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College: Engineering and Computer Science

Computer Simulations to Predict the Effectiveness of Intravascular Circulatory Support for Fontan Circulations

I. Introduction and Motivation

The incidence of congenital heart defects is approximated as 8 in 1,000 live births in the United States [2]. Congenital heart defects (CHD) represent a broad term to describe physical malformations in the heart or circulation of newly born children. The most severe cases of CHD involve the abnormal development of at least one of the ventricles (the pumping chambers of the heart). The majority of these patients must undergo a series of surgeries that effectively re-routes the blood vessels near the heart. The final surgical procedure connects the superior and inferior vena cava (the blood vessels that drain blood from the organs to the right heart) to the pulmonary arteries (the blood vessels that carry blood to the lungs from the right heart) [3]. A comparison of

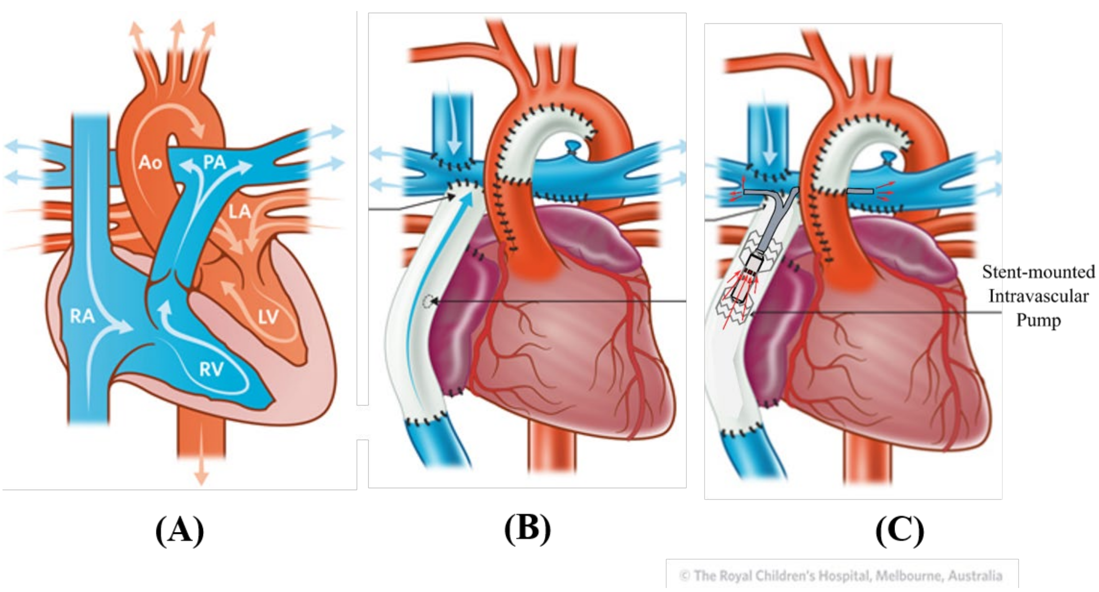


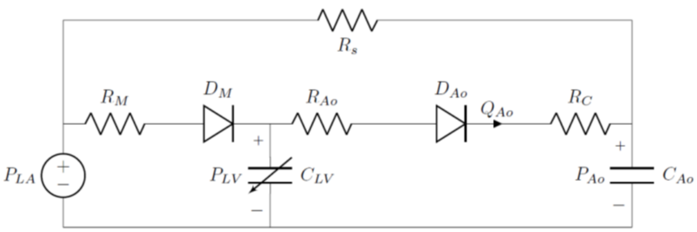
Figure 1. **(A)** A simplified diagram of the flow of blood through a normal heart, **(B)** diagram of blood flow through a heart with a congenital malformation (hyperplastic left heart syndrome in this case), **(C)** the proposed use of an intravascular blood pump in the Fontan circulation (image adapted from [1])

these circulations is shown in Figure 1A and Figure 1B. This new circulation, called the Fontan circulation, gives patients the opportunity to relatively healthy lives without the need for two functional ventricles [4]. However, when these patients reach adulthood, the lack of two ventricles eventually leads to heart failure [5]. Researchers have shown that using blood pumps, devices that supply circulatory support to heart failure patients, are effective therapy options for this population [6].

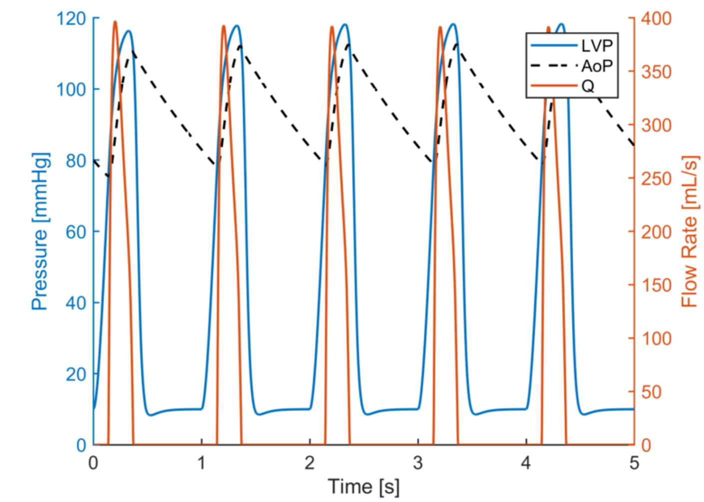
Intravascular blood pumps offer the potential to support patients with the Fontan circulation without the need for an additional open-heart surgical procedure. Intravascular blood pumps are devices that can be implanted via catheter-based procedures and are typically used clinically to provide partial support (2.5-5 L/min) for patients with acute heart failure (HF). Recently, Stretch et al. showed that the use of intravascular devices for short-term circulatory support in patients with acute HF increased ten-fold between 2007 and 2011 [7] and resulted in decrease mortality, from 41% to 33% over a 5 year period. Intravascular pumps have already been successfully used for the pulmonary circulation and the Fontan circulation [8, 9]. Despite their promise, there is limited clinical experience using intravascular pump technology, especially in specialized settings like the Fontan circulation. The long-term goal of the PI is to initiate the development of a Fontan specific intravascular pump (Figure 1C). To guide the design of this technology, this proposal will focus on developing computer simulations that will predict the level of pressure and flow needed to aid Fontan circulations and to optimize the placement of the device within the pulmonary circulation.

II. Methodology

Computer models of the human circulation are well documented [10]. The majority of researchers have created lumped element models representing the human circulation. Lumped element models



(A)



(B)

Figure 2. (A) Circuit representation of a normal systemic circulation and **(B)** Left ventricular pressure (LVP), aortic pressure (AoP) and aortic flow rate (Q)

take components and variables in the circulation, like valves, blood vessel elasticity and resistance, and represents them with linear electrical analogs like diodes, resistors, and capacitors. These models have successfully been used to model human circulation behavior under normal physiologic states, diseased states, and under the aid of circulatory support pumps [11-13].

A preliminary model with equations for the systemic circulation (the left side of the heart) has already been developed by the principal investigator (PI). The system of differential equations have been derived and solved numerically using MATLAB software. Figure 2A shows the lumped circuit representation developed by the PI. Valves in the heart are modeled as diodes, the elasticity of blood vessels are modeled as capacitors and the resistance of blood vessels to blood flow are modeled as electrical resistors. Lastly, the left ventricle is modeled as a time-varying capacitor. A total of four variables (left ventricular pressure, aortic pressure, left atrial pressure, and aortic flow) were solved by deriving the state-space equations and applying the appropriate initial conditions. The results from this initial simulation, shown in Figure 2B, demonstrate that it is possible to model the behavior of the systemic circulation using circuit analogies and a system of ordinary differential equations.

During this probationary faculty support program, the principal investigator (PI) will develop a set of new models, which build upon the existing work that has already been achieved. These models include 1) a complete and more complex representation of a normal circulation (which includes both the right and left hearts), 2) a model for the Fontan circulation (which is currently lacking in the field), and 3) a model for the Fontan circulation with circulatory support from an intravascular pump.

In the case of the normal circulation, a total of 8 state variables will be solved using the state space equations. The current circulation model developed by the PI will be modified and extended to include the right heart (pulmonary circulation). For the Fontan circulation, 9 state variables will be solved (since the superior vena cava and inferior vena cava pressures will be calculated separately). Lastly, 10 state variables will be calculated for the model representing the Fontan circulation with added circulatory support. The intravascular pump will act as a forcing function which acts on the circulation state variables, similar to Ferreira et al [14].The additional variable included the intravascular pump flow rate. Parameters like arterial resistance, capacitance, heart rate, and elastance will be taken from the literature. This includes reviewing other computer models published in relevant journals or from clinical research in peer-reviewed journal and conference proceedings. Various configurations of circulatory support in the Fontan circulation will be studied in the model to guide the development of a new intravascular pump.

The goal of this research is to produce preliminary data that results in the development of intravascular blood pumps designed specifically for Fontan patients. The PI has already begun collaborating with his former doctoral advisor, Daniel Levi M.D., at UCLA David Geffen School of Medicine regarding the submission of an NIH AREA grant. Dr. Levi, an interventional cardiologist, has extensive experience treating patients with the Fontan circulation. The PI has also worked with him on various projects pertaining to the development of Fontan patient-specific medical devices.

III. Timeline

The development of these three computer models will span the Spring 2019 semester. The model of the normal circulation will be completed by the end of the second week of the semester (February 8, 2019). This computer model will serve as the base results for other computer simulation results. The model for the Fontan circulation will be completed by the seventh week of the semester (March 15, 2019). Incorporation of the intravascular blood pump will be completed by the tenth week (April 5, 2019). By the end of the thirteenth week (April 26, 2019), sensitivity analysis of the model and model debugging will be completed.

IV. Significance

The development of medical devices that alleviate the pain of Fontan circulation patients is severely lacking relative to devices developed to treat adult heart failure therapies. This research aims to close this gap. As part of this proposed project, PI plans to gather preliminary data that will aid in procuring external funds to strengthen the research environment of the College of Engineering and Computer Science.

V. Impact on Instruction

This cardiovascular model has already been introduced in ECE 602 – Biomedical Engineering I. Graduate students enrolled in this course will be given access to the mathematical derivations and simulation protocols for modeling a healthy circulation. In addition, graduate students will be given an opportunity to work on this project as part of their Masters project or thesis submission.

VI. Dissemination

As part of the dissemination plan, a one page abstract will be submitted to the BMES Annual Meeting scheduled for October 2019. The results will also be included in an NIH AREA grant submitted in June 2019 in collaboration with UCLA.

VII. References

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