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# HYBRID MECHANICAL CIRCULATORY LOOPS – AN EMERGING NEED FOR TOTAL ARTIFICIAL HEARTS WITH NOVEL TECHNOLOGIES.

**Cardiovascular**

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## ABSTRACT

Circulatory assist devices need to be tested at various levels prior to human implantation. These include numerical simulations, lab and animal testing, tissue computability prior to human trials that would scale in terms of complexity of indications and participant load. Mock circulatory loops though not ideal offer the best current equivalents of gold standard for such purposes in the in vitro domain. These could be very simple hydraulic loops to complex hydraulic loop interface with computers. These need to replicate both right and left circulatory systems coupled with vascular compliances and resistances. It should recreate the perfusion rates and pressures that exist in normal systemic and pulmonary vasculature for both normal and heart failure models. These rigs greatly reduce the device evaluation costs by mimicking nature though vasomotor responses in the normal human body may require complicated evaluation models to be deciphered in future by use of evolving technologies. Following mechanical evaluation on the mock circulatory loop actual animal testing would give the experimental proof of concept. The basic requirements are that of a pump, flow channels, compliance chambers with monitoring of pressure and resistance changes using pressure and flow sensors. It serves as a safe low cost training and evaluating platform. Virtual mock loop simulation tool can simulate the hemodynamics using a lumped-parameter model for systemic/pulmonary circulation characteristic inputs values for impedance, systolic and diastolic ventricular compliance, beat rate, and blood volume and characteristics of the cardiac chambers and valves. VML contains several different lumped parameter models for selection and evaluation. It also stores and organizes data from different origins that makes comparison easier. For new total artificial heart models the advantage of a dual approach emerges with use of hybrid mechanical circulatory loop.

## KEYWORDS

MCL Mock Circulatory Loop, p-CFTAH-Pediatric Continuous Flow Total Artificial Heart, BIVAD – Biventricular Assist Devices, HMCL-Hybrid Mechanical Circulatory Loop

## INTRODUCTION

With changes in the technology and newer assist devices reaching the market there is need to change the in vitro evaluation platform too. Three critical areas need to be recognized. First being the need for advanced physical modeling tools- this makes evaluation of experimental setting prior to setting in mock rigs. Second is complete automation with closed loop control logic that makes evaluation standardized with accurate reproducibility standards. Finally at critical device interfaces like the aorta increasing local field fidelity ensures more accurate simulations to performance in vivo.

### Concepts – Anatomical and Physiological

Figure 1a shows the normal circulatory system and 1b shows the proportionate flow to different regions in a normal healthy adult.

Right ventricle ejects into the lungs at 15-30 mmHg and the pressure in the left atrium is on the order of 3-14 mmHg. Pulmonary system can have large flow at low pressures. The arterial circulation normally operates at 100- 140 mmHg in systole and 60-90 mmHg in diastole; these are the pressures at the ejection site the left ventricle (1).Normal right atrial pressure which is the return pressure of systemic circulation is 3-8 mmHg.

Transplant scenario is plagued by shortage of organs and artificial heart models are looking forward to better disruptive technology to attain necessary level of optimization. Performance validation and safety analysis assumes much importance as newer technology is being introduced for obtaining optimized performance level of these devices (2, 3). ISO and FDA certification requirements must be clearly understood when designing the mock circulatory loops that will be utilized for these evaluation accreditation.ISO 5198 is used for performance characterization and 14708-5 document is specific to circulatory support devices (4, 5, 6). ISO 14971 describes risk management techniques applied to medical devices, and serves as guidance on product life cycle safety determination. ISO 14971 serves as guidance on product life cycle safety determination (7).

Lumped parameter modeling can be applied to hydraulic models and has been used extensively to model the human circulatory system (8, 9, and 10).For LV device evaluation peripheral resistance, compliance and feed capacity- venous volume provides an effective model.

Responses at specific interfaces explain the mechanism of working of entire system (11, 12, and 13). Arterioles provide the largest pressure drop in the systemic circulation and mediate changes in resistance through vasoconstriction and vasodilatation. Both area and length play a role (14, 15).Clinically conditions can be recreated on rigs with proportional pinch valves as automated clamping of the tube can be done (16,17).Compliance is the capacitance that dampens the pressure wave and maintains the diastolic pressure. As a singular device compliance chambers are used to simulate this effect. Changes need to be evaluated during pumping as well as over a range of values to come closer to real life implantation situations which change with various parameters like age sex and disease states (18, 19).Volume expansion can be measured well in membrane chambers. Spring designs are plagued by high impedance due to seal friction and mass flow sensors should be used in case of pneumatic designs. Venous systems in body operated at near atmospheric pressure. The high volume in venous bed ensures adequate ventricular preload. If pump overdraws venous suction collapse would result. For mock loops a reservoir would serve adequate pressure head for left atrium (20, 21, and 22). When both systems are tested simultaneously then compliance chambers would serve the role adequately. Inertial effect of closed loop systems and changes to be replicated are issues when using reservoirs. Utilizing actuators and numerical models is a useful technique of simulating inertial effects.

The capability of researchers to extract geometry from medical imaging modalities, fabricate a representative model from material of choice, and integrating those geometries into experimental studies has become now crucial. The fidelity of the reflection of the physical system in computational models correlates to the accuracy of the determined parameters.

**CAD Model:** Images are used to extract geometry by segmentation. Boundaries of the model are constructed from data sets with regional subset. Integrated environment of segmentation methods and processing tools are available in commercial platforms. Multiple software and published algorithms is also available (23-26). Some of them have post processing tools. For STL model the geometry surface is a mesh of facets and vertices. Interpolation of the boundary between two vertices, and across a facet, is linear. Processing of the rough model is needed. Refinement is by removal of artifacts, smoothing the mesh profile and facet count modification. Alternative to STL is the non-uniform rational basis splines (NURBS).Here free surfaces of the model are defined by fitted nonlinear interpolations that matches the segmented geometry. Here the surface is smooth due to continuous curvature of underlying splines. FEA mesh or machining paths are thus simplified.

**Fabrication**- Additive manufacturing methods are the simplest form of producing an accurate model. Direct printing of distensible material, removes the need for a mold making step to deliver FSI models. The accuracy is typically regulated by the quality of the CAD model and the material choice (rigid or flexible). The fabrication method used is based on these material and accuracy choices. When using PIV or PTV methods, the refractive index of the material must match that of the system fluid (27, 28).For subtractive manufacturing which allows use of a wide range of materials at optimal cost can be used to produce a part with a CNC machine, the geometry of the CAD model forms the basis for cutting paths that are programmed through the use of CAD/CAM software. Rigid models destined for direct implementation as investigational pieces, molds for dip-spin techniques, and classic pour molds can be made using this approach.

Simple concept of a mock circulatory loop is given in Figure 3. Here a dual loop design with the implementation of a systemic venous reservoir is clearly shown. Changing the amount of air volume in the compliance chamber at rest affects the compliance of the system; less air space results in a lower compliance and vice versa. Total peripheral resistor simulating the systemic resistance and a pulmonary resistor with former is being actuated by a tuning clamp and the latter via a gate valve. Figure 4 shows the Timm's Queensland Model with its ability to set a wide range of circulatory parameters- arterial and venous compliance, pulmonary and systemic resistance, left and right atrial preloads, left and right Ventricular contraction .Numerical modeling supports performance enhancements in this method.

For evaluation of total artificial heart the University of Louisville, Kentucky mock circulatory loop is shown in Figure 5. This has also been used to illustrate function of the circulatory system with extracorporeal mechanical oxygenation, left ventricular assist, cardiopulmonary assist, and intra-aortic balloon pump (29, 30, and 31).

## DISCUSSION

In modeling of cardiovascular systems parameters need to be changed without stopping the system and analysis at a multitude of stationary settings in a battery testing method with anatomical geometry of interfaces being included is critical. Translating physiological conditions call for a reflective analog of the cardiovascular system. This analog must have the functional capacity to have runtime parameter control, recursiveness (as it is a closed loop system), and flow field similarity at the interfaces to the devices being tested. Regulatory agencies and scientific governing bodies ensure integral safety standards (32). When open data bases are utilized data sharing initiatives are crucial to common data sources in this field and higher utilization of repositories. Key software designs and hardware development as per regulatory approval need to be identified. Commercial engineering tools and open data bases are providing encouraging steps in this direction helping newer model to emerge with supporting computational tools. Computational models that are not based on hydraulic first principle are the key factors for the initial setbacks. Physical modeling packages that are built for the systems they are representing (hydraulic, mechanical, etc.) produce exceptional performance in these models (33, 34). Subsystem modeling should also be done to increase efficacy of prediction. Controlling arterial compliance with traditional sensors and hardware, inertial effects in the system interfere with efficient modeling. Novel control strategies could address this issue (35).Other pressing requirements are cutting the cost of model development and homogenize the models used by various teams. Use of computational device models would benefit those working on VADs and TAH. There is a need to implement code generation tools that were developed for regulated environments. Subsystem modeling of the mock circulatory loop can be tailored like inclusion of ventricular simulator, arterial compliance chamber, peripheral resistor, and pulmonary simulator etc. Desirable functionalities like nonlinear arterial compliance and change of all controlled set points in runtime could be incorporated into the emerging models. The use of parameter estimation via a computational model using experimental data as the optimization point is a powerful tool in characterizing custom assemblies.

## CONCLUSIONS

Modernization of design tools is crucial. This successfully implements high fidelity testing tools and technological development of devices. An integrated multi scale research tool approach for future requirements for evaluation of modified/novel devices would be a necessity very soon. Due to physical modeling and tuning software deploying stable and well performing process controllers has become increasingly easy. Microcontrollers should ensure the precise process control of the subsystem, communication with a host conductor that was coordinating the subsystems, and the ability to maintain safe subsystem operation in the event communications failed. Imaging modalities that give excellent resolution and the boundaries that are very clearly defined should be chosen. Loop functionality is assessed by the system's ability to change multiple parameters simultaneously and sequentially, to determine whether required conditions could be constructed. Currently virtual mock loop system could be helpful to assess pump performance before in vitro bench testing. This has been successfully demonstrated for pediatric continuous flow total artificial hearts and bi ventricular assist devices. For emerging total artificial heart design can be operated in the physical domain while all vascular elements can be in the numerical domain combing the advantages of the dual approach- as in hybrid mechanical circulatory loop ( figure 5). Virtual mechanical circulatory loops can evaluate a broader variety of devices over wider range of circulatory parameters at an affordable cost with better reproducibility too.

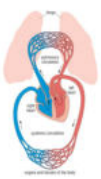

**Figure 1 a Normal Healthy Heart with closed loop circulation in series**

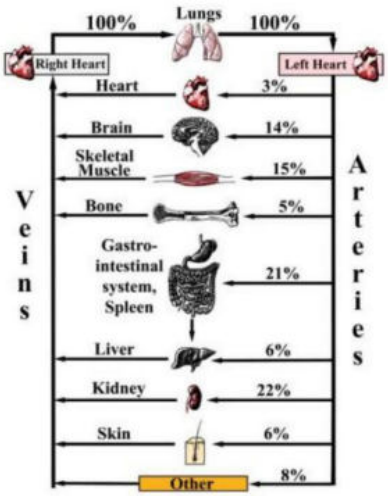


**Figure 1 b Flow distribution in a healthy normal adult at rest**

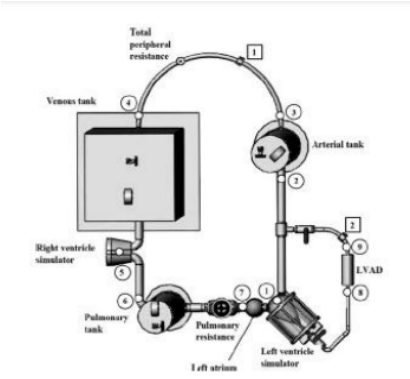


**Figure 3 Simple concept of a Mock Circulatory Loop by Liu**

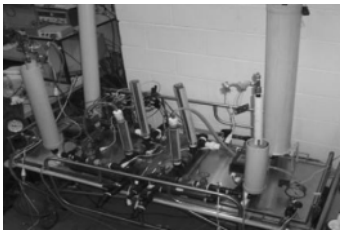

**Figure 4 Timm's Queensland University Model**

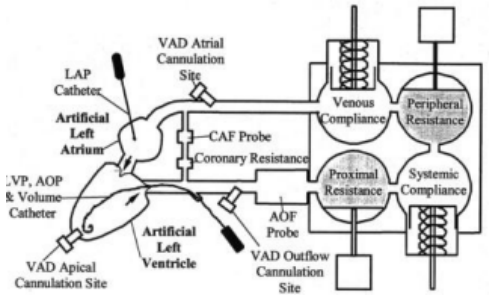


**Figure 5 University of Louisville, Kentucky mock circulatory loop.**

**Figure 5 Hybrid Mock Circulatory Loop**

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