Mechanical Simulators of the Cardiovascular System: An Alternative to Research Subjects and Patients

William D. Fraser

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Before the development of electrical analog and digital computer-based simulations of the cardiovascular system, animal models were the most common tools for investigating the detailed properties of the cardiovascular and cerebrovascular circulations, especially when human experimentation was not possible. However, as far back as the 16th century, William Harvey developed the concept of a mechanical analog to describe heart function and blood flow,^{11,13} though there is no evidence he constructed any such devices. In 1850 Weber²⁸ published a description of what appears to be one of the first working mechanical analogs, using portions of the small intestine with natural valves, to investigate the concept of the hydrostatic mean pressure. It was not until 1940 that Starr and Rawson developed a detailed mechanical model of the circulatory system in order to investigate congestive heart failure.²² Their model included mechanical versions of all four heart chambers, systemic and pulmonary circulations, capillary beds, flow meters, and the ability to regulate vascular resistance. Advances in materials and computer technologies have the potential to enable the development of much more sophisticated mechanical models for basic research, validation of computer based simulations, and training of physicians.

Cardiovascular Simulators for Teaching

Computer simulations of the cardiovascular and cerebrovascular systems are used as clinical teaching tools, including simulated pathologies.¹⁴ However, for training of medical students and physicians in hands-on procedures for radiology, cardiology, and cardiovascular surgery, mechanical systems that simulate the structure and fluid dynamics of some segments of the cardiovascular and cerebrovascular systems are becoming more common.^{1,6,17} Angioplasty, insertion of stents, and the use of other vascular probes and catheters can be demonstrated and practiced on mechanical analogs prior to real-world application, with the obvious advantages of increased patient safety and the ability to provide training when patients are not available. The use of 3D printing technology has allowed custom models that faithfully reproduce the vascular systems of individual patients, allowing clinicians to practice customized procedures prior to real-world use.¹

Research Systems

Investigating the exposure of human volunteers to extreme environments such as sustained acceleration, or thermal stress, is becoming more difficult and expensive, as Institutional Review Boards impose more constraints and safety requirements become more stringent. Computer simulations can provide an alternative approach, especially in those cases where one wishes to extrapolate to stress levels that would not be possible with human subjects. Dozens of research papers have been published describing mathematical models of the cardiovascular system, including detailed models of heart mechanics, respiratory function, and the complexities of blood flow in the brain and the impact of cerebrospinal fluid pressure on cerebrovascular fluid dynamics.^{21,24,26,27} Most of these have addressed basic research goals in understanding the interactions between various components of the system, though some have been developed as teaching tools. These models do require experimental data on the constitutive properties of blood vessels, the heart, and other soft tissue in order to determine the resistance,

From Silatyuk Research, Toronto, ON, Canada.

Reprint & Copyright © by the Aerospace Medical Association, Alexandria, VA. DOI: https://doi.org/10.3357/AMHP.4805.2017



Fig. 1. The mechanical model of the cerebrovascular system consists of an ascending carotid artery analog, a descending jugular vein analog, and a model of a rigid skull with a flow resistor. The flow is generated by adjusting the heights of the fluid containers (and thus the perfusion pressure).

inertia, and capacitance of the system components. Validation of these mathematical models requires data from patients, healthy human subjects, or animal models.

Mechanical models can be used to provide an alternative method to validate the computer simulations, since the constitutive properties of the blood vessel and heart analogs can be readily quantified. Since the work of Starr and Rawson²² described above, few mechanical models have been used, as the computer simulations have become more sophisticated. During the early development of improved cardiac bypass systems for open heart surgery, Anderson developed a mechanical analog with a motor driven heart model.^{2–4} A YouTube video is available demonstrating the simulator.³ Anderson was particularly

concerned with incorporating a nonsucking, four-chamber mechanical heart analog that produced pulsatile flow at the outlet and steady nonpulsatile flow at the inlet. Blood flow in a system with a nonsucking pump is dependent on systemic factors such as arterial and venous resistance and venous capacitance, not the properties of the pump such as stroke volume and beat rateunlike pumps that suck on the inlet side. More recently, similar circulation models have been developed to evaluate the designs of ventricular assist devices prior to their use in a clinical setting.²⁵ Variations on simple mechanical models of the cerebrovascular system have been used in the ongoing, and times heated, debate as to the role of gravity in influencing blood flow to the brain,^{16,18} the reasons for the high blood pressure of the giraffe,^{5,12,15,20} and the ability (or not) of some extinct dinosaurs to elevate their long necks to a near vertical position without losing consciousness.¹⁹

One mechanical simulator has been used to validate a mathematical model of cerebral blood under continuous positive G_z exposures. The mathematical model predicted that jugular vein collapse due to negative venous pressures and the subsequent increase in total cerebrovascular resistance would be sufficient to reduce cerebral perfusion to a level insufficient to support consciousness, i.e., G-induced loss of

consciousness (G-LOC).⁷ Determining jugular vein dimensions and blood flow velocity in humans during G_z exposures is not feasible. Therefore, to validate the role of the jugular vein collapse as the root cause of G-LOC, a mechanical surrogate of the head and neck was built⁸ incorporating a carotid artery, a jugular vein, a rigid skull with cerebrospinal fluid (water), and a linear cerebrovascular resistor (**Fig. 1**). Unable to test the system on a human centrifuge, the effect of G_z was simulated by incorporating a "heart" to "skull" distance approximately five times that of a human. Flow through the system was controlled by adjusting the height of the water-filled containers to adjust inlet and outlet pressures. The original mathematical model reproduced the fluid flow characteristics of the mechanical analog (with appropriate changes in neck vascular length and the constitutive properties of the analog vein and artery), confirming venous collapse as the primary mechanism regulating flow. The constitutive properties of the vinyl and dialysis tubing (as analogs of the carotid artery and jugular vein) could be easily measured in the laboratory, whereas the mathematical model of the actual human system used data collected from human subjects under high levels of positive pressure breathing.⁹ Thus the mathematical model, which accurately predicted the G_z level at which G-LOC was likely to occur,¹⁰ was validated by the mechanical model.

Future Applications

With the advent of recent manufacturing technologies, more sophisticated mechanical analogs of the cardiovascular and cerebrovascular systems, complemented by advanced computer simulations, could be applied to research issues of high altitude exposure or sustained acceleration. The accurate models of the cardiovascular and cerebrovascular anatomy of individual patients produced using imaging data and 3D printers¹ involve producing detailed blood vessel structures with dissolvable substrates that are coated with silicon. Using various thicknesses of silicon coatings, a simulator can be configured with a system of blood vessels with constitutive properties similar to actual arteries and veins, allowing more advanced mechanical simulators for investigating the mechanisms involved in orthostatic intolerance following long-term microgravity exposure,²³ or for designing G-LOC prevention technologies, including anti-G suits and positive pressure breathing. Anderson's models and more recent clinical training simulators have focused on modeling the supine patient. Modifying a mechanical model to allow transition from supine to sitting and standing, incorporating the ability to provide counterpressure to various parts of the systemic and pulmonary systems, and incorporating controllable resistance and capacitance elements to simulate myogenic, neurogenic, and metabolic influences would result in a powerful tool to validate current mathematical models of the cardiovascular system and a much enhanced research and teaching tool.

ACKNOWLEDGMENTS

The author has no conflict of interest to disclose.

Author and affiliation: William D. Fraser, M.Sc., DCIEM, Toronto, Ontario, Canada.

REFERENCES

- Alwais S. 3D printed vascular simulation models improve training and treatment. [Accessed 7 December 2016]. Available from http://blog. stratasys.com/2016/06/28/3d-printed-vascular-simulation/.
- Anderson RM. The gross physiology of the cardiovascular system. Tucson (AZ): Racquet Press; 1993.
- Anderson RM. The determinants of cardiac output. 2011; [Accessed 7 December 2016]. Available from https://www.youtube.com/watch?v= LftmowNNAbc&t=752s.
- Anderson RM, Fritz JM, O'Hare JE. The mechanical nature of the heart as a pump. Am Heart J. 1967; 73(1):92–105.

- Badeer HS. Is the flow in the giraffe's jugular vein a "free" fall? Comp Biochem Physiol A Physiol. 1997; 118(3):573–576.
- Cates CU, Gallagher AG. The future of simulation technologies for complex cardiovascular procedures. Eur Heart J. 2012; 33(17):2127–2134.
- Cirovic S, Walsh C, Fraser WD. A mathematical model of cerebral perfusion subjected to Gz acceleration. Aviat Space Environ Med. 2000; 71(5):514–521.
- Cirovic S, Walsh C, Fraser WD. A mechanical model of cerebral circulation during sustained acceleration. Aviat Space Environ Med. 2001; 72(8):704–712.
- 9. Cirovic S, Walsh C, Fraser WD, Gulino A. The effect of posture and positive pressure breathing on the hemodynamics of the internal jugular vein. Aviat Space Environ Med. 2003; 74(2):125–131.
- Code CF, Wood EH, Lambert EH, Bales EJ. Interim progress reports and concluding summary of 1942–46 acceleration physiology studies. In: Wood EH, editor. Evolution of anti-G suits, their limitations, and alternative methods for avoidance of G-induced loss of consciousness. Rochester (NY): Mayo Foundation Special Purpose Processor Development Group; 1990:409–430.
- 11. Fuchs T. The mechanization of the heart: Harvey & Descartes. Rochester (NY): University of Rochester Press; 2001.
- Gisolf J, Gisolf A, van Lieshout JJ, Karemaker JM. The siphon controversy: an integration of concepts and the brain as baffle. Am J Physiol Regul Integr Comp Physiol. 2005; 289(2):R627–R629.
- Gregory A. William Harvey: English Physician. 2000; [Accessed 7 December 2016]. Available from https://www.britannica.com/biography/ William-Harvey.
- Heldt T, Mukkamala R, Moody G, Mark RG. CVSim: an open-source cardiovascular simulator for teaching and research. Open Pacing Electrophysiol Ther J. 2010; 3:45–54.
- Hicks JW, Badeer HS. Siphon mechanism in collapsible tubes: application to circulation of the giraffe head. Am J Physiol. 1989; 256(2, Pt. 2):R567–R571.
- Hicks JW, Munis JR. The siphon controversy counterpoint: the brain need not be "baffling". Am J Physiol Regul Integr Comp Physiol. 2005; 289(2):R629–R632.
- Next Generation Harvey®—the cardiopulmonary patient simulator. 2016; [Accessed 7 December 2016]. Available from http://www.laerdal. com/ca/harvey.
- Seymour RS. Model analogues in the study of cephalic circulation. Comp Biochem Physiol A Mol Integr Physiol. 2000; 125(4):517–524.
- Seymour RS. Raising the sauropod neck: it costs more to get less. Biol Lett. 2009; 5(3):317–319.
- Seymour RS, Hargens AR, Pedley TJ. The heart works against gravity. Am J Physiol. 1993; 265(4, Pt. 2):R715–R720.
- 21. Shi Y, Lawford P, Hose R. Review of zero-D and 1-D models of blood flow in the cardiovascular system. Biomed Eng Online. 2011; 10:33.
- 22. Starr I, Rawson AJ. Role of the "static blood pressure" in abnormal increments of venous pressure, especially in heart failure. I. Theoretical studies on an improved circulation schema whose pumps obey Starling's Law of the Heart. 1940. Am J Med Sci. 1940; 19(4):499–500.
- Summers R. Development of the Digital Astronaut Project for the analysis of the mechanisms of physiologic adaptation to microgravity: validation of the cardiovascular system module. Acta Astronaut. 2008; 63(7–10):758–762.
- Tawhai MH, Clark AR, Burrowes KS. Computational models of the pulmonary circulation: insights and the move towards clinically directed studies. Pulm Circ. 2011; 1(2):224–238.
- Timms D, Hayne M, Mcneil K, Galbraith A. A complete mock circulation loop for the evaluation of left, right, and biventricular assist devices. Artif Organs. 2005; 29(7):564–572.
- van de Vosse FN. Mathematical modelling of the cardiovascular system. J Eng Math. 2003; 47(3):175–183.
- Wakeland W, Goldstein B. A review of physiological simulation models of intracranial pressure dynamics. Comput Biol Med. 2008; 38(9):1024–1041.
- 28. Weber E. The law of pulsatile flow and its application to the circulation. Primitive model of the circulation. [In German]. In: Berichte ueber die Verhandlungen der Konigl Sachsischer Gesellschaften der Wissen-Schaften zu Leipzig. Leipzig (Germany): Weidmanische Buchkandlung; 1850.