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Objective Content Validation of the Hemodynamic and Technical Parameters of the Orpheus™ Cardiopulmonary Bypass Simulator

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Abstract: The utilization of simulators for training is increasing in the professions associated with cardiac surgery. Before applying these simulators to high-stakes assessment, the simulator's output data must be validated. The aim of this study is to validate a Cardiopulmonary Bypass (CPB) simulator by comparing the simulated hemodynamic and technical outputs to published clinical norms. Three Orpheus™ CPB simulators were studied and compared to a published reference of physiologic and technical metrics that are managed during clinical CPB procedures. The limits of the simulators user modifiable variables were interrogated across their full range and the results were plotted against the published clinical norms. The data generated with the simulator conforms to validated clinical parameters for patients between 50 and 110 kg. For the pre- and post-CPB periods, the independent variables of central venous pressure (CVP), heart rate (HR), contractility, and systemic vascular resistance (SVR) must be operated between the limits of 7 and 12 mmHg, 65 and 110 beats/min, 28% and 65%, and 6 and 32 units respectively. During full CPB the arterial pump flows should be maintained between 3.5 and 5.5 LPM and SVR between 18 and 38 units. Validated technical parameters during cardioplegia delivery are expected at solution flow rates between 250 and 400 mL/min and 100 and 225 mL/min for antegrade and retrograde delivery routes, respectively. We have identified the limits for user-modifiable settings that produce data conforming to the physiologic and technical parameter limits reported in the peer reviewed literature. These results can inform the development of simulation scenarios used for high stakes assessments of personnel, equipment, and technical protocols. **Keywords:** cardiopulmonary bypass, simulation, education, validity. *J Extra Corpor Technol. 2021;53:263–9*

Cardiopulmonary bypass (CPB) is an invasive, high-risk, and complex technical procedure in which a heart-lung machine (HLM) is interfaced with a patient's vascular system. The physiologic function of the patient's heart and lungs is supplanted by the HLM, which removes blood from the patient, circulating it through a pump and oxygenator and returning it to the patient. During CPB it is common to chemically arrest the patient's heart rate by administering a cardioplegic solution from the HLM directly into the coronary arteries (antegrade route of delivery) or into the coronary sinus (retrograde route of delivery). Traditionally, clinical perfusionists, health professionals who operate extracorporeal circulation equipment, learned and practiced new skills, techniques, and technologies on human patients and animal subjects.

Recent advances in medical simulation technology have made it possible to interface HLM technologies to

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simulators, which act as human surrogates creating a safe environment to practice clinical procedures, demonstrate equipment function, and assess practitioner skills. The use of simulated patients has a clear advantage in protecting human patients from noncredentialed personnel, new practices, and new equipment (1). Increasingly, simulated patients are being applied to high-stakes assessments and evaluations in which interpretation of the outcome presumes a realistic experience (2,3). The Orpheus™ simulator was one of the first high-fidelity simulators designed for interface with extracorporeal technologies. It consists of a hydraulic surrogate patient, an electronic user interface, and a controlling computer. While a comprehensive description of the simulator is beyond the scope of this paper, one can be found in the 2007 descriptive work of Morris and Pybus (4).

The purpose of this project is to assess the use of the Orpheus™ CPB simulator as a valid surrogate for adult human subjects with regards to the physiologic and hemodynamic parameters experienced before, during, and after CPB. The application of this investigation is of critical importance if the simulator is to be applied to high stakes assessment of clinician competency, skill development and practice of clinical techniques, as well as design, development, and validation of new equipment.

MATERIALS AND METHODS

The methods described by Sargent in his review, "Verification and Validation of Simulation Models" were used to inform this protocol. We used a two-step combination of data-driven model validation methods, historical data validation, parameter variability, and face validity (5). In the first step, we generated a benchmark publication of hemodynamic and technical parameters observed during clinical adult CPB procedures. In the second step, we compared the data generated by the Orpheus™ CPB simulator to clinically validated measurement devices of proven accuracy, and to the benchmark data. Through this comparison process, limits were determined between which the simulator can be expected to produce valid hemodynamic and technical data.

Benchmark Clinical Parameters

Our first step toward validating the Orpheus™ CPB simulator involved collecting expert opinions regarding the normal limits of physiologic and technical parameters managed during clinical CPB procedures. A national survey was circulated within the professional community of clinical perfusionists. For a full description of the methods and the novel results of this survey, the reader is directed to our previous publication (6). The limits of the parameters necessary to validate the simulator are reproduced here. These parameters include the physiologic parameters of arterial blood pressure, central venous blood pressure, and coronary sinus pressures during retrograde cardioplegia delivery, as well as technical parameters from the HLM of arterial line pressure, arterial pump flow, cardioplegia system line pressures during antegrade and retrograde delivery.

Orpheus™ CPB Simulator Validation Testing

Three simulators, three clinical physiologic pressure monitors, two clinical flow probes, and two HLMs were applied to the validation testing. Quality assurance testing was performed on the simulators' internal measurement systems prior to data collection. Linear regression and Bland-Altman plots were used to confirm the agreement between the simulators' pressure and flow measurements and trusted clinical measuring systems. We sequenced each simulator through a systematic and standardized series of conditions that represented three phases of a surgical procedure (before, during, and after CPB). We interrogated two sets of user modifiable independent variables. The first set, central venous pressure (CVP), heart rate (HR), contractility (C%), and systemic vascular resistance (SVR), is incorporated into the setup conditions of the simulator and the second set, cardioplegia line pressure (CLPa = antegrade, CLPr = retrograde) coronary sinus pressure (CSP), and cardioplegia solution flow rates, are determined by the participants operation of the HLM.

Evaluation of the influence of the simulator's independent variables on the simulator's hemodynamic outputs. The Orpheus™ CPB simulator features four-user modifiable independent variables included in the software calculations for dependent hemodynamic variables. The independent variables of SVR, HR, C%, and CVP were individually assessed by adjusting their value across their full range and observing the influence on the dependent variables of cardiac output (CO) and mean arterial blood pressure (MAP). The direction and magnitude that individual independent variables have on dependent

Table 1. Patient hemodynamic ranges reported by surveyed perfusionists.

Arterial Pressure	High Limit (mmHg)	Low Limit (mmHg)
Pre CPB (sys/dia)	137 ± 21/83 ± 13	84 ± 12/48 ± 10
During CPB (MAP)	82 ± 9	54 ± 7
Post CPB (sys/dia)	121 ± 15/78 ± 12	83 ± 13/49 ± 10
Central Venous Pressure	Normal Limits (mmHg)	
Pre-CPB	11 ± 4	
During CPB	2 ± 2	
Post-CPB	12 ± 4	

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Table 2. HLM pressure/flow technical data reported from survey.

Pressure			Flow		
	High Limit (mmHg)	Low Limits (mmHg)		L/min/m^2	
Arterial	235 ± 77	125 ± 44	Arterial Pump	2.34 ± 0.35	
Line	Median = 250	Median = 123	Full Flow	–	
Pressure	Mode = 300	Mode = 150	(calculation)	–	
	High Limit (mmHg)	Low Limits (mmHg)		High Limit (mmHg)	Low Limits (mmHg)
Antegrade	246 ± 51	165 ± 53	Antegrade	359 ± 98	214 ± 71
Cardioplegia Line	Median = 250	Median = 180	Cardioplegia	Median = 350	Median = 200
Pressures	Mode = 250	Mode = 150	Pump Flow	Mode = 300	Mode = 200
Retrograde	141 ± 74	85 ± 48	Retrograde	236 ± 79	123 ± 49
Cardioplegia Line	Median = 140	Median = 85	Cardioplegia	Median = 235	Median = 120
Pressures	Mode = 100	Mode = 50	Pump Flow	Mode = 200	Mode = 100
Coronary	51 ± 31	30 ± 21			
Sinus	Median = 45	Median = 25			
Pressures	Mode = 45	Mode = 25			

Modified from J Extra Corpor Technol. 2020;52:165–72.

hemodynamic variables was investigated. This was completed to identify the limits within which these variables will dependably produce valid hemodynamic data representative of uncomplicated adult CPB procedures.

Evaluation of the influence of the HLM's independent variables on the simulator hemodynamic outputs and the resultant HLM technical outputs. *The Simulator/HLM interface*: The interface of the Orpheus™ simulator to a HLM introduces a second set of user-modifiable dependent variables. In the operating theater the clinicians operating extracorporeal equipment determine the filling pressures of the heart, the arterial and cardioplegia flow rates, and the route of cardioplegia delivery (antegrade or retrograde) as independent variables according to clinical protocols. These variables influence the arterial line pressure (ALP), MAP, CLPa, CLPr, and CSP. All must be monitored and maintained within clinically relevant ranges to assure proper perfusion of patient's tissue and avoid harming the patient or damaging the extracorporeal

Table 3. Recommended independent variable settings for uncomplicated adult CPB patient scenarios.

Pre/Post CPB	Small Adult‡	Medium Adult‖	Large Adult
Ideal Orpheus	50–70 kg	71–90 kg	91–110 kg
Set Points* and Acceptable Limits	1.25–1.77 BSA (m^2)	1.78–2.27 BSA (m^2)	2.28–2.77 BSA (m^2)
	C.O. = 2.9–4.1	C.O. = 4.1–5.2	C.O. = 5.3–6.4
	LPM	LPM	LPM
CVP (mmHg)	10 (7–12)	10 (7–12)	10 (7–12)
HR (beats/min)	70 (65–110)	70 (65–110)	70 (65–110)
Contractility (%)	35 (28–40)	45 (43–55)	55 (52–65)
SVR	25 (11–32)	16 (6–27)	11 (1–23)
On CPB			
Ideal Orpheus	Small Adult§	Medium Adult	Large Adult
Set Points* and Acceptable Limits	Pump Flow 3.5	Pump Flow 4.5	Pump Flow 5.5
	LPM	LPM	LPM
CVP (mmHg)	0 (−1 to 1)	0 (−1 to 1)	0 (−1 to 1)
HR (beats/min)†	†	†	†
Contractility (%)†	†	†	†
SVR	29 (20–38)	26 (18–33)	22 (16–32)
Cardioplegia Delivery			
Antegrade (mL/min)		250–400 mL/min	
Retrograde (mL/min)		100–225 mL/min¶	

* Set points are deemed acceptable if they produce hemodynamic data that is consistent with the benchmark ranges reported by experts (see Tables 1–2).
† HR and contractility (C%) settings have no hemodynamic influence during total bypass.
‡ Patient CO derived from 58 mL/kg/min (8).
§ Pump flow rates derived from benchmark value of 2.3 L/min/m^2 (Table 2).
‖ Average adult BSA in the USA are 1.8 and 2.05 m^2 for female and male adults (9).
¶ Retrograde cardioplegia, the root vent should be connected to the Orpheus and running at a flow rate that is approximately equal to the cardioplegia flow

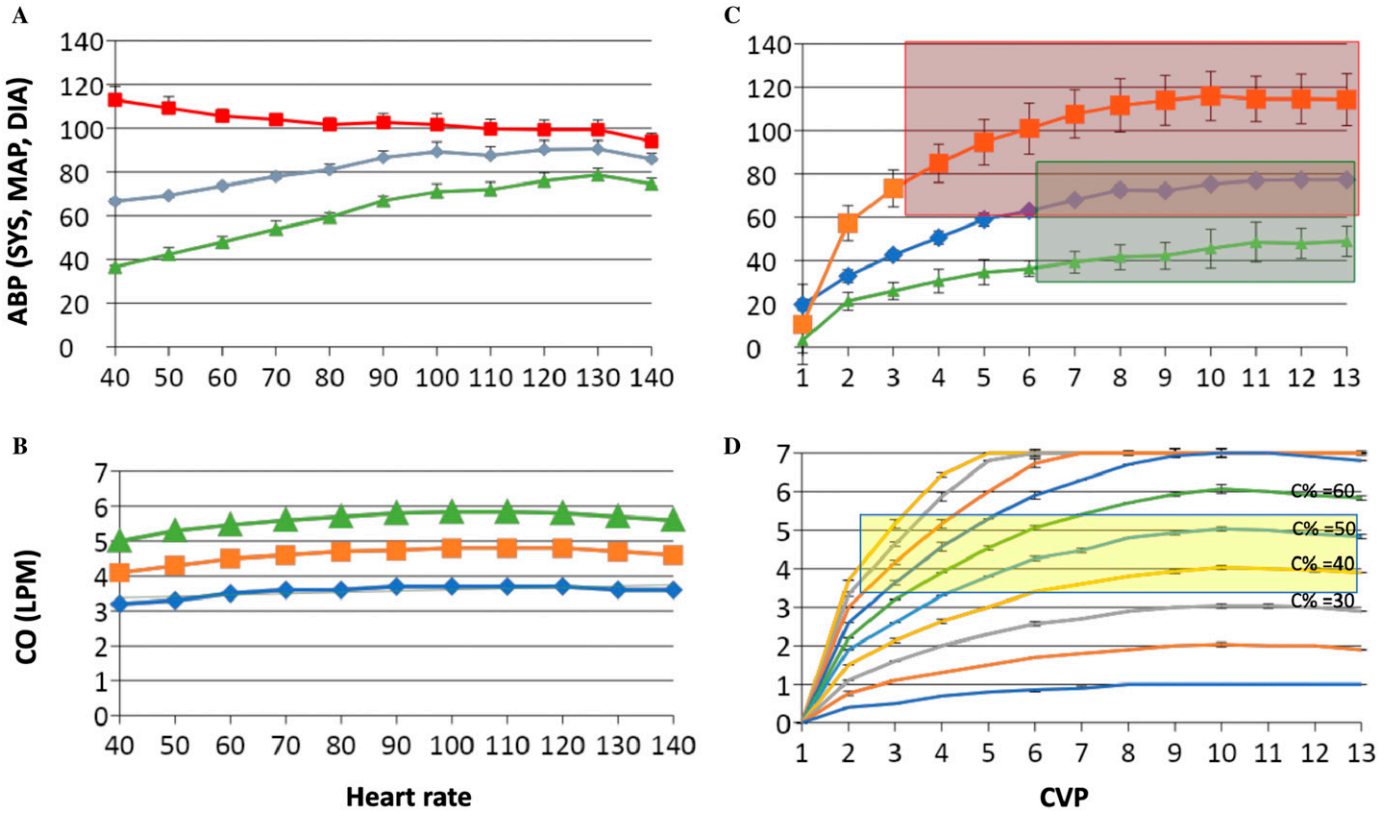

Figure 1. Influence of HR, CVP, and C% on ABP and CO. (A) Influence of HR on Systolic, Diastolic and Mean ABP (red, green, and blue lines, respectively). Sampled as a representative patient at SVR = 15—for full description of SVR on ABP, see Figure 2. (B) Influence of HR on emulated CO sampled with initial CO set to 3.5, 4.5, and 5.5 and CVP 10 (blue, orange, and green lines, respectively). (C) Influence of CVP on ABP for a typical adult patient sampled with initial CVP 10 mmHg, MAP 75 mmHg, CO 5 LPM (line color: red = systolic, green = diastolic, blue = mean). Shaded boxes identify the reported range of systolic and diastolic pressures +/− 1 SD from the benchmark survey and the CVP range that will produce them. (D) Influence of contractility (C%) and CVP on CO. C% was sampled between 10 and 100% across equal intervals (bottom line to top line respectively). The yellow shaded box identifies the C% and CVP settings that will produce adult CO values based on text book references (used with permission from Myles PS, Cui J. I. Br J Anaesth. 2007;99:309–11).

circuit. The independent variables of arterial and cardioplegia pump flows and route of cardioplegia delivery were altered across a wide range. The resultant dependent variables of MAP, ALP, CLPa, CLPr, and CSP were determined.

Data Analysis

The relationship between the independent variables of the Orpheus™ and the HLM were plotted against their dependent simulated physiologic and technical variables. Plots of the objective experimental data were superimposed with shaded boxes that represent referenced physiologic metrics and benchmark clinical parameters from the peer reviewed literature (6). Through this method the range and limits of the independent variable parameters, which produce data that conforms to the limits and range of the normal benchmark clinical parameters was identified.

RESULTS AND DISCUSSION

There were 335 total respondents of the benchmark clinical parameter survey (6). The geographic demographics of the respondents was similar to the American Board of Cardiovascular Perfusion's reported distribution of Certified Clinical Perfusionists[1] at the time of the study. The abbreviated results are presented in Tables 1 and 2.

Orpheus™ Simulator Performance Testing

Influence of independent variables on the simulator hemodynamic outputs. The influence of the independent variables of HR, CVP, and C% were tested for their influence on the dependent variables of ABP and CO.

Heart rate (Figure 1, Panel A and B): Across a range of representative normal adult COs (3–6 LPM), CO is

[1]American Board of Cardiovascular Perfusion, Inc, 2015 Booklet of Information, http://www.abcp.org/

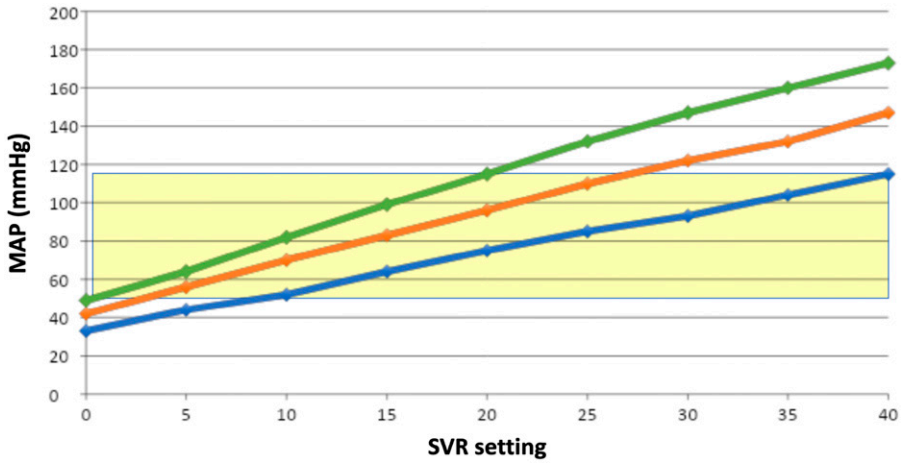

Figure 2. Influence of SVR on the simulated MAP: A representative example of the influence of the Orpheus's user-modifiable SVR variable on the simulated MAP across a range of blood flow that represent small (3.5 LPM = blue), medium (4.5 LPM = red), and large (5.5 LPM = green) adult patients (CVP 10). The horizontal borders of the yellow shaded box indicate the MAP values derived from the benchmark survey. MAP reference points (49–117 mmHg) were derived from the surveys reported systolic and diastolic ranges by producing the benchmark pressures with the simulator and recording the MAP from the clinical monitor.

directly related to HR between 40 and 100 beats per minute (BPM), not related to HR between 100 and 120 BPM, and inversely related to HR between 130 and 140 BPM. Conservatively, while valid hemodynamic data can be generated across the entire range of HRs, simulations of adult patients are easily managed between HR values of 65 and 110 BPM.

CVP (Figure 1, Panels C and D): The full range of the CVP variable is 0–12 mmHg and is determined by the volume of priming fluid added to the simulators' reservoir during setup. CVP values below 7 mmHg are irregular compared to the benchmark clinical parameter survey. To produce valid adult ABP before and after CPB and to generate a realistic blood volume displacement on initiation of CPB the ideal CVP for adult CPB simulation scenarios is 10 mmHg and can safely be manipulated between the limits of 7 and 12 mmHg.

Contractility (Figure 1, Panel D): Simulated CO between 3 and 6 LPM can be generated with C% values between 30 and 100%. Given the contribution and clinical limits of other variables, C% values between 35 and 55% are recommended for simulations of adult patients.

SVR: Figure 2 provides a representative diagram of the influence of SVR on MAP at three CO levels representative of the adult population. Conservatively, while valid hemodynamic data can be generated across the entire range of SVR, values between 1 and 32 are most appropriate for the simulation of adult CPB patients before and after the simulated CPB.

Evaluation of the influence of the HLM-independent variables on the simulator hemodynamic outputs and the resultant HLM technical outputs. Figure 3 demonstrates the influence of HLM flow and SVR on the MAP and ALP. The shaded boxes identify the normal MAP and ALP pressures determined in the clinical parameter benchmark survey. Across the expected blood flow range of 3–6 LPM for an adult patient, SVRs between 15 and 35 will produce valid MAP and ALP.

Simulator resistance to the HLM cardioplegic solution flow. Figure 4 demonstrates the relationship between antegrade cardioplegia flow and the cardioplegia line pressure (CLPa) as well as retrograde cardioplegia flow and the variables of cardioplegia line pressure (CLPr)

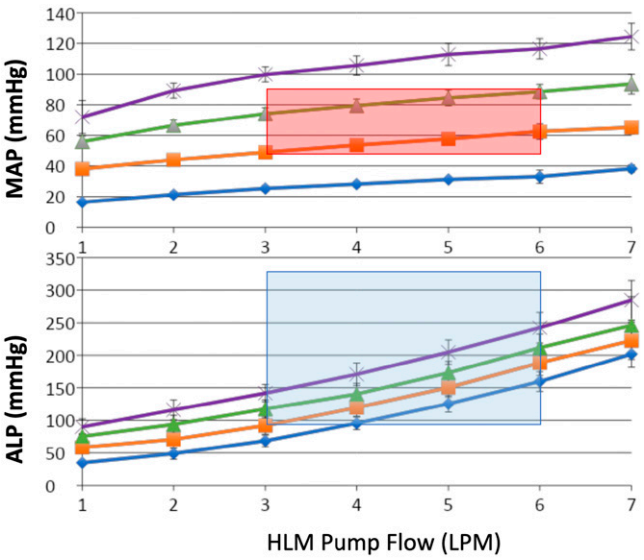

Figure 3. Range of MAP and ALP under normal adult CPB blood flows: The influence of HLM flow and SVR on ALP and MAP. SVR was varied across equal intervals from SVR = 10% (bottom line) through SVR = 40% (top line) respectively. Horizontal borders of the blue (ALP) and red (MAP) shaded boxes are based on the ALP and MAP benchmark survey values and vertical borders are determined by textbook references of adult CO.[8] The data is presented as mean ± SD.

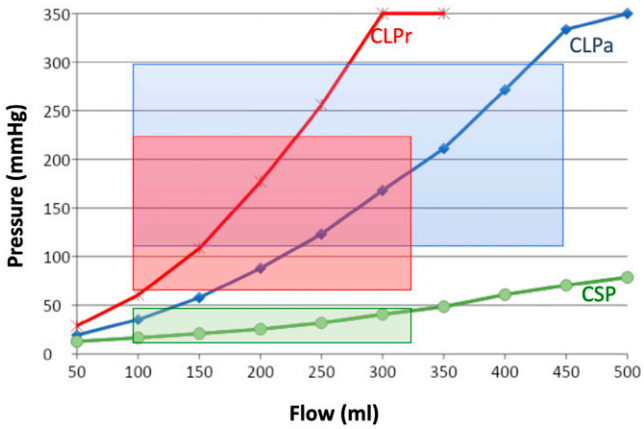

Figure 4. Range of cardioplegia pressures under normal flows: The relationship of the simulated antegrade/retrograde cardioplegia line pressure and coronary sinus pressures across the expected cardioplegia flow rates. The upper and lower borders for the blue (antegrade CLPa), red (retrograde CLPr), and green (CSP) indicate the benchmark survey values for cardioplegia pressure limits and the left and right borders indicate the benchmark survey values for expected cardioplegia flow rates as determined by the benchmark clinical parameters survey.

and simulated coronary sinus pressure (CSP). Antegrade cardioplegia delivery generates valid CLPa across a flow range of 250–400 mL/min. Retrograde cardioplegia delivery generates valid CLPr across a flow range of 100–225 mL/min. While delivering retrograde cardioplegia the simulated CSP is valid across a range of retrograde flows from 100 to 325 mL/min.

CONCLUSIONS

Generalizability of Results

This is the first report of the validation of a simulation model for CPB and as such may serve an important role in the administrative and procedural infrastructure for groups using the Orpheus™ to conduct research or assess the function of equipment or personnel. These results are generalizable to other groups using this same device and under the conditions described here. Additional validations of the testing environment and the assessment instrument would also be necessary to produce full confidence in any collected data. For groups that use a CPB simulator other than the Orpheus™ this work represents a generalizable method for validating their device and identifies a peer reviewed data set in the public domain to serve as the benchmark.

Recommended Reference Ranges for Adult CPB Scenarios

The Orpheus™ simulator is equipped to broadly control physiologic and technical hemodynamics. There are numerous configurations that may produce both valid and invalid outputs. For the most uncomplicated presentation that provides latitude for the scenario to progress in a variety of valid directions we have designed a table of recommended initial settings that will begin the simulation scenario within the validated ranges and cycle between the CPB and post-CPB phases.

During the application of simulation, uncomplicated patient data has the utmost importance. We have distilled the findings of this paper into a summary table that should prove to be a valuable resource for the simulation facilitator (see Table 3).

Quality Assurance Measures for the Valid Use of the Orpheus™ CPB Simulator

The transducers and flow meter that are integrated into the Orpheus™ system degrade with time. Therefore, prior to simulations, the pressure transducers and flow probe should be confirmed to correlate with a trusted clinical monitoring system across the expected range of use. Furthermore, the centrifugal pump that acts as the heart of the simulator is also known to degrade. The "health" of the centrifugal pump can be confirmed secondarily to the fidelity of the transducers by cycling the SVR variable across its full range and observing the developed MAP as illustrated in Figure 2. A centrifugal pump at the end of its viable life cycle will not generate hypertensive MAP pressures.

Limitations

Validity is based on comparison to a benchmark publication of uncomplicated adult patient parameters. These results may not be representative of pediatric patient scenarios or adult crisis management scenarios presenting patients in clinical extremes.

Summary of Investigation

This investigation evaluated the performance of multiple Orpheus™ CPB simulators as surrogates for a wide range of adult patients being supported with a HLM for cardiac surgery. The simulators' performance was evaluated before, during, and after simulated CPB. The independent variables influencing hemodynamic parameters were studied and compared to a novel publication of benchmark clinical parameters that was generated for this study (6). The benchmark clinical parameters publication was compiled through a survey of 335 clinical experts who have, on average, more than two decades of experience operating HLMs during cardiac surgery and who were geographically distributed without regional bias. Through direct comparison we have identified limits of simulator settings that produce data that is representative of normal clinical data for adults receiving cardiac surgery and are highly relevant to clinical educators and

equipment manufacturers as they represent the spectrum of hemodynamics that may be encountered during CPB across the majority of US centers. We have confirmed that the Orpheus™ simulator is able to consistently reproduce valid physiologic and technical hemodynamic data. Based on this analysis, it is reasonable to use the Orpheus™ CPB simulator as an element in a high-fidelity extracorporeal simulation environment where the validity of the physiologic and technical hemodynamic data is essential for accurate assessment. These applications may include educational training programs, high stakes skills assessment of students and professionals, medical device design usability testing, or product validation.

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