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Pulsatile In Vitro Simulation of the Pediatric Univentricular Circulation for Evaluation of Cardiopulmonary Assist Scenarios

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Abstract: The characteristic depressed hemodynamic state and gradually declining circulatory function in Fontan patients necessitates alternative postoperative management strategies incorporating a system level approach. In this study, the single-ventricle Fontan circulation is modeled by constructing a practical in vitro bench-top pulsatile pediatric flow loop which demonstrates the ability to simulate a wide range of clinical scenarios. The aim of this study is to illustrate the utility of a novel single-ventricle flow loop to study mechanical cardiac assist to Fontan circulation to aid postoperative management and clinical decision-making of single ventricle patients. Two different pediatric ventricular assist devices, Medos and Pediaflow Gen-0, are anastomosed in two nontraditional configurations: systemic venous booster (SVB) and pulmonary arterial booster (PAB). Optimum ventricle assist device strategy is analyzed under normal and pathological (pulmonary hypertension)

conditions. Our findings indicate that Medos ventricle assist device in SVB configuration provided the highest increase in pulmonary (46%) and systemic (90%) venous flow under normal conditions, whereas for the hypertensive condition, highest pulmonary (28%) and systemic (55%) venous flow augmentation were observed for the Pediaflow ventricle assist device inserted as a PAB. We conclude that mechanical cardiac assist in the Fontan circulation effectively results in flow augmentation and introduces various control modalities that can facilitate patient management. Assisted circulation therapies targeting single-ventricle circuits should consider disease state specific physiology and hemodynamics on the optimal configuration decisions. **Key Words:** Assisted circulation/methods—Fontan procedure/methods—Hemodynamics/physiology—Pulsatile flow—Ventricle-assist devices/utilization.

Single ventricle (SV) physiology introduces escalating energetic challenges in patients with congenital heart disease. The American Heart Association reports SV pathology as the leading cause of death from any birth defect less than 1 year of age (1) which requires the highest cost to treat any birth defect. Staged Fontan palliation has evolved based on

the clinical experience and has become a routine approach for SV management. Despite progress in the last decades (2), outcomes remain suboptimal (3,4) due to inherently inefficient physiology. Often, patients in the immediate postoperative period suffer from acute heart failure as well as side effects as their cardiovascular system requires long periods for hemodynamic adjustment. Recently, increasing numbers of SV patients surviving into adulthood classified as “failing Fontans” pose severe deteriorating hemodynamic state, and require circulatory assist. Recent studies indicate that application of a pediatric ventricular assist device (PVAD) (5), propeller pump (6) or an intraaortic balloon pump (7) to the Fontan circuit may augment venous flow, improve

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1 should quantify the acute volume shifts between each
2 compartment to accurately evaluate hemodynamic
3 adjustments and VAD performance. In addition,
4 **15** the indispensable effect of patient-specific anatomies
5 (i.e., fabricating using rapid prototyping to match
6 **16** vascular impedance) (29) on Fontan hemodynamics
7 which will critically influence the VAD selection
8 should also be taken into account. Along this line,
9 surgical templates of the intermediate high-risk
10 stages (i.e., Norwood operation) can also be imple-
11 mented in the current flow loop to explore the feasi-
12 bility of PVAD implementation to support a single
13 stage neonatal Fontan repair (9). As identified
14 earlier, accurate description of the TCPC hemody-
15 namics requires the simulation of respiration effects
16 which remains as a challenging task to be imple-
17 mented in future flow loop studies. Ongoing studies
18 focus on performance of PVAD at novel deployment
19 configurations such as the double inlet-double outlet
20 configuration (which is an extension of the recent
21 Optiflo conduit (30)) and the “ejector pump design”
22 which uses the flow energy of one caval low to drive
23 the other (Fig. 1).

24 Utility of distilled water in mock loops has been
25 shown by several investigators (31–33). For the
26 current study, the variation of viscosity affected only
27 the pressure field as the bellows pump discharges
28 constant flow rate regardless of the viscosity of the
29 working fluid. Based on the comparative nature of
30 this study, the variation in absolute pressure did
31 not pose any limitation to the results presented.
32 However, the effect of using lower viscosity fluid on
33 the flow profile was negligible due to the typical high
34 Womersley number (>10) in the large vessels. In addi-
35 tion, regardless of the relative increase in Reynolds
36 number with the use of distilled water, turbulence
37 phenomena have not been seen within any vessel
38 segment. Also, the effects of polycythemia that is
39 reported for some post-Fontan patients (34) were
40 also not included. For a more precise study with exact
41 patient specific parameters, a blood analog fluid and
42 the changes in red blood cell rheology should be
43 considered.

44 Although providing accurate local hemodynamic
45 information along the entire SV circulation circuit,
46 pulsatile venous flow waveforms clearly diverge from
47 the actual in vivo waveforms acquired by Doppler
48 Velocimetry (35). This is due to the neglecting of the
49 high respiratory dependency (i.e., 30–100%) of the
50 vena cavae flow in patients with TCPC (35–37) which
51 stems from the variation of intrathoracic pressure
52 (38) and abdominal pressure (39). Negative intratho-
53 racic pressure during inspiration decreases the left
54 atrial pressure and enhances both caval flows (18).

Limited acute in vivo animal studies (unpublished
data) have shown respiration to have a significant
impact on the pulmonary impedance in the Fontan
circulation. On the other hand, the increase in
abdominal pressure produced by the descending
diaphragm during inspiration enhances IVC flow
substantially (37). Moreover, our recent numerical
studies (22) revealed the indispensable effect of res-
piration and caval flow pulsatility on the internal
energy dissipation inside the TCPC. Therefore, an
accurate simulation of the TCPC hemodynamics
requires inclusion of respiratory effects (35), a
preload responsive cardiac simulator, and respiration
dependant splanchnic venous return (37).

The current study has inherent limitations related
to the selected devices and anastamotic con-
figurations. The Pediaflow Gen-0 VAD provided a
maximum output of 0.9 L/min at the highest settings
and had high nonlinear pump resistance. Our study
results indicate that in-line placement of the VAD in
the venous conduit is sub-optimal and that alterna-
tive configurations where the VAD is placed in par-
allel with the existing flow conduit may be preferable.
Future studies should consider the need to evaluate
the change in loading conditions on the heart. In
certain cases (such as dilated cardiomyopathy),
increased loading of the ventricle may be quite
detrimental in spite of any benefits derived from
reduced pulmonary pressures or enhanced pulmo-
nary perfusion. An elastance-based preload respon-
sive ventricle should be coupled to our existing
afterload model for this purpose. In spite of these
limitations, this study demonstrates that mechanical
support of Fontan patients is not a binary problem
that can be addressed through LVAD support alone
nor is it a matter of unloading the ventricle. VAD
support in these patients should be based on balanc-
ing the perfusion needs of the patient and careful
volume management of the major compartments of
the circulatory system with the goal of unloading
both the pulmonary circuit and heart.

CONCLUSION

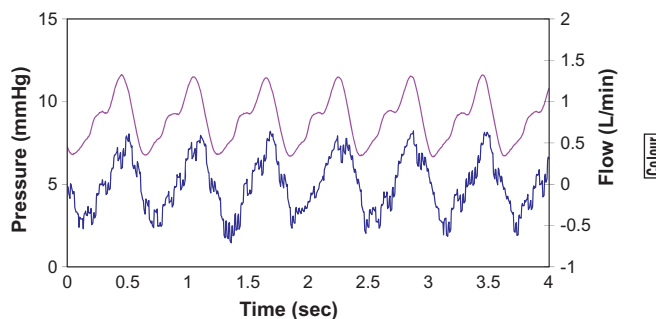
For traditional adult VAD deployment, the loca-
tion of anastomosis and pump selection in response
to hemodynamics and physiology is a major current
research interest and poses a very complex problem.
Pediatric patients with congenital circulation malfor-
mations complicate the problem even further due to
blood volume shifts, compliance remodeling during
early post-op, control of venous collapse, unsteady
venous flow dynamics and cardiopulmonary inter-
actions. The proposed experimental setup provides a

1 deployment allowed slightly better pulmonary perfu-
2 sion (4%). For hypertensive conditions, a similar con-
3 clusion, higher pulmonary flow increase with IVC
4 deployment (15.5% vs. 12.4%) could be drawn. It is
5 worth to note that average pulmonary pressure was
6 4 mm Hg higher in RPA configuration compared
7 with the IVC deployment. For the Pediaflow VAD,
8 PAB configuration allowed equally higher flow aug-
9 mentation in caval veins (20–23%) and pulmonary
10 arteries (30–48%) compared with SVB configura-
11 tion under both normal and hypertensive conditions.
12 Overall, these findings indicate that SVB configura-
13 tion is more favorable for Medos VAD, whereas, PAB
14 configuration should be preferred for Pediaflow
15 VAD insertion as mechanical support.

16
17 **VAD performance evaluation**
18 **(Medos vs. Pediaflow)**

19 In the SVB configuration, although the Pediaflow
20 was capable of increasing the total CV flow (50% in
21 normal and 29% in hypertensive condition), PA flow
22 is not affected or even reduced in normal and hyper-
23 tensive conditions, respectively. For RPA anastomosis,
24 CV flow augmentation provided by the Pediaflow
25 VAD is higher than Medos VAD: 91% versus 78%
26 and 55% versus 51% with respect to normal and
27 hypertensive conditions, respectively. In addition,
28 Pediaflow VAD anastomosed at the RPA was
29 notably more favorable in increasing PA flow under
30 pulmonary hypertension (28% vs. 12%) and dis-
31 played the same performance as the Medos VAD in
32 the normal conditions (both 46% PA flow increase).
33 In summary, the Medos pump in IVC configuration
34 provided the highest increase in PA (46%) and CV
35 (90%) flow under normal conditions. Superiority of
36 the Medos VAD in SVB configuration is primarily
37 based on the active suction from the systemic cir-
38 culation with this pulsatile VAD, and the increased
39 adverse resistance introduced by continuous flow
40 Pediaflow Gen-0. In contrast, for the hypertensive
41 conditions, highest PA (28%) and CV (55%) flow
42 augmentation is observed for the Pediaflow VAD
43 inserted as a PAB. Hence, our study suggests that
44 Pediaflow VAD in PAB configuration would be a
45 better candidate for aiding hypertensive Failing
46 Fontans, whereas, Medos VAD in SVB configuration
47 should be considered for the immediate postopera-
48 tive management of patients with functionally
49 normal vascular conditions.

50 Pulsatility of Medos VAD over the steady Pedia-
51 Flow discharge is another advantage that needs to be
52 taken account in assisted support of the Fontan
53 circuit. Along this line, insertion of PVADs to the
54 Fontan circulation allowed modulation of flow wave-



55 **FIG. 6.** Pressure (blue) and flow (red) waveforms measured at
56 inferior vena cava (IVC) (top) and left pulmonary artery (LPA)
57 (bottom) when Medos VAD inserted in systemic venous booster
58 configuration.

59
60 forms along the TCPC pathway (i.e., IVC, SVC, RPA,
61 and LPA). It is also found that the sinusoidal venous
62 flow waveforms disappeared (i.e., steady flow) when
63 the systemic venous compliance is increased. In con-
64 trast, pulsatile Medos VADs produced distinct flow
65 waveforms and high pulsatility even in the high
66 venous compliance condition ($C \gg 10$ mL/mm Hg)
67 as shown in Fig. 6.

68
69 **Limitations and future directions**

70 The present pulsatile in vitro Fontan flow loop
71 demonstrated its utility to simulate the single-
72 ventricle circulation and the hemodynamic effects
73 of surgical interventions, including the PVAD assist
74 to aid patients with degrading hemodynamics.
75 However, at this stage, the main objective of this
76 study was not to extract quantitative data on Fontan
77 hemodynamics but to develop a versatile bench-top
78 experimental setup with which we could compare
79 alternative VAD performances and possible deploy-
80 ment configurations, thus to explore the feasibility of
81 mechanical support in Fontan patients. There are
82 several limitations in terms of the accuracy of the
83 quantitative Fontan hemodynamics which need to be
84 addressed in the future.

85 Although PVAD insertion confirmed increased
86 pulmonary flow, cardiac output remained almost con-
87 stant due to the lacking Frank-Starling mechanism
88 under current settings of the flow loop. Minor
89 increase in aortic flow (2.7%) after PVAD anastomosis
90 is attributed to the active suction of fluid from
91 the visceral circulation. More physiological ventricle
92 function sensitive to afterload can be simulated
93 by implementing a feedback-controlled positive-
94 displacement pump (elastance-based control) as
95 described by Baloa et al. (28). Albeit our qualitative
96 observations confirmed the blood volume shift due
97 venous congestion or VAD discharge, future studies

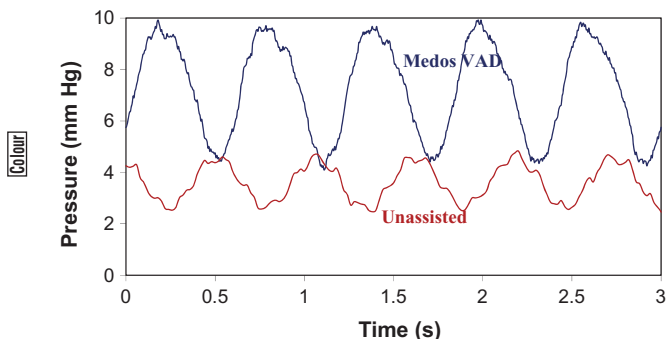


FIG. 5. LPA pressure for Medos VAD (blue) assisted circulation and unassisted circulation (red) under normal physiologic conditions.

pulmonary arteries was around 5 ± 3 mm Hg as shown in Fig. 5.

Pediaflow VAD anastomosis to the IVC segment caused adverse hemodynamics as the IVC flow decreased dramatically (-25%) causing venous stasis (i.e., volume shift) in the IVC compartment. In contrast, relatively larger cardiac output moved to visceral circulation, which increased the SVC flow substantially (106%). This allowed normal levels of pulmonary flow to be sustained in spite of the IVC flow reduction. However, Pediaflow insertion to RPA caused 49% reduction in RPA flow which is compensated by a dramatic increase in LPA flow (136%) based on the flow augmentation in both IVC ($+54\%$) and SVC ($+55\%$) segments. These nonintuitive results are primarily due to the increased (pulmonary) vascular resistance of the IVC (RPA) segments after VAD insertion due to the presence of the additional resistance of the pump itself. RPA deployment of Pediaflow VAD to aid pulmonary hypertension allowed 28% increase in overall pulmonary perfusion. In contrast, insertion through IVC caused further reduction in the pulmonary flow (-17%) due to the insufficient SVC flow augmentation ($+71\%$) relative to the reduction in IVC flow (-25%). On

average, pulmonary pressure was increased by 13 ± 7 mm Hg after Pediaflow VAD insertion.

DISCUSSION

Assisted cavopulmonary blood flow as a potential to serve as a bridge to neonatal SV Fontan repair (9,23–25) and long-term treatment option for failing Fontan physiology (26,27) has been demonstrated in animal models with commendable success. Along this line, bench-top studies as presented in this article are essential as, to this date, no animal model exists to study chronic single-ventricle physiology and compare efficacy of various cavopulmonary assist alternatives in moderate to long-term postoperative period. Our study confirms that mechanical assist in Fontan circulation incorporating VADs on either the systemic venous bed or at the pulmonary arteries provides cardiopulmonary flow augmentation. After Medos VAD insertion, both RPA and LPA pressure increased approximately $3\text{--}9$ mm Hg. These results indicate that present pressure head values increases pulmonary arterial flow significantly. In normal physiology, this translates to improved ventricular preload, creating higher cardiac output which, in certain circumstances, aids both immediate and long-term postoperative hemodynamics of functionally normal and “failing” Fontan patients. On the other hand, the flow delay and excessive pressure ($10\text{--}20$ mm Hg) caused by the Pediaflow VAD on its anastomosis branch is associated with the nature of the anastomosis used that were clearly suboptimal for the patient physiology analyzed in this study. Regardless of this design issue, the hemodynamic adjustments in the cavopulmonary circulation still provided a considerable level of pulmonary flow increase with the Pediaflow VAD.

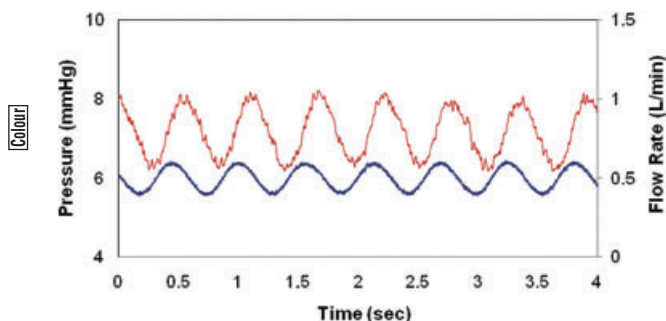
VAD deployment configuration (IVC vs. RPA)

The Medos VAD displayed similar performance in both RPA and IVC segments, although the IVC

TABLE 3. Variation of the hemodynamic parameters in response to different VAD insertions relative to “Failing Fontan” conditions

VAD configurations	QIVC (%)	QSVC (%)	QRPA (%)	QLPA (%)	QCV (%)	QPA (%)	Δ PIVC (mm Hg)	Δ PSVC (mm Hg)	Δ PRPA (mm Hg)	Δ PLPA (mm Hg)
SVB										
Medos VAD	66	41	12	19	52	16	0.0	2.1	0.0	0.3
Pediaflow VAD	-25	71	-18	-16	29	-17	6.3	14	4.0	10
PVB										
Medos VAD	57	49	15	10	51	12	5.2	7.5	2.4	6.7
Pediaflow VAD	54	55	-45	100	55	28	8.8	24	9.3	11

Q and Δ P indicate the percent flow variation and absolute pressure head change at the corresponding branch, respectively.



21 **FIG. 3.** Sinusoidal RPA flow (red) and pressure (blue) waveforms for unassisted circulation under normal physiological conditions.

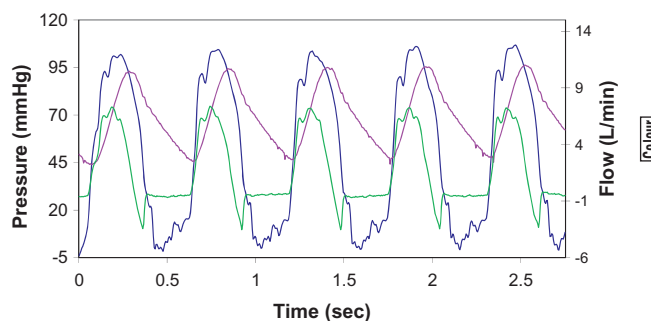


FIG. 4. Left ventricular pressure (blue), aortic pressure (red), and aortic flow (green) waveforms. Aortic waveforms were similar for both all VAD experiments.

and agrees with previous clinical (21) and computational (22) data.

The significant hemodynamic readjustments and volume shifts that took place with the introduction of assisted support compared with the baseline single-ventricle circulation are summarized in Table 2 qualitatively. Under normal vascular tone, insertion of the Medos pulsatile VAD to IVC in SVB configuration increased the flow within the IVC, SVC, LPA, and RPA segments by 120, 63, 43, and 61%, respectively. Increased IVC flow is accompanied with elevated pressure and larger fluid volume shifted to the IVC compartment. Anastomosis of Medos VAD to the RPA resulted in higher RPA flow (57%) and pressure (95%). In addition, based on the novel “ejector effect” of the PAB at RPA, the pressure at the left atrium, venous pressure (IVC and SVC), and also

LPA increased considerably (3–8 mm Hg). This caused significant flow augmentation at the LPA segment (37%) and volume shift toward pulmonary artery compartments. Under pulmonary hypertension, flow through the TCPC circuit was increased slightly (3–8%) relative to the normal conditions. Moreover, the blood volume shifted from pulmonary to systemic venous compartments causing venous congestion agrees with clinical observations. Medos VAD insertion to restore pulmonary flow obstruction, not only enhanced the systemic venous flow about 51%, but also increased PA flow about 12–16% compared with the hypertensive levels. To note, both VAD deployment configurations (i.e., IVC and RPA insertion) yielded similar hemodynamic improvements during pulmonary hypertension. The average pressure head added by the Medos VAD on the

TABLE 2. Configurations investigated the Fontan flow loop

Configuration	pVAD used	Observations	
		Hemodynamic	Volume shifts
1.0) Normal Fontan	None	Baseline	Baseline
1.1) SVB (IVC → TCPC)	1.1.1) Medos VAD	<ul style="list-style-type: none"> • QIVC ↑, PIVC ↑ • QSVC ↑, PSVC ↑ • QRPA ↑, PRPA ↑ • QLPA ↑, PLPA ↑ 	<ul style="list-style-type: none"> • Intermittent volume increase in IVC compartment
	1.1.2) Pediaflow Gen-0 VAD	<ul style="list-style-type: none"> • QIVC ↓, PIVC ↑ • QSVC ↑, PSVC ↑ • QRPA remained constant, PRPA ↑ • QLPA remained constant, PLPA ↑ 	<ul style="list-style-type: none"> • Rapid volume increase in IVC compartment
1.2) PAB (RPA → Left Atrium)	1.2.1) Medos VAD	<ul style="list-style-type: none"> • QIVC ↑, PIVC ↑ • QSVC ↑, PSVC ↑ • QRPA ↑, PRPA ↑ • QLPA ↑, PLPA ↑ 	<ul style="list-style-type: none"> • Intermittent volume increase in RPA compartments
	1.2.2) Pediaflow-Gen-0 VAD	<ul style="list-style-type: none"> • QIVC ↑, PIVC ↑ • QSVC ↑, PSVC ↑ • QRPA ↓, PRPA ↑ • QLPA ↑, PLPA ↑ 	<ul style="list-style-type: none"> • Rapid volume increase in IVC and RPA compartments

Pressure (P) and flow (Q) data were collected with and without two ventricular assist devices (VADs) in two anastomotic configurations; systemic venous booster (SVB) and pulmonary venous booster (PVB); and for two settings of pulmonary compliance (“normal” and “hypertensive”).

TABLE 1. Vascular parameters of the mock system simulating postoperative Fontan circulation in normal and hypertensive conditions

Parameter	Normal Fontan circulation	Hypertensive circulation
C_{SAB}	0.34	0.34
C_{IVC}	10	10
C_{SVC}	10	10
C_{PAB}	0.78	0.1
C_{PVB}	10	10
R_{SAB-L}	16	12
R_{SAB-U}	12	9
R_{IVC}	10	7.5
R_{SVC}	8	6
R_{PAB}	1.7	1.275
R_{PVB}	0.1	0.075

Shown are the parameters implemented on the mock loop. Parameters are taken from patient data presented in Ref. (12) and Ref. (5).

C, compliance (mL/mm Hg); R, resistance (mm Hg L/min); SAB, systemic arterial bed (-L, lower; -U, upper); SVB, systemic venous bed; PVB, pulmonary venous bed; PAB, pulmonary arterial bed; PVB, pulmonary venous bed.

Life Sciences, Irvine, CA, USA) attached to a six-channel differential amplifier (WPI Inc., Sarasota, FL, USA) in full bridge configuration. In-chamber pressure measurements were validated by conducting simultaneous measurements at locations before, inside, and after the chambers using *in-line* pressure ports. The pressure drop across each chamber is found around 2.5–3 mm Hg. Flow rate through each tubing segment was measured using transonic flow probes (9XL, Transonic Inc., Ithaca, MA, USA). A dedicated data acquisition module NI USB-6229 (NI Inc., Austin, TX, USA) with 16-bit resolution and multiplexing capabilities was employed for sampling and recording data. Distilled water ($\rho = 998 \text{ kg/m}^3$) was used as the working fluid.

Impedance matching and initial calibration

Combined vascular resistance and compliance constitutes the impedance of a particular vessel segment is given below,

$$Z = R + \frac{1}{i\omega C} \quad (1)$$

where Z, R, C, ω are the complex impedance, resistance, compliance of the vessel segment, and the associated flow waveform, respectively. In order to modulate the vascular impedance in a predictable manner, systemic calibration studies were conducted before the experiments. R and C of each vessel segment are characterized individually to accurately produce the desired normal and abnormal flow conditions. Vascular resistances are adopted from a

recent study (12) which incorporated 40 SV patients (age: 6–18), whereas, the compliances assigned to each vessel segment replicated the physiological range available in clinical reports (15,16) and literature (5,17–19) (See Table 1). In order to demonstrate how accurately the vascular resistances can be set using the clamp-type needle pinch valves, we conducted flow and pressure drop measurements at each vessel segment adjusting the pinch valves to different vascular resistances. The resistance data from this calibration were fit to a power regression equation ($\text{Log}(R) = 5.3073 + -6.5302 \text{ Log}(\text{meter-scale value})$, $R^2 = 0.889$).

Experimental procedure

Ejection function and cardiac output were set to 45% (20) and 1.6 L/min, respectively to represent the typical post-Fontan hemodynamics. Experiments incorporated a Medos pulsatile VAD (Medos Medizintechnik AG, Stolberg, Germany) with 10 mL stroke volume and a Gen-0 prototype of the Pediaflow centrifugal VAD (PediaFlow Consortium, Pittsburgh, PA, USA) with 350 mL/min flow rate. Alternative to the classical systemic support and total-heart-support configurations, two venous assist scenarios, with single VADs, were explored: the systemic venous booster (SVB) and pulmonary artery booster (PAB) (Fig. 1). Introduced by Rodefield et al. (9), the SVB refers to VAD anastomosis between the IVC and the TCPC, whereas, in the PAB a VAD is inserted in line between the TCPC and the RPA. Each VAD, anastomosed in both deployment configurations, was analyzed under physiologically normal conditions in order to evaluate the feasibility of mechanical support to improve postoperative Fontan hemodynamics. Experiments are repeated under pulmonary hypertension to evaluate mechanical assist as an aid for “failing” Fontan hemodynamics. In the bench-top loop, pulmonary hypertension is simulated with increased pulmonary resistance and loss of vascular compliance on the LPA and RPA compartments.

RESULTS

Unassisted Fontan circulation experiments produced sinusoidal pulsatile waveforms in both systemic and pulmonary venous compartments for both normal and hypertensive conditions (Fig. 3). Physiological aortic pressure and flow waveforms were produced in all experiments (Fig. 4). The variation of flow in the RPA and IVC segments; and LPA and SVC segments were proportional. This state is associated to the surgical design of the 1DO TCPC model

7 which comprises a modular pulsatile pump that can
run in either SV or biventricular mode selectively.
Each ventricular chamber incorporates inflow
(mitral/tricuspid) and outflow (aortic/pulmonary)
valves. The system further consists of trapped air
compliance chambers, variable resistance flow
clamps, and the prototype extra-cardiac total cavopulmonary connection anatomy.

8 For analytical purposes, the mock system elements
are designed in six different compartments analogo-
gous to the recent electric circuit analog lumped-
parameter models developed by our group (5,12) to
investigate congenital heart diseases. Pulmonary
obstructive disease and hypertension common in
9 "failing" Fontan patients is simulated adjusting the
pulmonary artery impedance taken from the clinical
data. The mock system includes the left atrium, left
ventricle, aorta, inferior and superior vena cava (IVC
and SVC), left and right pulmonary arteries (LPA
and RPA) to compose systemic circulation and
pulmonary circulations (Fig. 2). Ventricular pumping
action is simulated using a modified bellows metering
pump (GRI Inc., Bellville, OH, USA) with variable
stroke volume (20–40 mL) driven by a crank mecha-
nism and shaded pole motor (104 bpm). Low resis-
tance heart valves are constructed in-house from
0.005-m thin shim stock and a polypropylene sup-
porting mesh sandwiched between two polyacetal
rings and mounted at the inlet and outlet of the
bellows chamber. Each compliance chamber was fab-
ricated using closed acrylic tubes with an internal
diameter of 3¹/₄ inches equipped with luer and barbed
connectors to connect cannulas or pressure trans-
ducers. Hence, this versatile design allows insertion
of pediatric assist devices in several anastomotic
configurations to analyze multiple postoperative clinical
scenarios compared with the same baseline state. The
circulation system between the pump and chambers
is modeled using transparent Tygon tubing with 3/8"
diameter on the arterial side and 3/4" diameter on
the venous side to match the baseline vascular resis-
tances reported for typical pediatric circulation
10 (Table 1). Clamp-type needle pinch valves (Flow-rite
Controls Inc., Byron Center, MI, USA) with a
metered scale were installed on each vessel segment
to accurately set the resistance in the venous and
arterial segments. The change in vascular resistance
was determined from regression analyses of time
averaged flow and pressure data.

11 In order to represent the final surgical stage of the
Fontan procedure, idealized pyrex glass models of
the total cavopulmonary connection (TCPC) was
12 fabricated based on the anatomic MRI data of an
8-year-old TCPC patient (13), where the IVC was

13 anastomosed to the RPA across the SVC with zero
and one diameter offset configurations. Both models
had idealized planar vessel conduits with a constant
inner diameter of 13.4 mm. Flared connections with
a radius of curvature of 6.7 mm were employed at
the intersection of the vena cavae and the pulmo-
nary arteries to improve the efficiency of TCPC
geometry (14). One diameter offset TCPC results
are reported in this article.

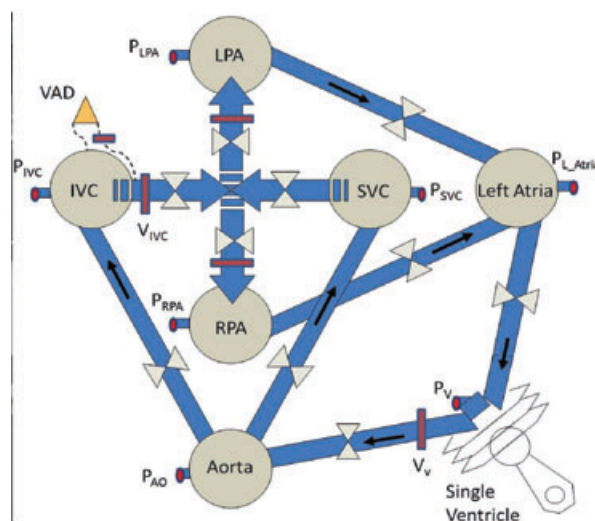
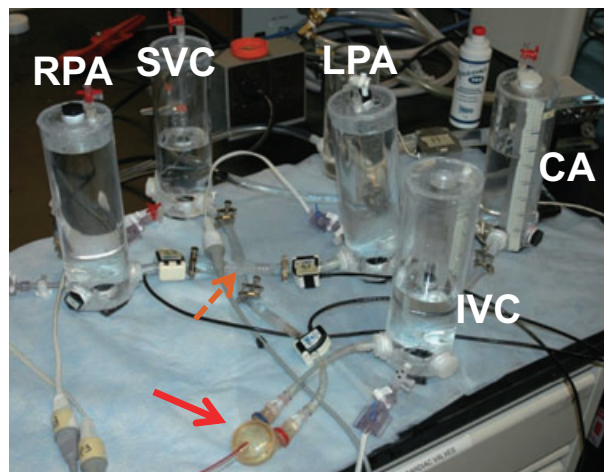


FIG. 2. Schematic representation of the Fontan flow mock loop (bottom) with ventricle assist device attached to IVC and TCPC in series: systemic venous booster (SVB). The compliance chambers are represented by dark grey circles. The grey double-triangles, orange rectangles, and the red circles represent the needle pinch resistors, velocity, and pressure measurement ports, respectively. Medos VAD inserted in SVB configuration and TCPC model are marked by solid red and dashed orange arrows on the flow loop picture (top), respectively.

14 anastomosed to the RPA across the SVC with zero
and one diameter offset configurations. Both models
had idealized planar vessel conduits with a constant
inner diameter of 13.4 mm. Flared connections with
a radius of curvature of 6.7 mm were employed at
the intersection of the vena cavae and the pulmo-
nary arteries to improve the efficiency of TCPC
geometry (14). One diameter offset TCPC results
are reported in this article.

15 Pressure measurements were performed at each
compliance chamber. Hence, six simultaneous
pressure measurements were performed using
TruWave disposable pressure transducers (Edwards

7 which comprises a modular pulsatile pump that can
run in either SV or biventricular mode selectively.
Each ventricular chamber incorporates inflow
(mitral/tricuspid) and outflow (aortic/pulmonary)
valves. The system further consists of trapped air
compliance chambers, variable resistance flow
clamps, and the prototype extra-cardiac total cavopul-
monary connection anatomy.

For analytical purposes, the mock system elements
are designed in six different compartments analogo-
us to the recent electric circuit analog lumped-
parameter models developed by our group (5,12) to
investigate congenital heart diseases. Pulmonary
obstructive disease and hypertension common in

8 “failing” Fontan patients is simulated adjusting the
pulmonary artery impedance taken from the clinical
data. The mock system includes the left atrium, left
ventricle, aorta, inferior and superior vena cava (IVC
and SVC), left and right pulmonary arteries (LPA
and RPA) to compose systemic circulation and
pulmonary circulations (Fig. 2). Ventricular pumping
action is simulated using a modified bellows metering
pump (GRI Inc., Bellville, OH, USA) with variable
stroke volume (20–40 mL) driven by a crank mecha-
nism and shaded pole motor (104 bpm). Low resis-
tance heart valves are constructed in-house from
0.005-m thin shim stock and a polypropylene sup-
porting mesh sandwiched between two polyacetal
rings and mounted at the inlet and outlet of the
bellows chamber. Each compliance chamber was fab-
ricated using closed acrylic tubes with an internal
diameter of 3¹/₄ inches equipped with luer and barbed
connectors to connect cannulas or pressure trans-
ducers. Hence, this versatile design allows insertion
of pediatric assist devices in several anastomotic
configurations to analyze multiple postoperative clinical
scenarios compared with the same baseline state. The
circulation system between the pump and chambers
is modeled using transparent Tygon tubing with 3/8”
diameter on the arterial side and 3/4” diameter on
the venous side to match the baseline vascular resis-
tances reported for typical pediatric circulation

9 (Table 1). Clamp-type needle pinch valves (Flow-rite
Controls Inc., Byron Center, MI, USA) with a
metered scale were installed on each vessel segment
to accurately set the resistance in the venous and
arterial segments. The change in vascular resistance
was determined from regression analyses of time
averaged flow and pressure data.

10 In order to represent the final surgical stage of the
Fontan procedure, idealized pyrex glass models of
the total cavopulmonary connection (TCPC) was
fabricated based on the anatomic MRI data of an
8-year-old TCPC patient (13), where the IVC was

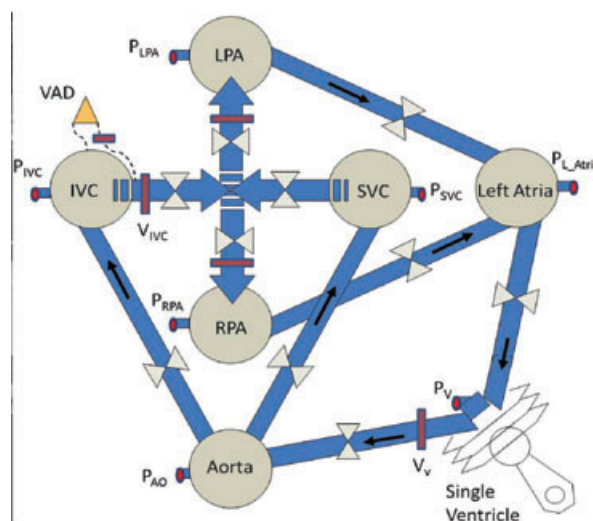
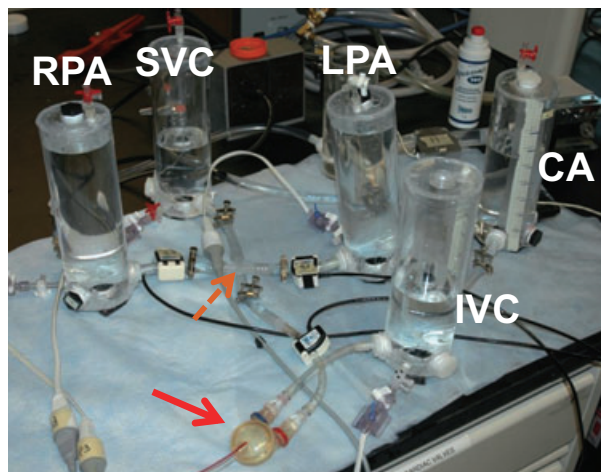


FIG. 2. Schematic representation of the Fontan flow mock loop (bottom) with ventricle assist device attached to IVC and TCPC in series: systemic venous booster (SVB). The compliance chambers are represented by dark grey circles. The grey double-triangles, orange rectangles, and the red circles represent the needle pinch resistors, velocity, and pressure measurement ports, respectively. Medos VAD inserted in SVB configuration and TCPC model are marked by solid red and dashed orange arrows on the flow loop picture (top), respectively.

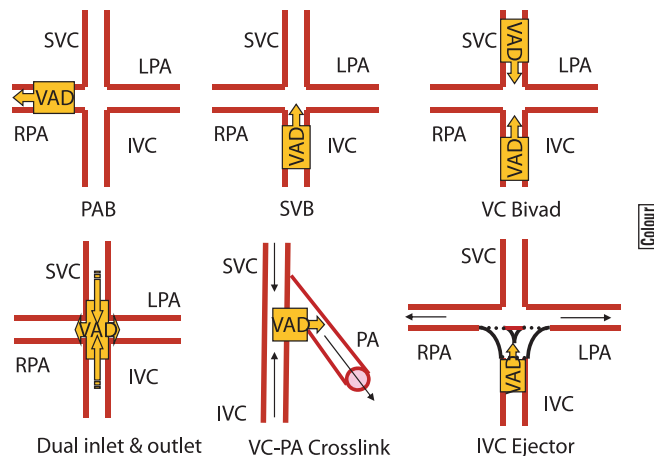
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1 ventricular preload, and reverse the Fontan Paradox
2 of underfilling of the pulmonary arteries with hyper-
3 tension in the pulmonary capillaries. Several opportu-
4 [4] nities exist for a VAD system to improve patient
5 outcomes during both immediate postoperative and
6 late “failing” states of the disease. Preliminary data in
7 humans and animals support the feasibility of circula-
8 tory assist (8,9), however, a major deficit is that the
9 current studies implement the conventional VAD
10 systems that are not specially designed for utilization
11 as booster pumps in lower-pressure flow assist
12 scenarios. The idea of Fontan VAD contrasts sharply
13 with the traditional concept of a left or right ventricu-
14 lar assist device (LVAD or RVAD) that generally
15 takes over the circulatory responsibilities from a
16 [5] damaged ventricle.

17 Many VAD programs have investigated standard
18 flow loops focusing only on the systemic compart-
19 ments for testing device performance both in contin-
20 uous (10) and pulsatile (10,11) modes. Although
21 these simple systems allow for the assessment of
22 VAD performance for conventional physiologies,
23 few are able to mimic the hemodynamic conditions
24 of nontraditional physiologies, such as the Fontan
25 patients, and thus provide limited insight on the effec-
26 tiveness of VAD insertion for patients with congeni-
27 tal heart defects. In vitro set-ups for Fontan patients
28 are scarce and have been limited to steady venous
29 flow conditions that emphasize the use of devices as
30 a left ventricular support and generally ignore the
31 effects of the surgically constructed pulmonary
32 conduit on venous return, fluid balance, and cardiac
33 function in the SV. A reliable bench-top pediatric
34 single-ventricle pulsatile flow loop is necessary to
35 investigate the feasibility of using VADs other than
36 [6] as a LVAD in the postoperative period. Using the
37 VAD in a fashion that simultaneously reduces venous
38 stasis and restores cardiac output may reduce post-
39 operative morbidity and prove to be superior to
40 the current LVAD paradigm which most directly
41 addresses the problems associated with ventricular
42 overloading associated with poor ventricular
43 performance. The ideal experimental workbench
44 should enable systemic evaluation and optimization
45 of assisted circulation strategies for short or moder-
46 ate term VAD use in “failing” Fontans as well. The
47 goal of mechanical support for Fontan patients
48 should translate from decreasing the workload of the
49 SV to extending the life of the entire cardiopulmo-
50 nary circuit and thereby extending the time that
51 patients may be bridged to transplant on VAD
52 support.

53 The pediatric mock circulation system introduced
54 in this study reproduced physiological and pathologi-



55 **FIG. 1.** A cartoon of possible venous ventricle assist device [20]
56 configurations (VAD) for cardiopulmonary support in Fontan
57 patients. VADs are inserted (from top left to bottom right)
58 between pulmonary artery-to-venous bed (pulmonary artery
59 booster-PAB), systemic venous return-to-TCPC (systemic
60 venous booster-SVB), dual caval veins-TCPC (CV-Bivard) (9),
61 double-inlet double outlet (5), vena cava to pulmonary arteries
62 crosslink (uses a VAD with a single inlet and outlet to connect
63 between the two vessels), IVC ejector pump. In this study, SVB
64 and PAB configurations are studied. SVC, IVC, RPA, LPA refer
65 to superior vena cava, inferior vena cava, right and left pulmo-
66 nary artery, respectively.

67 cal states (pulmonary hypertension) with realistic
68 hemodynamics. Our results demonstrated its utility
69 to simulate the Fontan circulation and the hemody-
70 namic effects of insertion of various existing VADs.
71 The present bench-top flow loop was designed with
72 the objective of (i) reproducing both the physiologi-
73 cal and pathological conditions that are commonly
74 observed during the early and long-term postopera-
75 tive life after Fontan procedure; and (ii) evaluation of
76 the feasibility of cardiopulmonary support in single-
77 ventricle patients. Likewise, the proposed flow loop
78 should facilitate the deployment of alternative
79 PVAD anastomosis configurations (Fig. 1). Particu-
80 larly the present flow loop design (i) allows tuning of
81 the vascular resistance and compliance of the indi-
82 vidual arterial and venous compartments within the
83 clinical ranges; (ii) provides an ability to adjust
84 patient-specific pediatric flow rate; and (iii) allows
85 practical insertion of PVADs, data acquisition instru-
86 ments (pressure-flow probes), and anatomical Fontan
87 models.
88

89 **MATERIALS AND METHODS** 90

91 **Mock circulation loop** 92

93 The entire SV Fontan circulation is modeled in
94 vitro by constructing a bench-top pediatric flow setup