A mock circulation loop for in vitro haemodynamic evaluation of aorta

Xuhui Li, Zhenfeng Li and Duanduan Chen *
School of Life Science, Beijing Institute of Technology, Beijing, China

*Corresponding author e-mail: duanduan@bit.edu.cn

Abstract. Haemodynamic conditions play a crucial role in the pathological development of aortic dissection (AD). However, it is challenging to quantitatively and precisely capture the flow features in vivo. In this study, a mock circulation loop (MCL) embedded with patient-specific aortic phantoms was proposed. In order to evaluate perfusion characters, a normal aortic model and an AD model were established with twelve main branches. The system is capable of replicating the aortic geometry, vascular compliance, characteristic resistance, and peripheral resistance of the cardiovascular system. By altering controlling parameters, it can mimic various cardiovascular conditions. The physiological healthy rest cardiac condition was reproduced and the rationality and accuracy of the system was confirmed by comparing the measured flow data from the MCL with a normal aortic phantom and the in vivo ultrasound velocimetry of healthy volunteers (maximum discrepancy was 4.69%). Different flow features between the normal and AD phantoms were quantitatively compared by pressure sensors and ultrasonic flow sensors under the same condition. Therefore, the proposed MCL can be applied as a research tool for in vitro haemodynamic analysis of the aorta. Moreover, it can be applied to evaluate the performance of interventional devices and to provide a realistic platform for trainings on interventional treatments.

1. Introduction
Aortic dissection (AD) is a severe cardiovascular condition associated with a high morbidity and mortality. It is initiated by a tear that allows the blood to surge into a space between the intima and media layers, splitting the aortic wall into two passages: the true lumen (TL) and the false lumen (FL). Patients with an AD are usually accompanied with other vascular-related complications, such as hypertension, TL collapse and FL dilation and the subsequent end-organ malperfusion (organ ischaemia). [1]. Data from International Registry of Aortic Dissection (IRAD) suggests increased adverse outcomes in the acute phase for patients with resistant hypertension [2]. Besides, malperfusion syndrome also remains a significantly adverse risk factor for the survival of AD [3]. The visualization of the detailed information on local haemodynamic environment of AD and the connecting visceral branches is essential to understand the pathological features influenced by the AD structure.

Computational biomechanical modelling has been proved its practicality and reliability in researching many aortic applications. However, most of these studies are based on the assumption that the effect of the vessel wall motion was neglected [4]. Fluid-structure interaction (FSI) simulations are capable to capture this motion but with a prohibitively expensive cost for computational time, especially
for the complex structure of AD models [5]. Recently, the systematic development of the mock circulatory loop (MCL) is able to provide a suitable test platform for reproducing physiological or pathological hemodynamic environment by mechanically representing the human cardiovascular system. The in vitro aortic model with human anatomy and elastic properties was applied in the MCL to evaluate the haemodynamic parameters. In this situation, the effects of the vessel wall motion were taken into consideration to conduct a more realistic and efficient simulation.

This study aimed to investigate the special haemodynamic characters caused by the AD structure. An MCL system incorporated with patient-specific aortic models fabricated by elastic silicone as a research tool to evaluate the haemodynamic environment of AD was established. Windkessel models are used at in vitro research to represent the effects of the distal vasculature. A normal and an AD model with patient-specific anatomy were fabricated. The MCL embedded with the normal model was set to reproduce physiological condition to validate the function of the system. Based on which, flow parameters of the AD model were acquired under the same settings and haemodynamic features were analyzed.

2. Materials and Methods

2.1. Patient-specific silicone models fabrication
This study was approved by the Institutional Review Board of Chinese PLA General Hospital (S201703601) and all subjects provided written informed consent. A normal model and an AD model made of silicone were constructed from the patient-specific scans. The anatomy of the normal model was obtained by a patient with sudden abdominal pain and ruled out for aorta or visceral artery disease by aortic computed tomography angiography (CTA) using a 16-detector row scanner (Aquilion; Toshiba Medical Systems, Japan). The AD model was reconstructed from CTA scans of a chronic Type B AD patient using a same type scanner. The branches of the reconstructed geometry was extended for the convenience of connecting. Figure 1a displays the complete aortic geometries of the normal aorta (left) and AD (right) patient which started from the ascending aorta (AAo) and extended to the iliac artery. All branches were divided into upper-arch group, abdominal group and iliac group based on the location and the function parameters. The reconstructed normal and AD aortic anatomy was used to manufacture the compliant aortic model shown in Figure 1b.

![Figure 1. The reconstructed geometry and established model of the normal aorta and the AD](image)

2.2. Mock circulation loop
The MCL along with a schematic of the main components is shown in Figure 2. The cardiac pulsatile flow was generated by a gear pump driven by the servo motor. A passive one-way valve was arranged as the aortic valve to prevent reflux. Compliance chambers was adopted to simulate the Windkessel effect. Vascular resistance was replicated by the effective selection of the electric proportional control valves. A compliance chamber and a valve were attached to the inflow of the aortic model via a connection tube. Side branches of the aorta were equipped with Hoffman pinchcocks to mimic the character resistance of aortic bifurcations and thus manually adjust the flow distribution ratio (FDR). The four branches of each group were collected to a compliance chamber and all branches were collected
to an proportional valve which represents the peripheral resistance (PR). The pinchcocks, compliance chambers and the proportional valve consisted of the three-elements Windkessel model to properly control the boundary conditons (BCs) at the branches. The efflux flowed into an acrylic reservoir executing the duty of the atrium and veins.

![Figure 2. Schematic of the MCL setup](image)

A hydraulic transducer (CYYZ11, Star Sensors, China) and an ultrasonic flowmeter (ME20PXL291, Transonic Systems, Inc., USA) were installed at the connection tube attached to the inflow of the aortic model to measure the pressure and flowrate of AAo. Other movable pressure sensors (HSCDANT005PGAA5, Honeywell, USA) and another ultrasonic flowmeter (ME9PXL1668, Transonic Systems, Inc., USA) were located at the downstream of the branch vessels to measure the pressure and flowrate of effluent fluid. Here, water was used as the circulating fluid, in a similar fashion to the study conducted by Rezaienia et al [6].

### 2.3. Experimental operation

Velocities of vital branches of aorta were measured using a Doppler ultrasound machine from 20 healthy volunteers. The AAo flowrate curves was served as the base control waveform of the pump and transformed to physiological healthy rest conditions by changing the cardiac output features and PR as shown in Table 1. The FDR was calculated by the measured branches serving as the standard FDR. Pinchcocks were modified to reproduce the standard FDR using the normal model inserted in the MCL. Then, the patient-specific AD model were joined to the MCL under the same condition. The FDR and pressure of all the branches were acquired and compared with that of the normal model to investigate the special characters induced by the AD structure.

### 3. Results and Discussion

The haemodynamic evaluation was accomplished by comparing the haemodynamic features including pressure and FDR at each branch of the normal and AD models under reproduced physiological healthy rest conditions. The local flow parameters could be highly influenced by the dissection anatomy of the AD model and revealed the pathological characters of the AD structure.

#### 3.1. Functional verification of MCL

MCL functional verification was firstly attained by simulating the pressure under the healthy rest condition using the normal silicone aortic model. After adjusting the MCL PR settings to achieve heart rate (HR), AAo systolic pressure (AoPsys) and diastolic pressure (AoPdias) shown in Table 1, the experimental results of the normal model was obtained. The measured experimental PR, HR under the physiological condition achieves a good consistence with that of the reference data. However, the measured CO, AoPsys and AoPdias were lower than the reference data. The reason inducing this phenomenon is that the reference PR represents the total resistance of vascular system while the experimental PR is actually the vascular resistance excluding the phantom and branches in our model.
Hence, this theoretically higher PR results in lower CO and pressures. However, the aim of this research is to compare the haemodynamic features between the normal aorta and the AD model, hence this difference is acceptable when the settings of the MCL keep at the same level.

Table 1. Experimental results and reference data.

| Experimental result | Reference data |
|---------------------|----------------|
| PR (Dyne·s·cm⁻⁵)    | 1466           | 1430           |
| CO (L/min)          | 4.85           | 5.2            |
| HR (bpm)            | 60             | 60             |
| AoPsys              | 108.34         | 120            |
| AoP dias            | 70.80          | 80             |

3.2. Comparison between the normal and the AD model

The aortic pressure waveforms and pulsatile aortic flowrate waveforms are measured at AAo of the normal and AD model under the same condition and shown in Figure 3a. Compared with the AAo pressure of the normal model, the AD model showed similar pressure waveforms under the same MCL setting. The AD model represented a higher systolic pressure, which was 117.36 mmHg, and a slightly increasing diastolic pressure with a value of 72.68 mmHg. The pattern of the flowrate curve was almost identical with that of the normal model.

Figure 3. The pressure and flow rate waveform of normal and AD model at AAo

The pressure waveforms at each branch of the two models were also captured. Figure 4 shows that, in general, the AD model had a higher systolic pressure value which is similar to the AAo pressure. In particular, the branches of the cerebral group locating at the upstream of the dissection affected region showed relatively smaller systolic pressure differences between the normal model and the AD model (4.92% ± 0.91%) compared to branches locating at distal (9.11% ± 1.74%).

Figure 4. The pressure waveform of normal and AD model at each branch
This result suggested that the double-barrel anatomy of the AD had larger resistance than the normal aorta, resulting in a higher afterload. The specific morphological structure of AD can result in increased aortic pressure due to the high resistance. Peak systolic blood pressure was seen as informative cardiovascular risk factors [7]. It is reported that the occurrence of an AD may be related to long-term hypertension [8]. Clinical studies have shown that elevated afterload is the cause of LV diastolic dysfunction [9]. LV diastolic dysfunction has been found in AD patients [10]. The special morphological structure of the AD may aggravate the degree of hypertension experienced and cause LV diastolic dysfunction.

Figure 5 shows the FDR of the standard data and the measured data. As for the experimental results of normal model, the FDR under the physiological condition was in good agreement with standard FDR with a maximum difference of 4.69%. This result illustrated that the MCL could reproduce specific FDR acting as proper BCs. Hence, the MCL functional verification was secondly attained. Compared the FDR of the AD model with normal model, the total blood flow to the branches of upper-arch group increased while the flow to the branches of iliac group decreased. The FDR of the branches shows a lower flowrate to the downstream of the dissection-affected region.

Figure 5. FDR of the standard data, normal model and AD model

The normal and AD models were connected to the MCL under the same setting of the Windkessel models to exclude the influence of the BCs. Thus, the difference of the FDR was mainly affected by the morphological structure. Malperfusion remains a significant adverse risk factor for survival for acute AD and the leg malperfusion is an important symptom [11]. Ischaemic complications can arise when the dissection compromises blood flow by extrinsic compression of the TL by the FL [12]. Although the AD anatomy in this study was reconstructed with a chronic patient which had a relatively stable vascular anatomy, decrease FDR to the iliac group was still observed. Due to the high resistance character of the dissection-affected region, the flowrate to downstream of the dissection-affected region was lower while the flowrate to upstream of the dissection-affected region was higher. As for a more severe collapsed TL in acute AD, the decreasing perfusion to the lower limbs could be aggravated. The pressure increased more at the distal branches of the AD model, which may contribute to the low perfusion of lower limbs.

4. Conclusion
An MCL system was developed for the in vitro haemodynamic evaluation of aorta. Patient-specific models and Windkessel models in this study consisted the configuration of blood circulation system. This newly developed MCL could provide an accurate method to evaluate the realistic haemodynamic characters. The function of the MCL was verified by reproducing a physiological condition. The obtained experiment pressure and FDR at normal model was similar with that of the reference data. This study performed the comparison of the haemodynamic features of the normal and AD models such as pressure and branch perfusion. The higher aortic pressure observed at AD model showed the high resistance character of the specific ‘double-barrel’ morphological structure. The AD structure could also
cause visceral ischemia as flowrate to the downstream of the dissection-affected region was lower. Actually, the experiment FDR of the AD showed a lower flowrate to the iliac group.

In this MCL, in vitro phantoms can be changed to other vessels and the BCs can be easily modified by altering parameters of the resistance and compliance components. Therefore, this MCL could satisfy not only producing various haemodynamic conditions but also researching multiple vascular diseases. Besides, it also has the ability to evaluate the performance of cardiovascular assistance devices when applied to patient-specific models prior to practical clinical surgery. On the other hand, it can help to optimize the design of cardiovascular assistance devices through in vitro testing.

Acknowledgments
National Key R&D Program of China (2018AAA0102602), National Natural Science Foundation of China (81970404, 81770465, 81911530224), Beijing Nova Program (Z181100006218008), Beijing Natural Science Foundation (Z190014).

References
[1] Fattori R, Montgomery D, Lovato L, et al. Survival after endovascular therapy in patients with type B aortic dissection: a report from the International Registry of Acute Aortic Dissection (IRAD). [J]. jacc cardiovascular interventions, 2013, 6(8): 876-882.
[2] Delsart P, Ledieu G J, Ramdane N, et al. Impact Of the Management of Type B Aortic Dissection on the Long-Term Blood Pressure [J]. American Journal of Cardiology, 2017, 120 (3).
[3] Deeb G M, Patel H J, Williams D M. Treatment for malperfusion syndrome in acute type A and B aortic dissection: A long-term analysis [J]. journal of thoracic & cardiovascular surgery, 2010, 140(6-supp-S): 0-0.
[4] XuHuanming, LiZhenfeng, DongHuiwu, et al. Hemodynamic parameters that may predict false-lumen growth in type-B aortic dissection after endovascular repair: A preliminary study on long-term multiple follow-ups [J]. Medical Engineering & Physics, 2017.
[5] Aortic dissection simulation models for clinical support: fluid-structure interaction vs. rigid wall models [J]. Biomedical Engineering Online, 2015, 14(1): 34.
[6] Rezaienia M A, Rahideh A, Alhosseini Hamedani B, et al. Numerical and In Vitro Investigation of a Novel Mechanical Circulatory Support Device Installed in the Descending Aorta [J]. Artificial Organs, 2015, 39(6): 502-513.
[7] Bortolotto L A, Safar M E. Blood pressure profile along the arterial tree and genetics of hypertension [J]. Arquivos Brasileiros De Cardiologia, 2006, 86(3): 166-169.
[8] Czermak B V, Waldenberger P, Fraedrich G, et al. Treatment of Stanford type B aortic dissection with stent-grafts: preliminary results [J]. radiology, 2000, 217(2): 544-50.
[9] Left ventricular remodeling in patients with acute type B aortic dissection after thoracic endovascular aortic repair: Short- and mid-term outcomes. [J]. International Journal of Cardiology, 2018.
[10] Shingu Y, Shiiya N, Mikami T, et al. Left Ventricular Diastolic Dysfunction in Chronic Aortic Dissection [J]. annals of thoracic surgery, 2007, 83(4): 0-1360.
[11] Nakahira A, Ogino H, Matsuda H, et al. Postural change causing leg malperfusion resulting from expansion of a patent false lumen in type B aortic dissection [J]. journal of thoracic & cardiovascular surgery, 2007, 134(4): 1046-1047.
[12] Fattori R, Botta L, Lovato L, et al. Malperfusion Syndrome in Type B Aortic Dissection: Role of the Endovascular Procedures [J]. Acta Chirurgica Belgica, 2008, 108(2):192-197.