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Development of a Custom Extracorporeal Circuit for Endovascular Resuscitation Research

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Our aim was to demonstrate the utility and applicability of in vitro extracorporeal circuits in endovascular resuscitation research. The method for building an inexpensive in vitro extracorporeal circuit for endovascular resuscitation research is described. In this study, aortic cannulas and pump combinations were evaluated in the in vitro extracorporeal circuit. Then one aortic cannula and pump set up was evaluated in a post-mortem swine model. Flow data was collected and compared among groups. The peristaltic pump generated the highest flow as compared with the other pump combinations at any given catheter size. The peristaltic pump combined with the 10 Fr cannula produced the highest flow overall at 2,304 ml/min. This same combination produced a peak flow of 886 ml/min at the aortic root in the swine model. The flow generated in the swine model was less than half of that generated in the in vitro model. However, all flow was channeled through one outflow tract in the in vitro model whereas the swine aorta has several branches of outflow. As such, a 50% reduction in flow or greater is anticipated at the level of the aortic root. An in vitro extracorporeal circuit for endovascular research can be built for less than US$10,000, with most of the materials being reusable, and can be used to generate representative data that may be anticipated in a swine model.

Keywords: *Extracorporeal Circuit; Endovascular Resuscitation; Endovascular Research*

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INTRODUCTION

Traumatic injury constitutes the leading cause of loss of life in patients between 16 and 40 years of age [1]. Prompt resuscitation of patients presenting in extremis with deranged physiology is critical to survival [2]. Conventional resuscitation measures include fluid administration, surgery, and the use of drugs such as vasopressors. Extracorporeal circuits have been used in organ support for many years, but this has largely been limited to refractory organ failure and is rarely used during acute resuscitation.

This paradigm is changing with the advent of endovascular resuscitation where catheter-based therapies are used to manipulate physiology, usually as a bridge to definitive intervention. An early example of this is resuscitative endovascular balloon occlusion of the aorta (REBOA) [3]. While compelling, the experience of REBOA in patients in cardiac arrest has been poor and has prompted the exploration of therapies such as selective aortic arch perfusion and emergency preservation and resuscitation [4,5].

Common to these therapies is the need for an extracorporeal circuit to deliver a perfusate. This has generally involved the adaption of commercially available circuits like those found in cardiopulmonary bypass or extracorporeal membrane oxygenation [4,6]. The expense of these products can be prohibitive for labs. Furthermore, these materials are not meant to be reused and are not easily customizable.

Research in this nascent area is critical to progressing our understanding of these adjuncts. The aim of this study is to describe the laboratory fabrication of a practical and customizable extracorporeal circuit for endovascular resuscitation research.

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METHODS

Building the Circuit

A United Biologics™ (Santa Ana, CA) silicone aorta model was used to build the circuit. All materials used

Table 1 A list of materials necessary to build a circuit and their associated costs.

Item	*Cost (US$)*
Silicone aorta model	5,100
10 feet of tubing	10
Connectors and stopcocks	600
1,000 zip ties	15
Zip tie gun	50
Pulsatile pump	3,500
Reservoir	110
Total	**9,385**

are listed in Table 1. A series of tubing, connectors, and stopcocks (Figure 1) make up the circuit. Zip ties were critical to maintain the integrity of the circuit at connecting points as high flows delivered by the pumps could cause a breakdown at these relative weak points. Pumps were included to drive flow in the circuit. A reservoir was also incorporated to hold excess fluid in the circuit and to allow for easy addition of fluid into the system. Fluid was made up of 20% glycerol in water to replicate the density and viscosity of blood and added to the system via the reservoir [7]. Aortic cannulas of varying sizes were included in the circuit after the pump and connected the circuit to the aorta model. An in-line flow probe was included in the circuit to measure the flow the pump generated through the aortic cannula.

To replicate low level perfusion in the system, a United Biologics™ FlowTek125 pulsatile pump was added to the circuit to deliver a low level mean arterial pressure (MAP). The complete circuit with labeled components is depicted in Figure 2.

Model Development

Aortic cannula size and pump configuration were both varied. Aortic cannula sizes included 6, 8, and 10 Fr, each 80 cm in length. Harvard Apparatus (Holliston, MA) centrifugal and peristaltic pumps were used. Centrifugal pumps use rotational kinetic energy to propel fluid forward whereas peristaltic pumps use roller heads. Pump configurations included a single centrifugal pump, two centrifugal pumps in series as well as in parallel, and a peristaltic pump. Given the circuit set up, all of these configurations could be incorporated into the system with relative ease.

For each run, the pulsatile pump was set to a pulse of 80 and flow of 10%. External compression with a clamp was applied to the aorta model 5 cm distal to the aortic cannula tip to mimic the presence of an occluding balloon, which prevents distal perfusion and maintains maximum pressure in the aortic arch. Centrifugal pump flow was set to maximum in each case. Peristaltic pump flow was set to the maximum flow tolerated by the system. The peristaltic pump setting for each catheter is represented in Table 2. Each run began with a short 5–10 s baseline to establish that the initial measured MAP was within the 10–20 mmHg range followed by a 5-min run. Flow was measured proximal to the aortic cannula tip.

In Vivo Study

The circuit with the peristaltic pump and the 10 Fr aortic cannula was selected, as it demonstrated the highest flow rate in the in vitro study, to examine the reliability of the circuit when used in vivo. This was done in a single post-mortem swine model, and, as such, did not require formal approval. The animal required femoral arterial access for placement of the aortic cannula intravascularly. The cannula's associated balloon was inflated in zone 1 (the thoracic aorta) corresponding with the region of occlusion in the in vitro model. The animal's chest was opened to place a flow probe around the aortic root. A run was completed using blood that had been exsanguinated from the animal shortly beforehand.

Data Collection and Analysis

All flow data were captured continuously using the PowerLab system (AD Instruments, Colorado Springs, CO). For in vitro model development, flow data was averaged every 20 s for a total of 15 data points per 5-min run. For the post-mortem swine model, flow data was averaged every 3 s for a total of 15 data points as the run was 45 s long. All data were exported to Microsoft Excel (Redmond, WA) for storage and analysis. Data were analyzed and graphed using GraphPad version 8 (San Diego, CA).

RESULTS

Using an aortic model and a "home-made" circuit, flow generated from a variety of pumps and catheters in different combinations were evaluated. Figure 3 summarizes these findings. The peristaltic pump was able to generate more flow than the centrifugal pump at any given catheter size. The peristaltic pump combined with the 10 Fr cannula produced the highest flow at 2,304 ml/min.

To test the applicability of the model to the in vivo model, the circuit using the peristaltic pump and the 10 Fr aortic cannula was selected. Figure 4 demonstrates the flow generated in the aortic root; the flow peaked initially at 886 ml/min but then deteriorated to as low as 698 ml/min and was 700–800 ml/min for the remainder of the run.

DISCUSSION

An in vitro vascular model for extracorporeal research was successfully and relatively inexpensively built as reflected in Table 1. The bulk of these costs comes from durable equipment that can be reused for a long time. Moreover, they afford researchers the ability to develop

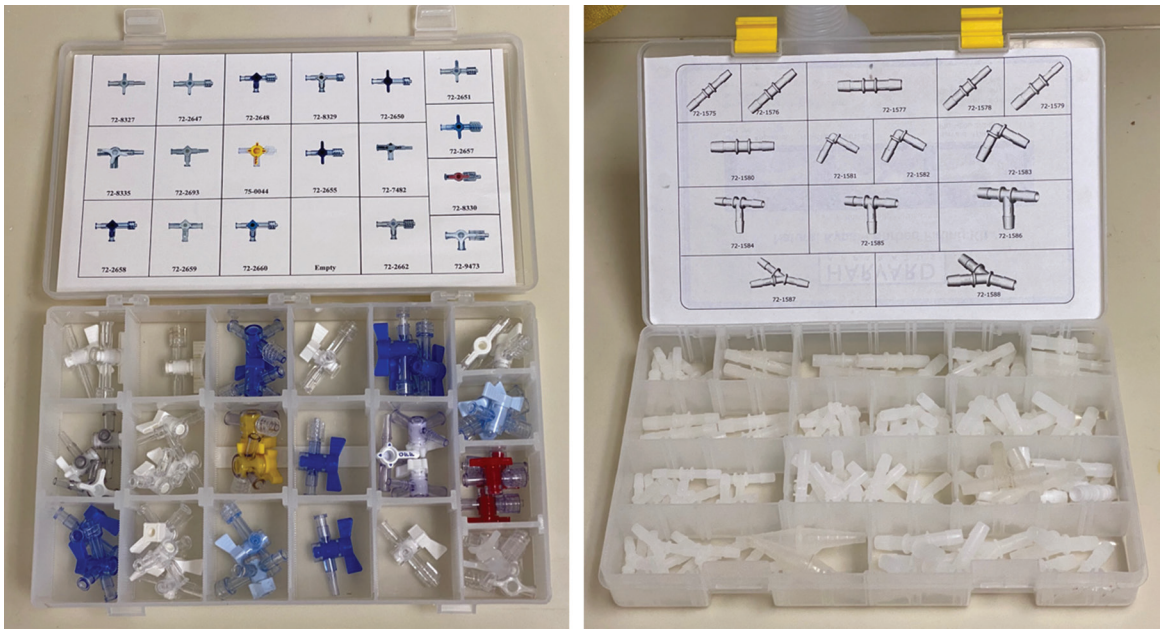

Figure 1 The kits from which connectors and stopcocks were used to build the circuit.

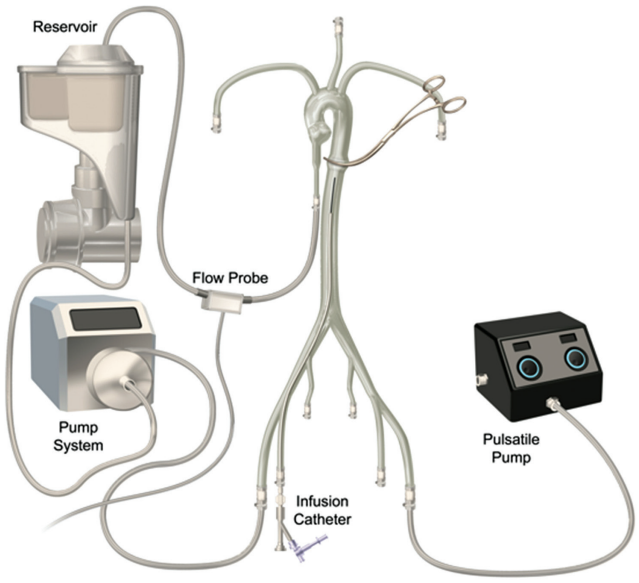

Figure 2 The in vitro vascular circuit.

Table 2 Peristaltic pump flow corresponding with each catheter.

Catheter Size (Fr)	*Peristaltic Pump Flow (rpm)*
6	120
8	170
10	215

methodology, gather preliminary data, and troubleshoot problems in endovascular research prior to moving to an animal model, which introduces many high costs.

The in vitro model was successfully used to evaluate the flow capacity of different catheters and pumps. It is not surprising that higher flow rates were generated using larger catheters with any given pump or pump combination. However, the model provided important information as to what flow could be generated with a given circuit.

In the swine model, flow rates at the aortic root did not exceed 900 ml/min. Initially this may appear to be a flaw with the model. However, given that the model had only one outflow through which all the fluid was traveling as opposed to the animal model that has branches off of the aortic arch, a 50% reduction or more in flow at the aortic root is anticipated. In addition, the swine model has an initial peak of flow that then decreases in contrast to the in vitro model where that does not occur in an appreciable way. This too makes sense as the in vitro model is a circuit where fluid always moves forward, whereas the animal model does not have the same luxury likely resulting in some back pressure and reduced flow. Although these differences are limitations of the model, they do also suggest that measurements made in the in vitro model may be translatable to the animal model for research purposes.

Another limitation of the in vitro model was the inability to maximize pump flow when using the peristaltic pump secondary to circuit failure. This required the use of the maximum pump flow that the circuit could handle rather than the true maximum pump flow.

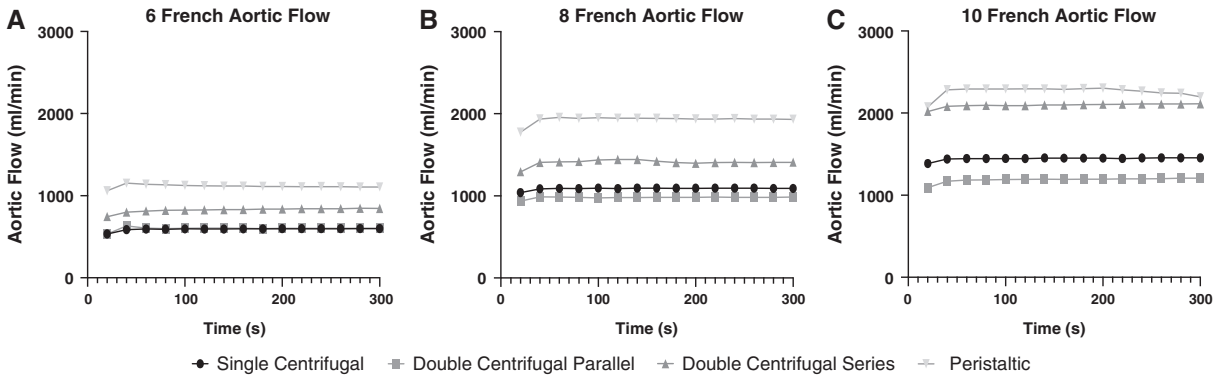

Figure 3 Flows generated through each aortic cannula by each pump combination. (**a**) 6 Fr catheter. (**b**) 8 Fr catheter. (**c**) 10 Fr catheter.

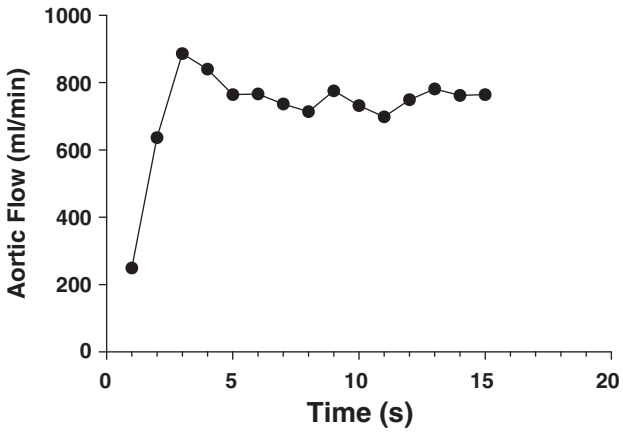

Figure 4 Aortic root flow generated in the swine model using a 10 Fr catheter and the peristaltic pump.

This is probably a consequence of the tubing and connector quality as they are not medical grade. However, this does again demonstrate the importance of using zip ties when building circuits, particularly if high pressures or flows will be run through the circuit. More importantly, we would maintain that the expense justifies the use of circuits such as this as a lot of information can be derived using this inexpensive system.

CONCLUSIONS

We believe that this cost-effective in vitro model will be of great value to many laboratories exploring endovascular resuscitation and catheter-based therapies. It will help remove some of the financial burden and enable more investigators to further research in this field.

Ethics Statement

(1) All the authors mentioned in the manuscript have agreed to authorship, read and approved the manuscript, and given consent for submission and subsequent publication of the manuscript.
(2) The authors declare that they have read and abided by the JEVTM statement of ethical standards including rules of informed consent and ethical committee approval as stated in the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Author Contributions

All authors have substantially contributed to the study and manuscript writing.

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