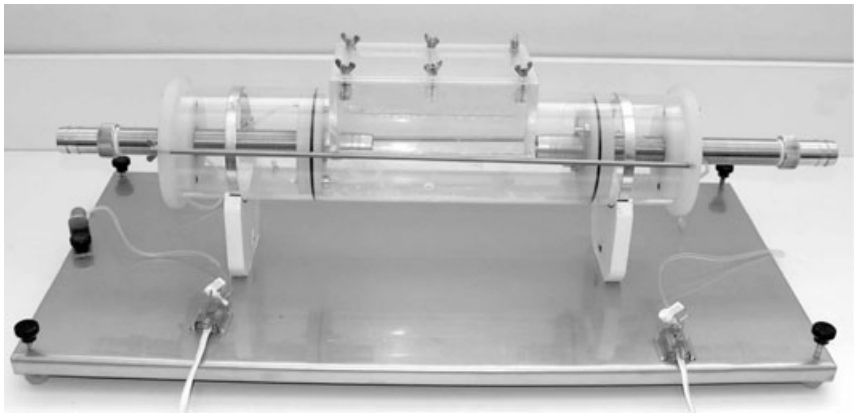

FIG. 3. Test compartment module.

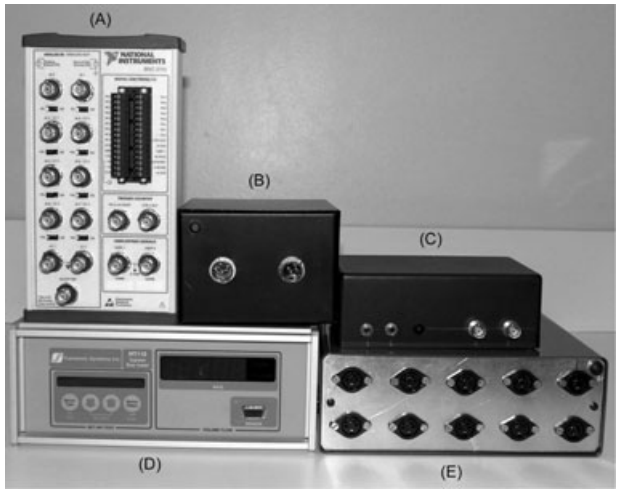

FIG. 4. Acquisition system consists of the (A) acquisition device, (B) power supply, (C) thermometer, (D) ultrasonic flow meter, and (E) signal amplifier device for pressure acquisition.

system is designed to have a fully developed flow pattern into the tubes at the section in which the transducer is placed. It is possible by having a sufficient section length according to the equation:

$$\frac{l_e}{D} = 0.06Re \quad \text{(Laminar flow)} \tag{2}$$

$$\frac{l_e}{D} = 4.4(Re)^{\frac{1}{6}} \quad \text{(Turbulent flow)} \tag{3}$$

$$Re = \frac{\rho VD}{\mu} \quad \text{(Reynolds number)} \tag{4}$$

where l_e is the entrance length, D the internal diameter of the tube, μ is the fluid viscosity, ρ is the fluid density, and V is the fluid velocity.

The temperature transducer (PT100 KN 2515, Heraeus Sensor Technology, Diadema, SP, Brazil) is connected to the reservoir of the mock system to measure the instantaneous local temperature value. Depending on the experiment goal, it is important to keep the temperature range within the physiologic level. A pressure transducer (TruWave Disposable Pressure Transducer, Edwards Lifesciences, São Paulo, SP, Brazil) is placed in the test compartment module to investigate the behavior of the simulator. An ultrasonic flowmeter (HT110, Transonic Systems, Ithaca, NY, USA) is placed downstream of the test compartment module and it is used to acquire hydrodynamic information of the mock system. All measured signals are amplified by devices developed in our laboratory and acquired by a data acquisition board slotted in the PC (PCI-6036, National Instruments, Austin, TX, USA) through a connector block (BNC-2110, National Instruments).

The monitoring program is written in LabView (National Instruments). Figure 6 presents the block diagram developed to monitor the whole system and this main program is composed of two subprograms (Figs. 7 and 8). The program processes all acquired data and shows all measured signals in a computer program front panel developed in LabView. The signals are sampled at 1 kHz and low-pass filtered at 60 Hz in order to acquire a reasonable sampling rate and to remove unwanted signal components, respectively. The instantaneous measured signals are monitored in real time, but they can also be stored in a text file.

RESULTS

The test was performed simulating a normal healthy person in the resting condition and also in a pathologic state. At normal conditions, the values of the systolic pressure, diastolic pressure, heart rate, and cardiac output were given as 120 mm Hg, 80 mm Hg, 60–90 bpm, and 5–6 L/min; however, those values at the pathologic condition were different. In this study, the results of the flow, pressure, and temperature were evaluated according to the physiologic and pathologic states and they were compared with literature results.

Figures 9 and 10 show the front panel with all physiologic and pathologic measured signals. The temperature range alarm was fixed between 32 and 39°C, although it was controlled by a thermostat to stabilize at 36.5 ± 0.5°C. The temperature was kept stable during the whole experiment to avoid change in the fluid viscosity. Liquid viscosity tends to fall with temperature increase. The mean flow was about 4.86 L/min, the mean arterial pressure was

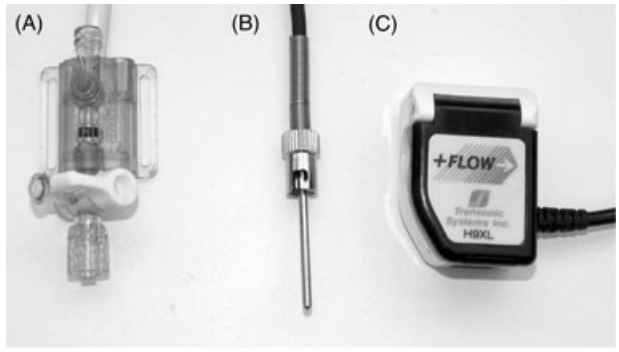

FIG. 5. Pressure (A), temperature (B), and flowmeter (C) sensors.

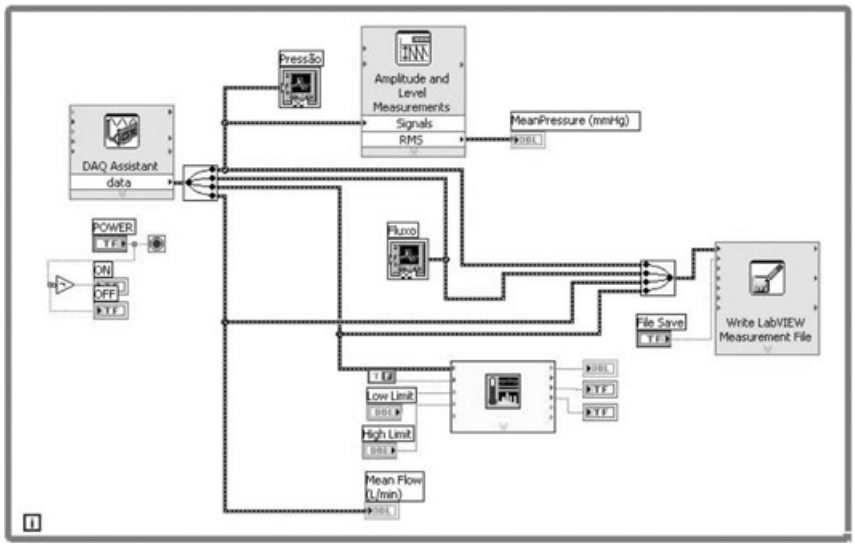

FIG. 6. Block diagram developed to monitor the whole system.

about 95 mm Hg, and the systolic/diastolic peaks were about 120 and 70 mm Hg, respectively. All these values were within physiologic levels. However, the values of the pathologic state were given as 3.94 L/min, the mean arterial pressure was about 139 mm Hg, and systolic/diastolic peaks were about 210 and 70 mm Hg, respectively. The value of the heart rate was fixed at 80 bpm without a waiting phase for filling the ventricular chamber between strokes.

According to the results of the physiologic and pathologic flow waveform, it is possible to see a multiphase pulse starting with a sudden increment with an abrupt decrement after the systolic peak, but also with a backflow at the end of the pulse. In the pathologic simulation, pressure and flow changes were caused by an increment in peripheral resistance imposed on the system. The pressure pulse follows the same pattern, and also, it is possible to note the dicrotic notch more evidently.

DISCUSSION AND CONCLUSION

The mock circulatory system has been designed to mimic the physiologic and pathophysiologic characteristics of the cardiovascular system. The main aim of this simulator was to perform an accurate evaluation of the natural vessel segments, stents, endoprostheses, and artificial hearts prior to in vivo experiments. The system has proven an accurate environment to simulate in vivo conditions, and the experiments have shown to be valuable in the research and development of medical devices. A set of transducers, such as pressure, temperature, and flowmeter, with actuators, such as electrical resistance, tourniquets, and compliance chamber, was used to control and monitor the system. It is helpful to analyze and replicate several kinds of physiologic

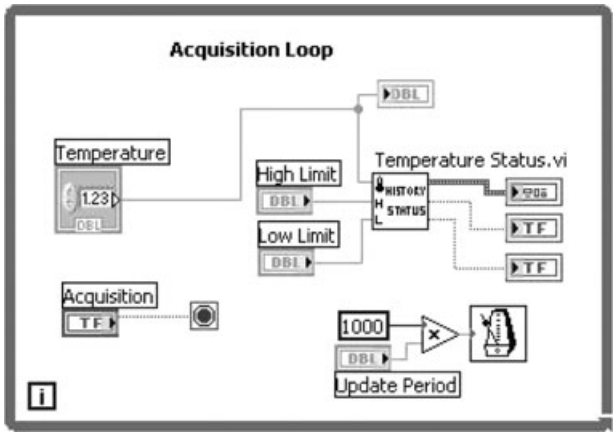

FIG. 7. Temperature acquisition block diagram.

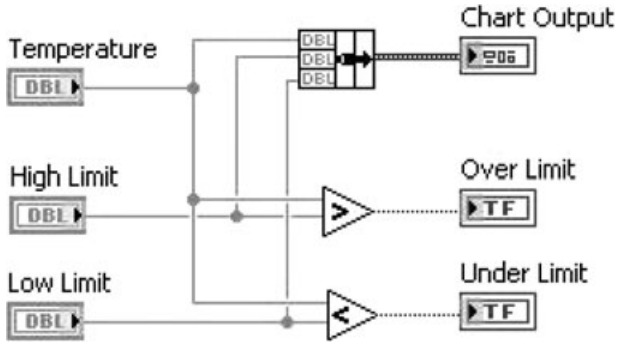

FIG. 8. Temperature range alarm block diagram.

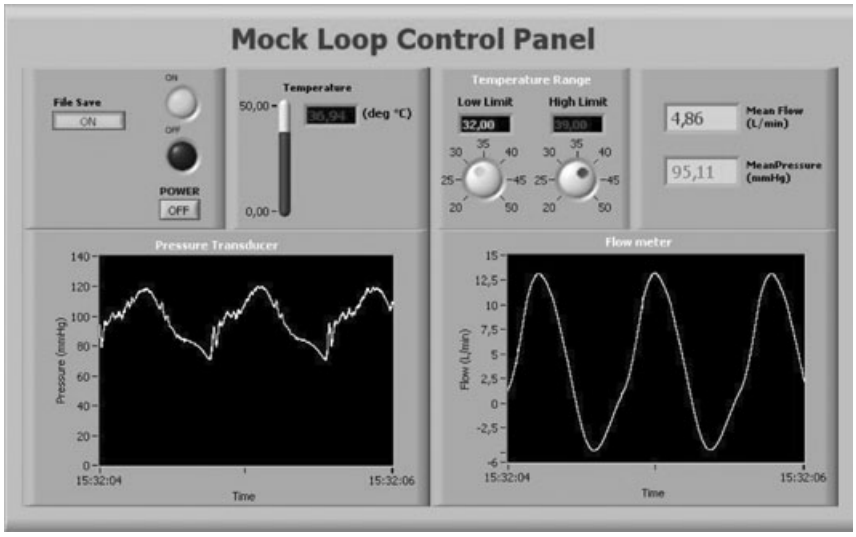

FIG. 9. Front panel with physiologic measured signals.

and pathologic conditions. This article describes the first experiment to validate the mock system.

During systole, blood is ejected through the open aortic valve and the flow rapidly rises to a peak somewhere in the first one-third of the systole. After the ventricular systole is completed, the aortic valve is closed by a retrograde surge of blood flow, represented by a dicrotic notch on the pressure pulse (Figs. 9 and 10) and it causes some changes in the slope angle of the waveform.

When blood is ejected into the aorta, it generates a pressure wave that travels along the arteries. The pressure pulse is also determined by the elasticity of the blood vessels. The shape of the pulse provides early information about a developing arterial vascular disease and the pulse waveform analysis can often detect changes very early even in asymptomatic diseases.

The control of the arterial pressure is a complex problem because it can be altered by many factors. The systemic arterial pressure is determined by the relationship between cardiac output and systemic peripheral resistance. An uncompensated reduction in either leads to a reduced pressure in the arterial system and this indicates a decreased blood flow through the organs. Conversely, a high arterial pressure indicates an increased cardiac workload and/or a high peripheral resistance. The cardiac output is the volume of fluid expelled by the pump system per minute and it is determined by the heart rate and stroke volume.

A compensatory mechanism can be set as follows: a reduction in cardiac output can be compensated for by a corresponding increase in peripheral resistance. Likewise, a reduction in peripheral resistance can be controlled by a corresponding increase in cardiac

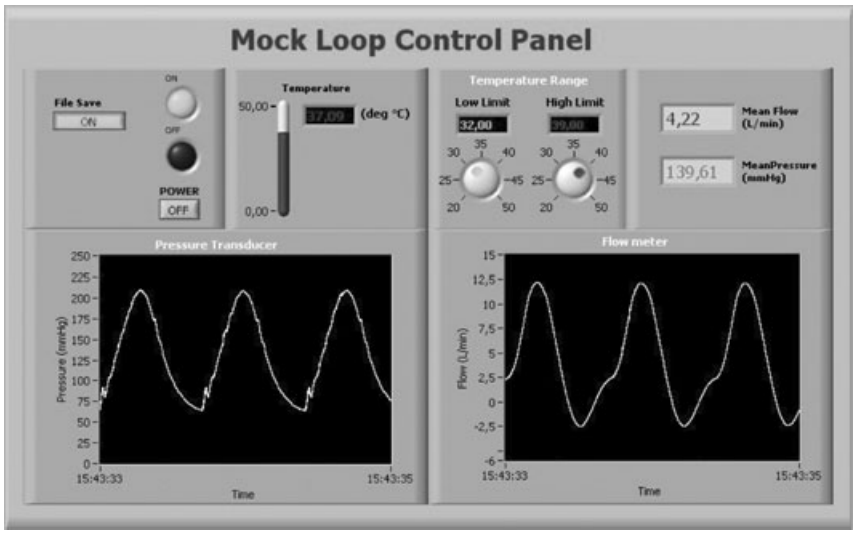

FIG. 10. Front panel with pathologic measured signals.

output. In the same way that changes in the compliance of the system can be balanced by changes in the peripheral resistance, a reduction in ventricular stroke can be adjusted by an increase in heart rate.

Even though some basic physics principles are related to blood flow as described in Eq. 1, pressure and flow waveform patterns are highly influenced by factors such as wall roughness and compliance, pulsatile flow, turbulence, backflow, and collateral vessels. These variables will contribute to pressure and flow waveform modeling. The introduction of pathologic disturbance such as atherosclerosis, which is caused by the formation of multiple plaques within the arteries, causes changes in physiologic pressure and flow pulse.

The results of the pressure and flow waveforms measured in the mock system have demonstrated good repeatability and reproducibility. It is necessary to guarantee data consistency and stability. The experiments have promoted values of pressure, flow, and temperature in the physiologic and pathologic level. The changes are performed in the peripheral resistance of the system in order to increase pressure and decrease flow magnitude to replicate the pattern of a downstream stenotic condition as it occurred in the pathologic case. The pressure and flow waveform generated by the mock system has some intrinsic characteristics promoted by the inertia generated with the use of a direct current motor in the pump system and compliance characteristics caused by the use of silicone tubes. The noise observed in the pressure pulse occurs because of the monolayer silicone tubes used and also because of the disturbance caused by the stainless steel plug used for pressure measurement. According to the vessel segment into the body, the artery is a multiplayer structure (tunica intima, tunica media, and tunica adventitia) and this will change some characteristics of the damping and pressure pulse propagation. The stainless steel connector is plugged to a silicone tube segment, which causes changes in the local compliance pattern.

Because the mock system is set to work at a fixed rate, without a waiting phase for filling the ventricular chamber between strokes, it causes a flow waveform with a short diastolic period and also with some misinformation of that period.

The mock circulatory system developed in our laboratory to perform experiments under physiologic and pathologic conditions will enable us to focus our investigations on the cardiovascular field. Further investigations are needed to address the performance of the mock system for the evaluation of cardiovascular devices and improvement of vascular surgery techniques.

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