Use of Mock Circulatory Loops for Standardized Performance Testing of Mechanical Circulatory Support Devices: An Interlaboratory Study

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Synopsis

There is a need to standardize how mock circulatory loops can be used as a non-clinical tool for evaluating the performance of mechanical circulatory support devices under pathophysiologic conditions. FDA is facilitating an interlaboratory study to establish consensus bench test methods for predicting device performance in patients.

Introduction

Heart Failure (HF)

- Disease having high clinical significance (6.7 million Americans affected between 2017-2020 [*Tsao CW et al., Circulation, 2023*])
- Impacts cardiovascular hemodynamics (Fig. 1 – cardiac pulses)
- Different HF conditions (e.g., acute myocardial infarction, cardiogenic shock) lead to variability in diagnostic cardiac indices (e.g., left ventricle (LV) pressure and flow, stroke volume)

Mechanical Circulatory Support (MCS)

- One of the few surgical options for end-stage HF patients
- Devices with implantable/extracorporeal mechanical pumps maintaining adequate tissue perfusion
- Device hemodynamic performance evaluated (per ISO 14708-5) using: a) bench testing, b) animal studies, and c) clinical trials

Study Need / Current Knowledge Gap

- *In vivo* device-patient interactions are complex due to varying HF hemodynamics, and therefore need to be evaluated
- Bench testing in pre-market submissions often only contain non-physiologic pressure drop (ΔP)-flow rate curves (Fig. 1 – HQ curve) with no assessment of device-patient interaction in a cardiovascular mock circulatory loop (MCL)
- Standardized physiologic *in vitro* tests are needed because we mainly have to rely on animal and human studies for evaluating device hemodynamic performance

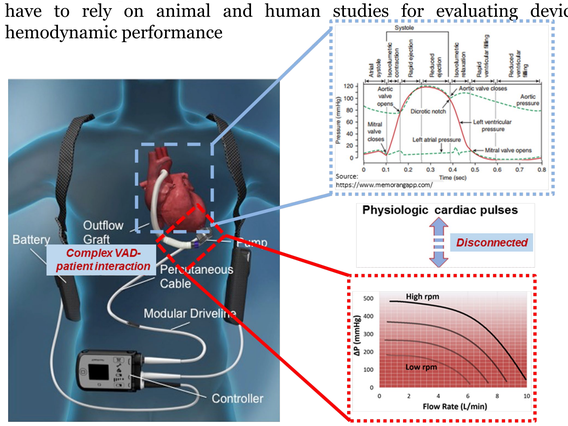


Figure 1. An image showing an implanted MCS device (i.e., ventricular assist device (VAD)) along with the knowledge gap in current *in vitro* testing.

Objective: We aim to standardize the use of mock circulatory loops (MCLs) as a regulatory science tool to assess device hemodynamic performance under clinically relevant HF patient conditions

Materials and Methods

Interlaboratory Study

- Goal: To establish consensus bench test methods using MCLs for evaluating device hemodynamic performance in simulated HF patients
- Study participants: Device manufacturers, third-party test laboratories, and MCL experts
- FDA is currently pursuing research collaboration agreements with external stakeholders with functional MCLs
- Consensus study plan includes: 1) Description of MCL test setup, 2) target test conditions, 3) standardized test protocol, 4) output performance metrics, and 5) acceptance criteria

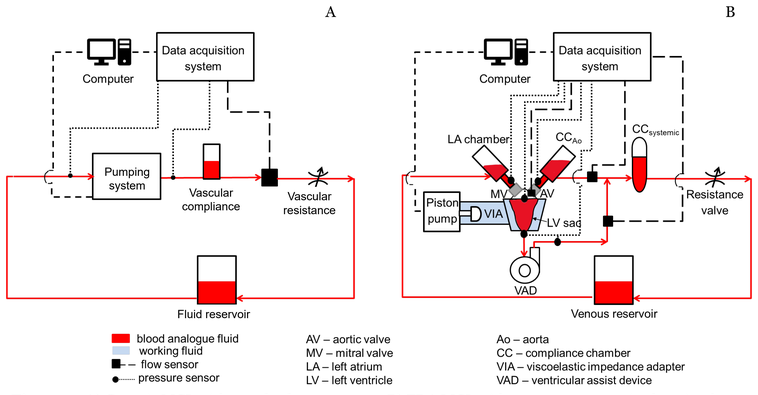


Figure 2. A) Generic MCL with standard components, B) FDA MCL with components required to simulate different pathophysiologic conditions.

1) Mock Circulatory Loop (MCL) Test Setup

- *In vitro* tool that simulates cardiovascular hemodynamics in a benchtop setting
- Generic MCL components (Fig. 2A): pumping system, vascular compliance, vascular resistance, heart valves, fluid reservoir, hemodynamic sensors, data acquisition system, blood analog fluid
- FDA engaged with stakeholders to determine acceptable MCL components

FDA MCL Components (Fig. 2B)

Piston pump, VIA, and LV sac – generate pulsatile LV blood flow and pressure

Compliance chambers – mimic vascular elasticity

Resistance valve – mimics systemic vascular resistance

Venous reservoir – collects the large blood volume of the veins

LA – reservoir for venous return to the heart

MV & AV – maintain unidirectional flow

Programmable VAD – pumps blood from the LV apex to the Ao

Pressure sensors – measure LV, Ao, LA, and VAD pressures

Flow sensor – measures cardiac output and VAD flow

2) Target Test Conditions

- Target pathophysiologic conditions and corresponding cardiac hemodynamic indices (Table 1) were identified through engagement with clinicians, real-world clinical evidence, and published reports
- Proposed test conditions represent a range of heart failure patients with and without MCS devices

3) Standardized Test Protocol (*followed by each participating laboratory*)

- Calibrate hemodynamic sensors and document calibration report
- Characterize MCL test system across its entire operating range and document system specifications
- Document detailed description of the MCL test setup along with schematic and pictures

Materials and Methods

Table 1. Proposed target test conditions representing clinically relevant HF patient pathophysiologies. (HR: heart rate, CO: cardiac output, SAP: systolic arterial pressure, DAP: diastolic arterial pressure)

Test Condition	HR (bpm)	CO (L/min)	SAP (mmHg)	DAP (mmHg)	LA Pressure (mmHg)	VAD Connected?
Healthy adult at rest	70	5	118	76	6	No
Healthy adult during exercise	120	13	186	111	9	No
Mild hypertension	76	7	140	85	6	No
Hypertension	76	7	168	87	6	No
Coronary artery disease	100	5	108	69	7	No
LV hypertrophy with hypertension	72	3	160	125	6	No
LV hypertrophy with right heart disease	76	4.4	130	88	15	No
Mild heart failure	80	6	130	80	6	No
Advanced heart failure	90	6	140	80	6	No
Cardiogenic shock	90	3	80	50	>15	No
Mild heart failure	80	6	130	80	6	Yes, Full Support
	80	6	130	80	6	Yes, Partial Support
	80	6	130	80	6	Yes, Not Running
Advanced heart failure	90	6	140	80	6	Yes, Full Support
	90	6	140	80	6	Yes, Partial Support
	90	6	140	80	6	Yes, Not Running

3) Standardized Test Protocol [*cont'd*]

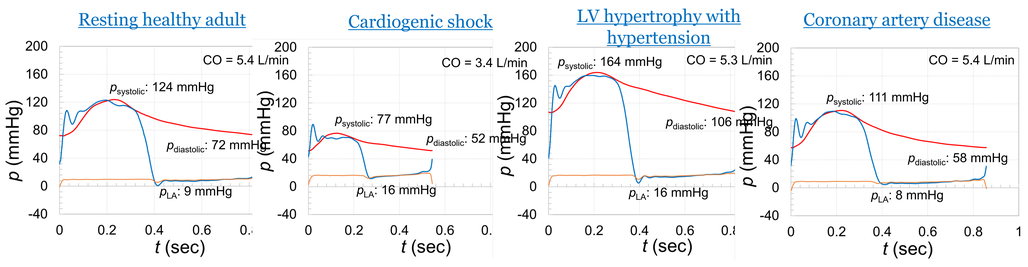
- Report test fluid (blood analog fluid) properties (e.g., viscosity, density)
- Determine and report number of test runs and device samples to achieve 95% confidence/95% reliability
- Document input and output parameters to be measured
- Start testing at all the proposed target test conditions (Table 1)
- Record and save raw and post-processed data
- Submit all information documented under test protocol to lead study lab for analysis

4) Output Performance Metrics

- CO, Ao/LA/LV pressures, LV end diastolic/end systolic pressures and volumes, cardiac cycle time, systemic vascular resistance, ejection fraction
- Acceptance criteria determined based on consensus from study participants and supported with clinical evidence/published data

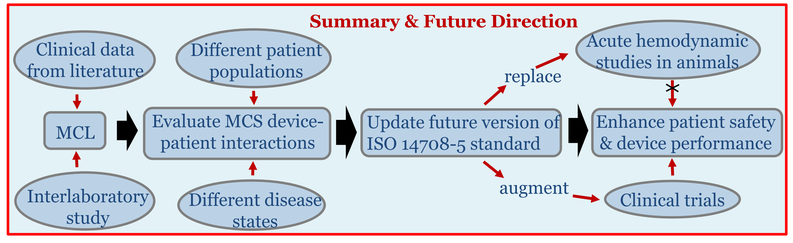
Results and Discussion

FDA Preliminary Test Results



- Differences between the target and simulated hemodynamics range between 2 – 12 mmHg for blood pressure, 0.3 – 1 L/min for cardiac output, and 0.001 – 0.01 s for cardiac cycle time, thus demonstrating good reproducibility
- Results from the interlaboratory testing are expected to vary due to the different MCL capabilities and complexities
- Common trends in output performance metrics, such as cardiac output and pressure waveform features, are being established across all the test laboratories.

Summary & Future Direction



Acknowledgments: This research is funded in part by a FY 2023 Critical Path Award