DESIGN AND LUMPED-PARAMETER MODELLING
OF AN MRI-COMPATIBLE MOCK LOOP FOR
AORTIC-VALVE APPLICATIONS

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ABSTRACT

INTRODUCTION

Cardiovascular diseases are a group of disorders of the heart, the heart valves and of the blood vessels, and are the number one cause of death globally (source: WHO). The treatments include either the fixing or the replacement of a non-functional part by means of cardiovascular devices. Cardiovascular devices’ performance must be assessed during a preclinical testing phase [5], and they must be tested under physiological conditions, which involves the use of pulsatile flow. This is generally done by using mock circulation loops, which are hydraulic circuits that mimic the cardiovascular circulation in different conditions. These mock loops provide good control and measurements of macroscopic fluid-dynamic parameters such as flow rates and pressures [6]; however, they provide no information about local fluid dynamic quantities, such as the velocity field of the fluid in the device. Other techniques like echocardiography [14] and phase contrast MRI provide information about the velocity field of the fluid in selected bi-dimensional planes [12], [13]. Computational Fluid Dynamics is the gold standard for obtaining information about the velocity field and its development in time in a three-dimensional volume, however the results are related to fluid dynamic calculations (as opposed to measurements), hence depend on the proper choice of the model used [11].

MRI 4D-flow is a relatively new technique that can provide the velocity field in the interested three-dimensional volume and its evolution in time, and it is related to a real device [12], [15], [16]. The 4D-flow technique relies on the use of an MRI-scanner. The main challenge with dealing with the MRI measurements is the placing of instrumentation and pumping systems, which are generally made by ferromagnetic materials. The MRI-scanner generates an electro-magnetic field which is not compatible with metallic materials. After an analysis of the literature, the existent mock loops developed to this purpose provided
physiological flow and pressure waveforms, but with some limitations, including the use of pneumatically driven devices [18], or pumping systems which are not easily available or replaceable, such as MRI-compatible pumps [19] or gear pumps [21], or the transmission of rigid movement along high distances which carries mechanical constraints [20]. Moreover, the solutions rely on the possibility to place the instrumentation and the generators inside the MRI-room, behind a safety line: that is not feasible in non-research-purpose hospitals.

The aim of this work was to design an MRI-compatible pulsatile mock loop for the testing of cardiovascular devices. The instrumentation and pumping system were intended to be placed into the control room, while the test section was intended to be placed in the MRI-scanner, for the mock loop to be exploitable in non-research-oriented hospitals too (see Figure I). The focus was placed upon an aortic valve, but the project was carried out requesting a certain degree of versatility, so that with some adjustments the mock loop can be adopted to study other cardiovascular diseases and devices. The design phase was aided by means of lumped parameter modelling approach. The design specifications include the ability to reproduce physiological pulsatile flow and pressure conditions in the test section regardless of imposed heart rate and stroke volume; the easiness of transportation, assembling and disassembling phases; the availability and replaceability of the components; the user-friendliness of the management of the mock loop during the MRI acquisitions.

MATERIALS AND METHODS

Initial circuit configuration

Based on the design specifications, the initial circuit configuration (Figure I) was composed by: a submersible centrifugal pump to allow the initial filling and the debubbling of the circuit; a pulsatile volumetric piston pump, controlled by an external driver, that can provide the set flow waveform; service valves, placed immediately after and before the volumetric pump, in order to obtain unidirectional fluid flow and avoid negative pressures downstream the pump, made of flexible silicone to facilitate the connection of the pump with the rest of the circuit [24]; a phantom of the region of interest, consisting in a flexible PVC cylindrical 10 cm tube with internal diameter of 25 mm; a three-elements afterload, simulating the impedance of the systemic circulation, composed by a
characteristic resistance, a compliance chamber and a peripheral resistance, already available in the μBS Lab [25]; and finally several-metres-long delivery and returning tubes, with 25 mm internal diameter, made out of flexible silicone rubber, material chosen both for its MRI-compatibility and in order not to have high pressures at the pump outlet. The tubes purpose was to carry the fluid from the pumping system to the test section and back.

![Figure I. Initial concept of the circuit](image)

The fluid utilized to carry out the experiments was water (density=1000 kg/m^3; viscosity=0.001 Pa·s). The imposed flow rate during the systolic phase follows the analytical expression by Swanson and Clark (Figure II) [23].

![Figure II. Swanson and Clark’s systolic waveform](image)

**Lumped parameter model**

The design phase was supported with the aid of a lumped parameter model, which was developed to assess the choice of the tube’s material and to study different configurations of the circuit for it to comply to the design specifications. The model was implemented on Simulink® (The MathWorks, Inc.). Its electrical equivalent is showed in Figure III.

![Figure III. Lumped parameter model of the circuit](image)

**Verification of the model**

The initial configuration of the set-up, with two lengths of the delivery tube (configuration A, length = 11 metres; configuration B, length = 4 metres), was used to verify the ability of the model to predict flow and pressure waveforms. The verification was qualitative, by looking at the pressure and flow curves, and quantitative by the evaluation of the determination coefficient ($R^2$) between the measured pressures and flows and the data from the simulations.
**Final configuration of the circuit**

Since the initial concept of the circuit did not comply with design specification of providing physiological flow and pressure conditions in the test section, the model was used to preliminary simulate a variety of circuit configurations in order to get physiological flow rates and pressure in the test section. The simulations demonstrated that the best configurations were three:

**Configuration C:** this layout involves an additional valve in the test section, placed at the site where the aortic valve is expected to be, i.e. upstream the aorta phantom;

**Configuration D:** a resistance element is applied at the distal part of the delivery tube;

**Configuration E:** both the additional aortic valve and the resistance.

The aortic valve was a flexible silicone valve, deriving from a previous thesis work carried out in the lab. The final configuration of the circuit is shown in Figure IV.

**Testing protocol**

The tests were carried out in pulsatile flow regime, with changing heart rate between 40, 60 and 80 bpm, and stroke volume between 30, 50 and 70 mL, to simulate the hemodynamic conditions of different subjects. The measurements accesses are shown in Table I and Figure III.

<table>
<thead>
<tr>
<th>Signal</th>
<th>One valve</th>
<th>Two valves</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery tube pressure</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Upstream pressure</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Aortic pressure</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Pump output</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Aortic flow rate</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

*Table 1. Signal measured in the different configurations.*

![Figure IV. Final configuration of the circuit. Accesses for flow and pressure measurements.](image)
RESULTS

Model verification

In Table II and III the results for configurations A and B are shown, respectively. Model accuracy is evaluated through the vicinity of the $R^2$ coefficient to 1. Both the tables refer to the 70 mL SV case. The other SVs cases showed no relevant differences. The $R^2$ were evaluated after the manual superimposing of the curves, eliminating the offset in both the pressure/flow axis and time axis.

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>Aortic pressure</th>
<th>Aortic flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.9977</td>
<td>0.9292</td>
</tr>
<tr>
<td>60</td>
<td>0.9955</td>
<td>0.9547</td>
</tr>
<tr>
<td>80</td>
<td>0.7779</td>
<td>0.9259</td>
</tr>
</tbody>
</table>

*Table II. $R^2$ for $SV=70$ mL, configuration A*

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>Aortic pressure</th>
<th>Aortic flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.8512</td>
<td>0.9292</td>
</tr>
<tr>
<td>60</td>
<td>0.9127</td>
<td>0.7823</td>
</tr>
<tr>
<td>80</td>
<td>0.7015</td>
<td>0.6605</td>
</tr>
</tbody>
</table>

*Table III. $R^2$ for $SV=70$ mL, configuration B*

In general, the model fitted the data well in terms of predicting the dynamic behaviour of pressure and flow rate for both configurations in 40 bpm and 60 bpm HR cases, except for an over-/underestimation of parameters such as average or peak pressure or flow rates, or phase shift. This is likely due to the simplifications done in the model with respect to non-linear elements. At 80 bpm in configuration A the model fails to describe the aortic pressure curve in terms of average pressure, while the flow rate is phase-shifted in time. In configuration B, the aortic flow is always phase-shifted in time, likely due to an underestimation of the delivery tube’s inertance. In Figure V an example of the predicted flow and pressure waveforms is shown.

![Aortic pressure and aortic flow rate from the simulations and experimental tests in configuration A, for $SV=70$ mL and HR=80 bpm.](image)

Choice of the best configuration
The three configurations C, D and E were simulated and then tested.

**Influence of additional valve (Configuration C):** An example of the obtained result for SV=70 mL and HR=60 bpm is shown in Figure VI. The waveform of the aortic flow rate is coherent with the one imposed by the pump. The backflow that was observed in configuration A is totally avoided by the valve’s presence. In the diastole phase some oscillations are present, both in the flow rate and pressure. The aortic pressure waveform is almost physiological, if compared with the Vismara’s results [7], except for the presence of a marked dicrotic notch, that is likely due to the valve’s non-ideal closure behaviour, and the systolic-diastolic pressure difference, which is 20 mmHg instead of the physiological 40 mmHg. The average pressure is 100 mmHg, which is physiologically accurate.

**Influence of additional resistance (Configuration D):** The aortic flow presents a physiological waveform only in 60 bpm case. The flow in 40 bpm presents a backflow reaching -2 L/min, as expected from the simulations. In the 80 bpm HR case, the flow presents a backflow in the early-diastole phase and a peak in the end-diastole phase. The aortic pressure presents an almost physiological
Waveform, with a systolic-diastolic pressure difference of 15 mmHg, in 70 mL SV and 60 bpm HR case, and lower in the 40 bpm HR case. The results for 60 bpm HR, 70 mL SV case are shown in Figure VII.

**Influence of additional valve and resistance (Configuration E):** In the 70 ML, 40 bpm case the flow waveform is not physiological, presenting a backflow during diastole (Figure VIII). Since the pressure upstream the valve is higher than the aortic pressure, the valve does not close during diastole. In the 80 and 60 bpm HR cases, the flow waveform is almost-physiological, as well as the aortic pressure, which displays no oscillations in the diastole phase.

In Table IV the results for the peak pressure in the 70 mL SV case are shown, for three configurations.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>HR=40 bpm</th>
<th>HR=60 bpm</th>
<th>HR=80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>173</td>
<td>236</td>
<td>338</td>
</tr>
<tr>
<td>D</td>
<td>196</td>
<td>265</td>
<td>386</td>
</tr>
<tr>
<td>E</td>
<td>206</td>
<td>250</td>
<td>377</td>
</tr>
</tbody>
</table>

*Table IV. Peak delivery tube pressures for 70 mL SV and different HRs.*

The adding of a resistance in the delivery tube increases the pressure of about 50 mmHg with respect to the configuration without the resistance. A too high pressure in the pump outlet could lead to failure of the connection between the components.

**Hemodynamic evaluation for configuration C**

**Flow rates:** In Table V all flow-related parameters are shown, for 70 mL, 50 mL and 30 mL SV.

In general, the higher the SV, the higher the backflow; while the opposite is true for the HR. That is because the higher the heart rate, the quicker is the diastolic phase. The systolic time didn’t change significantly for different SV and the same
HR, while decreases for higher HR, which is physiologically accurate. The average flow rate is the comparable to the pump output one. The systolic peak of the aortic flow was higher than the pump output peak for HR=40 bpm and lower for HR=60 bpm, 80 bpm. That is due to how the waveform is transported inside the delivery tube. The comparison between the systolic peaks is shown in Figure IX. The SV of the pump output and of the aortic flow rate were evaluated to compute the accumulation of fluid in the delivery tube during the experiments. The stroke volumes are not equal; however, they differ by a few millilitres. This difference could be due to measurement errors, and overall is acceptable.

![systolic peak](image)

Figure IX. Comparison between the systolic peak of the aortic flow rate and of the pump output.

<table>
<thead>
<tr>
<th>SV=70 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV-PO</td>
<td>61.27</td>
<td>65.94</td>
<td>65.96</td>
</tr>
<tr>
<td>SV-AFR</td>
<td>65.18</td>
<td>63.60</td>
<td>65.18</td>
</tr>
<tr>
<td>BF</td>
<td>-5.21</td>
<td>-6.15</td>
<td>-4.79</td>
</tr>
<tr>
<td>Qao,mean</td>
<td>4.03</td>
<td>6.32</td>
<td>8.69</td>
</tr>
<tr>
<td>Qao,peak</td>
<td>15.14</td>
<td>17.48</td>
<td>23.93</td>
</tr>
<tr>
<td>Ts</td>
<td>0.55</td>
<td>0.41</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=50 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV-PO</td>
<td>45.54</td>
<td>45.37</td>
<td>46.00</td>
</tr>
<tr>
<td>SV-AFR</td>
<td>44.62</td>
<td>48.41</td>
<td>47.34</td>
</tr>
<tr>
<td>BF</td>
<td>-4.78</td>
<td>-2.23</td>
<td>-3.18</td>
</tr>
<tr>
<td>Qao,mean</td>
<td>3.06</td>
<td>4.85</td>
<td>6.31</td>
</tr>
<tr>
<td>Qao,peak</td>
<td>10.55</td>
<td>12.79</td>
<td>17.29</td>
</tr>
<tr>
<td>Ts</td>
<td>0.53</td>
<td>0.40</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=30 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV-PO</td>
<td>25.83</td>
<td>26.73</td>
<td>26.88</td>
</tr>
<tr>
<td>SV-AFR</td>
<td>26.87</td>
<td>28.65</td>
<td>29.20</td>
</tr>
<tr>
<td>BF</td>
<td>-2.97</td>
<td>-2.11</td>
<td>-1.65</td>
</tr>
<tr>
<td>Qao,mean</td>
<td>1.79</td>
<td>2.87</td>
<td>3.89</td>
</tr>
<tr>
<td>Qao,peak</td>
<td>6.64</td>
<td>7.81</td>
<td>10.64</td>
</tr>
<tr>
<td>Ts</td>
<td>0.51</td>
<td>0.41</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Table V: Flow-related parameters for Configuration C. SV-PO: Stroke volume of pump output (mL). SV-AFR: stroke volume of aortic flow rate (mL). BF: backflow of the aortic valve (mL). Qao,mean: aortic flow average (L/min); Ts: systolic time (s).

**Pressure:** All pressure-related parameters are shown in Table VI.
<table>
<thead>
<tr>
<th>SV=70 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ppeak</td>
<td>173</td>
<td>235.67</td>
<td>338</td>
</tr>
<tr>
<td>Pao, mean</td>
<td>79.6</td>
<td>103</td>
<td>132</td>
</tr>
<tr>
<td>S-DPD</td>
<td>17.9</td>
<td>19.6</td>
<td>27.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=50 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ppeak</td>
<td>143</td>
<td>172</td>
<td>260</td>
</tr>
<tr>
<td>Pao, mean</td>
<td>72.2</td>
<td>82.8</td>
<td>97.2</td>
</tr>
<tr>
<td>S-DPD</td>
<td>13.2</td>
<td>13.7</td>
<td>19.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=30 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ppeak</td>
<td>102</td>
<td>146</td>
<td>195</td>
</tr>
<tr>
<td>Pao, mean</td>
<td>49.5</td>
<td>45.1</td>
<td>64.2</td>
</tr>
<tr>
<td>S-DPD</td>
<td>6.62</td>
<td>9.07</td>
<td>12.0</td>
</tr>
</tbody>
</table>

Table VI. Pressure related parameters for configuration C. Ppeak: peak delivery tube pressure (mmHg); Pao,mean: average aortic pressure (mmHg); S-DPD: systolic-diastolic pressure difference (mmHg).

The higher the HR/SV, the higher the average aortic pressure and the systolic-diastolic pressure difference, which, however, never reaches the physiological 40 mmHg. The average pressure for 70 mL SV, 60 bpm HR is physiological (102 mmHg).

The peak pressure in the delivery tube is relatively high. The higher value is measured with 70 mL stroke volume and 80 bpm heart rate. For that reason, having a stroke volume higher than 70 mL and a heart rate higher than 80 bpm may lead to failure of the connections at the pump outlet.

**CONCLUSIONS**

The aim of this work was to design an MRI-compatible mock loop for aortic-valve applications, with easily available and replaceable materials, and easy to assemble and disassemble, and managed during the experiments.

The behaviour of the initial concept of the circuit did not comply with the design specification of providing physiological flow rates and pressures in the test section. Hence, different elements were added to the mock loop for it to comply to the design specifications. The inclusion of these elements was simulated with the aid of the lumped parameter model.

Overall, the model seemed to provide good results in terms of predicting the dynamic behaviours of pressure and flow rates. It did not predict with high accuracy parameters such as peak or average flow and pressure, which were often under- or overestimated. This is likely due to the simplifications used in the lumped parameters model. Nonetheless, the model was detailed enough to be use as a preliminary design-oriented tool, in the awareness that any model-aided
prediction should be verified via experimental tests.

With the addition of a second valve, the backflow that affected the flow wave shape in the initial configuration was avoided, and the flow rate in the test section could be considered physiological. At rest hemodynamic conditions (represented by 70 mL stroke volume and 60 bpm heart rate), the aortic pressure presented an almost physiological curve with mean value of 100 mmHg and systolic-diastolic difference of 20 mmHg, which can be considered physiological.

The presence of an additional resistance allowed the dampening of unwanted oscillations and less distortion of the waveforms. However, the flow rate was considered to have a physiological waveform only for 60 bpm heart rate. Moreover, the pressures at the outlet of the pump resulted up to almost 400 mmHg, 50 mmHg higher than the configuration with just the additional valve. The addition of the second valve in aortic position to this configuration provided some advantages regarding the backflow, but for some heart rates the valve did not close properly during diastole.

The results from configuration D and E suggest that probably an adjustable resistance to be regulated at different imposed heart rate would be needed, in addition to the second valve, for the circuit to work at its best with every heart rate. However, the mock loop is intended to be used in MRI rooms, which require versatile and easily manageable set-ups; therefore, having a resistance to be adjusted every time the pumping conditions are changed does not comply with this design specification. Moreover, the system was thought for the testing of aortic valve applications, so, as shown from Configuration E, a resistance upstream the valve could corrupt the correct behaviour of a prosthetic valve.

In conclusion, the configuration C layout complies with the design specifications, as it displays physiological waveforms in the aorta phantom position, the components are easily available and replaceable, and the circuit can be easily assembled, disassembled, and managed during the acquisitions.
INTRODUZIONE

Le malattie cardiovascolari sono un gruppo di disturbi del cuore, delle valvole cardiache e dei vasi sanguigni e sono la principale causa di morte a livello globale (fonte: OMS). I trattamenti comprendono la riparazione o la sostituzione di una parte non funzionale mediante dispositivi cardiovascolari. Le prestazioni dei dispositivi cardiovascolari devono essere valutate durante una fase di test preclinico [5] e devono essere testate in condizioni fisiologiche, che includono l’esposizione a un flusso pulsatile. Questo è fatto usando simulatori idraulici, che sono circuiti idraulici che imitano la circolazione cardiovascolare in condizioni diverse. I simulatori idraulici forniscono parametri fluidodinamici grossolani per quanto riguarda le portate e le pressioni [6]; tuttavia, non forniscono informazioni sul campo di velocità del fluido nel dispositivo.

Altre tecniche come l’ecocardiografia [14] e la MRI a contrasto forniscono informazioni sul campo di velocità del fluido in un piano bi-dimensionale selezionato [12],[13]. La fluidodinamica computazionale è il gold standard per le informazioni sul campo di velocità e il suo sviluppo nel tempo in un volume tridimensionale, tuttavia i risultati sono relativi ai calcoli fluidodinamici e dipendono dalla scelta appropriata del modello utilizzato.

MRI 4D-flow è una tecnica relativamente nuova che può fornire il campo di velocità nel volume tridimensionale interessato e la sua evoluzione nel tempo, ed è relativo a un dispositivo reale [12],[15],[16]. Il 4D-flow si basa sull’uso di uno scanner MRI. La principale sfida con le misure di risonanza magnetica è la collocazione di strumentazione e sistemi di pompaggio, che sono generalmente realizzati da materiali ferromagnetici. Lo scanner MRI genera un campo elettromagnetico non compatibile con i materiali metallici. Dopo un’analisi della letteratura, i simulatori idraulici esistenti forniscono flussi fisiologici e forme d’onda di pressione, ma con alcune limitazioni, tra cui l’uso di dispositivi azionati
pneumaticamente [18], o sistemi di pompaggio che non sono facilmente disponibili o sostituibili, come pompe compatibili con risonanza magnetica [19], [21], o la trasmissione del movimento rigido lungo grandi distanze che comporta vincoli meccanici [20]. Inoltre, le soluzioni si basano sulla possibilità di collocare la strumentazione e i generatori all'interno della sala di risonanza, oltre una linea di sicurezza: ciò non è fattibile in ospedali non a scopo di ricerca.

Lo scopo di questo lavoro è stato quello di progettare un simulatore idraulico pulsatile compatibile con risonanza magnetica per il test dei dispositivi cardiovascolari. La strumentazione e il sistema di pompaggio sono stati pensati come destinati a essere collocati nella sala di controllo, mentre la sezione di test doveva essere collocata nello scanner MRI, in modo che il simulatore idraulico potesse essere sfruttato anche in ospedali non orientati alla ricerca (vedi Figura I). L'attenzione è stata posta su una valvola aortica.

La fase di progettazione è stata coadiuvata mediante un approccio di modellazione a parametri concentrati.

Le specifiche di progetto comprendono la capacità di riprodurre condizioni fisiologiche e di flusso pulsatile nella sezione del test indipendentemente dalla frequenza cardiaca e dal volume della corsa imposti; la facilità delle fasi di trasporto, montaggio e smontaggio; la disponibilità e la sostituibilità dei componenti; la facilità della gestione del simulatore idraulico durante le acquisizioni MRI.

**MATERIALI E METODI**

**Configurazione iniziale del circuito**

La configurazione iniziale del circuito (Figura I) era composta da: una pompa centrifuga sommergibile per consentire il riempimento iniziale e il degorgogliamento del circuito; una pompa a pistone volumetrica pulsatile, controllata da un driver esterno, in grado di fornire una specifica forma d'onda del flusso; valvole di servizio, poste immediatamente dopo e prima della pompa volumetrica, per ottenere un flusso unidirezionale del fluido ed evitare pressioni negative a valle della pompa, realizzate in silicone flessibile per facilitare il collegamento della pompa con il resto del circuito [24]; un fantoccio della regione di interesse, costituito da un tubo cilindrico flessibile in PVC da 10 cm con diametro interno di 25 mm; un postcarico a tre elementi, che simulà l'impedenza della circolazione...
sistemica, composta da una resistenza caratteristica, una camera di compliance e una resistenza periferica, già disponibile nel laboratorio μBS [25]; e infine lunghi tubi di ritorno e di mandata, con diametro interno di 25 mm, realizzati in silicone flessibile, materiale scelto sia per la compatibilità MRI che per non avere alte pressioni all'uscita della pompa.

Il fluido utilizzato per effettuare gli esperimenti è stato l’acqua (densità = 1000 kg / m^3; viscosità = 0,001 Pa * s). La portata imposta durante la fase sistolica segue l'espressione analitica di Swanson e Clark [23] (Figura II).

Modello a parametri concentrati

La fase di progettazione è stata supportata con l'ausilio di un modello a parametri concentrati, che è stato sviluppato per valutare la scelta del materiale del tubo e per studiare diverse configurazioni del circuito affinché questo fosse conforme alle specifiche di progetto. Il modello è stato implementato su Simulink® (The MathWorks, Inc.). Il suo equivalente elettrico è mostrato in Figura III.

Verifica del modello

La configurazione iniziale del set-up, con due lunghezze del tubo di erogazione (configurazione A, lunghezza = 11 metri, configurazione B, lunghezza = 4 metri), è stata utilizzata per verificare la capacità del modello di prevedere le forme d'onda di flusso e pressione. La verifica è stata qualitativa, osservando le curve di pressione e di flusso e quantitativa mediante la valutazione del coefficiente di...
determinazione ($R^2$) tra le pressioni e i flussi misurati e i dati delle simulazioni.

**Configurazione finale del circuito**

Poiché il concetto iniziale del circuito non era conforme alle specifiche di progetto relative alle condizioni fisiologiche di flusso e pressione nella sezione di test, il modello è stato utilizzato per simulare preliminarmente una varietà di configurazioni circuitali al fine di ottenere portate fisiologiche e pressione nella sezione di test. Le simulazioni hanno dimostrato che le migliori configurazioni erano tre:

**Configurazione C**: aggiunta di una valvola aggiuntiva nella sezione di test, a monte del fantoccio dell'aorta.

**Configurazione D**: aggiunta di una resistenza nella parte distale del tubo di mandata; **Configurazione E**: aggiunta della valvola aortica e della resistenza.

**Protocollo di prova**

I test sono stati effettuati in regime di flusso pulsatile, con frequenza cardiaca (HR) variabile tra 40, 60 e 80 bpm, e volume di eiezione (SV) tra 30, 50 e 70 bpm, per simulare diverse condizioni del paziente. Gli accessi per le misure sono mostrati nella Tabella I e nella Figura III.

<table>
<thead>
<tr>
<th>Segnale</th>
<th>1 V</th>
<th>2 V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressione tubo di mandata</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Pressione a monte</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Pressione aortica</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Uscita della pompa</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Portata aortica</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

Tabella I. Segnali misurati nelle differenti configurazioni (1 V= una valvola; 2 V= due valvole).
RISULTATI

Verifica del modello

Nella Tabella II sono mostrati i risultati per R² valutati per la configurazione A. Nella Tabella III sono mostrati i risultati per R² valutati per la configurazione B. Le tabelle si riferiscono al caso SV = 70 mL. Gli altri casi di SV non hanno mostrato differenze significative. L'R² è stato valutato dopo la sovrapposizione manuale delle curve, eliminando l'offset sia nell'asse di pressione / flusso che nell'asse del tempo.

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>Pressione aortica</th>
<th>Portata aortica</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.9977</td>
<td>0.9292</td>
</tr>
<tr>
<td>60</td>
<td>0.9955</td>
<td>0.9547</td>
</tr>
<tr>
<td>80</td>
<td>0.7779</td>
<td>0.9259</td>
</tr>
</tbody>
</table>

*Tabella II. R² per SV=70 mL, configurazione A*

<table>
<thead>
<tr>
<th>HR (bpm)</th>
<th>Pressione aortica</th>
<th>Portata aortica</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.8512</td>
<td>0.9292</td>
</tr>
<tr>
<td>60</td>
<td>0.9127</td>
<td>0.7823</td>
</tr>
<tr>
<td>80</td>
<td>0.7015</td>
<td>0.6605</td>
</tr>
</tbody>
</table>

*Tabella III. R² for SV=70 mL, configurazione B*

In generale, il modello ha predetto bene i comportamenti sperimentali in termini di previsione del comportamento dinamico della pressione e della portata per entrambe le configurazioni nei casi di HR 40 bpm e 60 bpm, fatta eccezione per una sovrastima / sottostima di parametri quali la pressione media o di picco di portate e pressioni, o lo sfasamento. Questo è probabilmente dovuto alle semplificazioni fatte nel modello rispetto agli elementi non lineari. A 80 bpm nella configurazione A il modello non riesce a descrivere la curva di pressione aortica in termini di pressione media, mentre la portata è sfasata nel tempo. Nella configurazione B, il flusso aortico è sempre sfasato nel tempo, probabilmente a causa di una sottostima dell'inserzione del tubo di mandata.

Figura V. Pressione e portata aortiche a confronto
Scelta della migliore configurazione

Le tre configurazioni C, D ed E sono state simulate e quindi testate.

Influenza della valvola addizionale (configurazione C): Un esempio del risultato ottenuto per SV = 70 mL e HR = 60 bpm è mostrato nella figura VI. La forma d'onda della portata aortica è coerente con quella imposta dalla pompa. Il retroflusso osservato nella configurazione A è totalmente evitato dalla presenza della valvola. Nella fase diastolica sono presenti alcune oscillazioni, sia nella portata che nella pressione. La forma d'onda della pressione aortica è quasi-fisiologico, se confrontato con i risultati di Vismara [7], ecetto per la presenza di un’onda dicotoma marcata, che è probabilmente dovuto al comportamento di chiusura non ideale della valvola, e la differenza di pressione sistolico-diastolica di 20 mmHg invece del fisiologico 40 mmHg. La pressione media è di 100 mmHg, che è fisiologicamente accurata.

Influenza della resistenza addizionale (configurazione D): il flusso aortico presenta una forma d'onda fisiologica solo nel caso di 60 bpm. Il flusso a 40 bpm presenta un retroflusso che raggiunge -2 L / min, come previsto dalle simulazioni.

Nel caso HR 80 bpm, il flusso presenta un retroflusso nella fase della diastole iniziale e un picco nella fase della diastole terminale. La pressione aortica presenta una forma d'onda quasi fisiologica, con una differenza di pressione sistolico-diastolica di 15 mmHg, in 70 ml di SV e un caso di 60 bpm di HR e inferiore nel caso di 40 bpm di HR. I risultati per 60 bpm HR, 70 mL SV sono mostrati in Figura VII.

Influenza della valvola addizionale e della resistenza (configurazione E): Nel caso di 70 mL, 40 bpm, la forma d'onda del flusso non è fisiologica, presentando un retroflusso durante la diastole.

Figura VI. Configurazione C, SV=70 mL e HR=60 bpm.
Poiché la pressione a monte della valvola è superiore alla pressione aortica, la valvola non si chiude durante la sistole. Nei casi HR 80 e 60 bpm, la forma d'onda del flusso è quasi fisiologica, così come la pressione aortica, che non mostra oscillazioni nella fase diastolica (Figura VIII).

Nella Tabella IV sono mostrati i risultati per la pressione di picco nel caso SV da 70 mL, per tre configurazioni. L'aggiunta di una resistenza nel tubo di mandata aumenta la pressione di circa 50 mm Hg rispetto alla configurazione senza la resistenza. Una pressione troppo alta all'uscita della pompa potrebbe portare al guasto della connessione tra i componenti.

Figura VII. Configurazione D, SV=70 mL e HR=60 bpm.

Figura VIII. Configurazione E, SV=70 mL e HR=40 bpm.

<table>
<thead>
<tr>
<th>Configurazione</th>
<th>HR=40 bpm</th>
<th>HR=60 bpm</th>
<th>HR=80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>173</td>
<td>236</td>
<td>338</td>
</tr>
<tr>
<td>D</td>
<td>196</td>
<td>265</td>
<td>386</td>
</tr>
<tr>
<td>E</td>
<td>206</td>
<td>250</td>
<td>377</td>
</tr>
</tbody>
</table>

Tabella IV. Massima pressione nel tubo di mandata.

Valutazione emodinamica per la configurazione C

Portate: nella tabella V sono riportati tutti i parametri relativi al flusso, per 70 ml, 50 ml e 30 ml SV.

In generale, maggiore è lo SV, maggiore è il retroflusso; mentre è vero il contrario
per l’HR. Questo perché più alta è la frequenza cardiaca, più veloce è la fase diastolica.

Il tempo sistolico non varia per SV diversi, mentre diminuisce per HR più alti, il che è fisiologicamente accurato.

La portata media è quella fisiologica.

Il picco sistolico del flusso aortico era superiore a quello della pompa per HR = 40 bpm e inferiore per HR = 60 bpm, 80 bpm. Ciò è dovuto al fatto che la forma d'onda è stata trasmessa all'interno del tubo di erogazione. Il confronto tra i picchi sistolici è mostrato nella Figura IX.

Gli SV dell'uscita della pompa e della portata aortica sono stati valutati per calcolare l'accumulo di fluido nel tubo di erogazione durante gli esperimenti. Gli SV non sono uguali; tuttavia, differiscono di alcuni millilitri. Questa differenza potrebbe essere dovuta a errori di misurazione e nel complesso è accettabile.

<table>
<thead>
<tr>
<th>SV=70 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV-PO</td>
<td>61.27</td>
<td>65.94</td>
<td>65.96</td>
</tr>
<tr>
<td>SV-AFR</td>
<td>65.18</td>
<td>63.60</td>
<td>65.18</td>
</tr>
<tr>
<td>BF</td>
<td>-5.21</td>
<td>-6.15</td>
<td>-4.79</td>
</tr>
<tr>
<td>Qao,mean</td>
<td>4.03</td>
<td>6.32</td>
<td>8.69</td>
</tr>
<tr>
<td>Qao,peak</td>
<td>15.14</td>
<td>17.48</td>
<td>23.93</td>
</tr>
<tr>
<td>Ts</td>
<td>0.55</td>
<td>0.41</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=50 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV-PO</td>
<td>45.54</td>
<td>45.37</td>
<td>46.00</td>
</tr>
<tr>
<td>SV-AFR</td>
<td>44.62</td>
<td>48.41</td>
<td>47.34</td>
</tr>
<tr>
<td>BF</td>
<td>-4.78</td>
<td>-2.23</td>
<td>-3.18</td>
</tr>
<tr>
<td>Qao,mean</td>
<td>3.06</td>
<td>4.85</td>
<td>6.31</td>
</tr>
<tr>
<td>Qao,peak</td>
<td>10.55</td>
<td>12.79</td>
<td>17.29</td>
</tr>
<tr>
<td>Ts</td>
<td>0.53</td>
<td>0.40</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=30 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV-PO</td>
<td>25.83</td>
<td>26.73</td>
<td>26.88</td>
</tr>
<tr>
<td>SV-AFR</td>
<td>26.87</td>
<td>28.65</td>
<td>29.20</td>
</tr>
<tr>
<td>BF</td>
<td>-2.97</td>
<td>-2.11</td>
<td>-1.65</td>
</tr>
<tr>
<td>Qao,mean</td>
<td>1.79</td>
<td>2.87</td>
<td>3.89</td>
</tr>
<tr>
<td>Qao,peak</td>
<td>6.64</td>
<td>7.81</td>
<td>10.64</td>
</tr>
<tr>
<td>Ts</td>
<td>0.51</td>
<td>0.41</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Tabella V: Parametri relative alle portate nella configurazione C. SV-PO: Volume di eiezione dell’uscita della pompa (mL). SV-AFR: volume di eiezione della portata aortica (mL). BF: retroflusso della valvola aortica (mL); Qao_mean: media del flusso aortico(L/min); Ts: tempo di sistole (s).
**Pressioni:** tutti i parametri relativi alla pressione sono riportati nella Tabella VI. Maggiore è l'HR / SV, maggiore è la pressione aortica media e la differenza di pressione sistolica-diastolica, che tuttavia non raggiunge mai i 40 mmHg fisiologici. La pressione media per 70 mL SV, 60 bpm HR è fisiologica (102 mmHg).

<table>
<thead>
<tr>
<th>SV=70 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ppeak</td>
<td>173.17</td>
<td>235.67</td>
<td>337.8</td>
</tr>
<tr>
<td>Pao, mean</td>
<td>79.64</td>
<td>102.60</td>
<td>131.66</td>
</tr>
<tr>
<td>S-DPD</td>
<td>17.88</td>
<td>19.60</td>
<td>27.93</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=50 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ppeak</td>
<td>142.68</td>
<td>171.65</td>
<td>260.06</td>
</tr>
<tr>
<td>Pao, mean</td>
<td>72.18</td>
<td>82.75</td>
<td>97.18</td>
</tr>
<tr>
<td>S-DPD</td>
<td>13.2</td>
<td>13.7</td>
<td>19.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SV=30 mL</th>
<th>40 bpm</th>
<th>60 bpm</th>
<th>80 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ppeak</td>
<td>101.52</td>
<td>145.73</td>
<td>194.5</td>
</tr>
<tr>
<td>Pao, mean</td>
<td>49.48</td>
<td>45.12</td>
<td>64.23</td>
</tr>
<tr>
<td>S-DPD</td>
<td>6.62</td>
<td>9.07</td>
<td>12.00</td>
</tr>
</tbody>
</table>

Tabella VI. Parametri relative alla pressione per la configurazione C, SV=70 mL. Ppeak: massima pressione del tubo di mandata (mmHg); Pao, mean: pressione aortica media (mmHg); S-DPD: differenza di pressione sistolico-diastolica (mmHg).

La pressione di picco nel tubo di erogazione è elevata. Il valore più alto viene misurato con il volume della corsa di 70 ml e la frequenza cardiaca di 80 bpm.

Per questo motivo, avere un volume di eiezione superiore a 70 ml e una frequenza cardiaca superiore a 80 bpm può portare al fallimento delle connessioni all'uscita della pompa.

**CONCLUSIONI**

Lo scopo di questo lavoro era di progettare un simulatore idraulico compatibile con la risonanza magnetica per applicazioni con valvola aortica, con materiali facilmente sostituibili e facilmente reperibili, e facile da assemblare e smontare, e da gestire durante l’utilizzo.

Il comportamento del layout iniziale del circuito non era conforme alla specifica di progetto di fornire portate e pressioni fisiologiche nella sezione di prova. Quindi, diversi elementi sono stati aggiunti al circuito per soddisfare le specifiche di progettazione. L'inclusione di questi elementi è stata simulata con l'aiuto di un modello a parametri concentrati.

Nel complesso, il modello sembra fornire buoni risultati in termini di previsione dei comportamenti dinamici della pressione e delle portate. Non ha predetto parametri quali il picco o il flusso e la pressione medi, che sono stati spesso sottostimati o sovrastimati. Ciò è probabilmente dovuto alle semplificazioni utilizzate nel modello.
dei parametri concentrati. Tuttavia, il modello è stato considerato sufficientemente dettagliato per prevedere diverse configurazioni di circuito, tenendo conto che una valutazione sperimentale deve essere sempre eseguita.

Con l'aggiunta di una seconda valvola, il retroflusso precedentemente visto nella configurazione iniziale del circuito per le diverse frequenze cardiache è stato totalmente evitato dalla presenza della valvola e la portata nella sezione di test poteva essere considerata fisiologica. A 70 mL SV e 60 bpm HR, la pressione aortica presentava una curva quasi fisiologica con un valore medio di 100 mmHg e una differenza sistolica-diastolica di 20 mmHg, che può essere considerata fisiologica.

La presenza di una resistenza aggiuntiva ha permesso lo smorzamento delle oscillazioni e la minore distorsione delle forme d'onda. Tuttavia, si è ritenuto che il flusso avesse una forma d'onda fisiologica solo per la frequenza cardiaca di 60 bpm. Inoltre, le pressioni all'uscita della pompa hanno raggiunto 400 mmHg, 50 mmHg in più rispetto alla configurazione con solo la valvola aggiuntiva. L'aggiunta della seconda valvola in posizione aortica a questa configurazione ha fornito alcuni vantaggi per quanto riguarda il retroflusso, ma per alcune frequenze cardiache la valvola non si è chiusa correttamente durante la diastole.

I risultati della configurazione D ed E suggeriscono che probabilmente sarebbe necessaria una resistenza regolabile rispetto alla frequenza cardiaca imposta, oltre alla seconda valvola, affinché il circuito funzioni al meglio con ogni frequenza cardiaca. Il simulatore idraulico è destinato ad essere utilizzato in stanze MRI, che richiedono configurazioni versatili e facilmente gestibili; pertanto, avere una resistenza regolabile, da regolare ogni volta che vengono modificate le condizioni di utilizzo non è conforme a questa specifica di progetto. Inoltre, il sistema è stato pensato per applicazioni della valvola aortica, quindi, come mostrato dalla Configurazione E, una resistenza a monte della valvola potrebbe corrompere il corretto comportamento di una valvola protesica.

In conclusione, il layout di configurazione C è conforme alle specifiche di progetto, poiché mostra le forme d'onda fisiologiche nella posizione del fantoccio dell’aorta, i componenti sono facilmente disponibili e sostituibili e il circuito può essere facilmente assemblato, smontato e gestito durante gli esperimenti.
INTRODUCTION

Cardiovascular diseases (CVDs) are a group of disorders of the heart, of the heart valves and of the blood vessels. Cardiovascular diseases are the number one cause of death globally. An estimated 17.9 million people died from cardiovascular diseases in 2016, representing 31% of all global deaths. Of these deaths, 85% are due to heart attack and stroke. (source: World Health Organization).

The treatments of cardiovascular diseases include open-heart surgery and transcatheter surgery. Open-heart surgery requires the opening of the chest of the patient and the stopping of the beating heart, and the connection to an extra-corpooreal circulation circuit. This technique carries some serious issues both during the surgery and in the post-operative period. Lately, most treatments use the transcatheter technique, which allow to fix or replace a non-functional part without stopping the heart from beating and without opening the chest, allowing the access of the cardiac structures through a blood vessel.

A cardiovascular device to be implanted or a surgical technique’s performance must be assessed in the testing phase. Specifically, a device should display a proper functionality with respect to the application in which it is used (patient’s age, gender, everyday activity, …). This preclinical assessment is generally done by using mock circulation loops that are able to mimic the cardiovascular circulation in different conditions.

The mock circulation loops provide good control and measurements of macroscopic fluid dynamic parameters regarding flow rates and pressures. However, the velocity profile inside the device and other parameters such as wall shear stresses could be useful to properly evaluate the device performance, and how its presence affects the hemodynamics in terms of recirculation and vortexes.

Today, echocardiography and PC-MRI are used in order to evaluate some parameters such as wall shear stresses and to visualize the velocity field on a selected plane, but not in a three-dimensional volume. The golden standard in visualizing the velocity profile inside a three-dimensional volume is Computational Fluid Dynamics (CFD), a technique consisting in
simulating the diseases and the effect of the treatment. The main disadvantage of CFD is that it is not a representation of the real-world measurements, but the result of fluid dynamics calculations, which are carried out on the ground of certain modelling assumptions. For example, CFD calculations at high flows require specific turbulence models which are not always easy to implement and verify.

MRI 4D-flow is a technology that allows the visualization of the in vitro flow streamlines in a three-dimensional volume of interest, bridging the gap between CFD and the other in vitro technologies: the 4D flow measurements are capable of showing the velocity field in the three-dimensional space and its evolution in time, with a lower spatial and temporal resolution with respect to CFD, but regarding a real device.

Since cardiovascular devices performance must be assessed under physiological conditions, they are generally subjected to pulsatile flow rate. To bring pulsatile flow rate inside an MRI scanner is a challenge, because MRI technology uses an electro-magnetic field which interact with ferromagnetic materials. Since the instrumentations and actuators are generally made of metallic materials, these must be placed at a safety distance with respect to the scanner. The existing mock loops intended to be placed in the MRI scanner face some limitations due to this reason, mainly regarding the waveform control and the use of not easily available and replaceable components. Moreover, the solutions often rely on the possibility of placing the instrumentation inside the MRI scanner room, behind a safety line, which is not feasible in non-research-oriented hospitals.

The aim of this work is to design a mock circulation loop which should be able to provide physiological flow and pressure waveforms in the test section, to be placed upon the MRI scanner table. The mock loop will comprise a pulsatile volumetric pump which generates physiological waveform, and silicone tubing carrying the fluid from outside the MRI scanner room to the test section. The mock loop is intended to be easy to assemble and to disassemble. Moreover, the mock loop should be easy to be managed during the experiments, to optimize the acquisition time inside the MRI-room. The focus was put upon an aortic heart valve, but with some adjustments the mock loop can be adopted to study variety of cardiovascular diseases and other cardiovascular devices.
The design was carried out through lumped parameter modelling approach. The lumped parameter model was developed starting by the circuit at its initial form, verified with respect to the layout, and then used to simulate different configurations for the circuit.

This script will be subdivided into five chapters:

- Chapter 1: Anatomy and physiology of the cardiovascular system;
- Chapter 2: State of the art and design specifications;
- Chapter 3: Materials and methods;
- Chapter 4: Results and discussion;
- Chapter 5: Conclusions and future developments.
1. ANATOMY AND PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

1.1 The cardiovascular system

The cardiovascular system is a closed hydraulic circuit that allow blood to circulate inside the body. It consists in three elements: the heart, the blood and the vessels. The heart is at the centre of the system, pumping the blood from its chambers to every cell of the body and then recollecting it once it returns. The blood travels through vessels of two types: the arteries, which carry the blood from the heart to the body, and the veins, which allow the blood to return to the heart. The arteries progressively reduce their diameter and grow in number through bifurcations while approaching the organs and tissues, becoming first arterioles and then capillaries. The gas exchange happens at capillaries level. The capillaries merge into venule and then merge again in veins and carry the blood back to the atria.

Figure 1.1 is a sketch of the path of blood inside the human body.

[Figure 1.1: Scheme of the blood circulation. RA= right atrium; RV= right ventricle; LA= left atrium; LV= left ventricle; T= tricuspid valve; P= pulmonary valve; AO= aortic valve; M= mitral valve.]
The venous blood, rich in carbon dioxide and waste products, travels from the extremities of the body through the venous vessels and it is collected in the right atrium, from which it passes into the right ventricle through the tricuspid valve. The right ventricle moves the venous blood through the pulmonary artery to the lungs for it to be oxygenated through the pulmonary circulation. The oxygenated blood is then recollected into the left atrium, and then into the left ventricle. The left ventricle moves the blood in order to give the body tissues and organs oxygen through the systemic circulation. The blood then returns to the right atrium through the superior and the inferior vena cava.

1.1.1 The heart

The heart is a hollow organ contained inside the thoracic cavity, above the diaphragm, a muscle which separates the thoracic cavity from the abdominal one. Its dimensions are about the one of a human fist and its weight ranges from 250 to 350 g. Inside of it there are four chambers, two atria and two ventricles, which collect and eject the blood, respectively. The two ventricles are separated by a wall called ventricular septum. Atria and ventricles are separated by valves. The cardiac muscle generates the necessary force to push the blood into the blood vessels, while the presence of the four valves ensures the right direction of the flow and prevents the retrograde flow. A scheme of the heart is shown in Figure 1.2.
1.1.2 Heart valves

The heart valves are structures that determine a pathway of blood flow through the heart by allowing the blood to flow unidirectionally. The valve are passive elements – meaning that they do not require an internal source of energy to work. Their open or closed state depends on the difference of pressure between upstream and downstream the leaflets.

The human heart has four valves: two atrioventricular valves (AV, mitral valve and tricuspid valve), that separate atria from ventricles; two semilunar valves (SL, aortic valve and pulmonary valve), that separate the ventricles from the arteries leaving the heart. All four valves lie in a plane called the valvular plane, as shown in Figure 1.3.

![Figure 1.3: Valvular plane. (a) Anterior; (b) Posterior; (c) Left; (d) Right; (e) Septal.]

1.1.2.1 Semilunar valves

The aortic valve separates the left ventricle from the ascending aorta. It consists of an aortic annulus attached to the ventricular wall, from which three thin, crescent-shaped leaflets originate facing toward the aorta. Downstream the leaflets there are three outpouchings of the aortic root, called the sinuses of Valsalva, from which the coronaries originate. The three cusps are called left coronary, right coronary and non-coronary cusp with respect to the
coronary vessel that originates in the corresponding sinus. The junction of the sinuses with the aorta is called the sino-tubular junction.

During the systole, the flow entering the aorta is not characterized by all-parallel fluid streamlines: there are vortexes in the three sinuses of Valsalva. It is believed that these vortexes help the valve to close quicker with respect to a straight cylinder situation, creating a pressure difference that pushes the leaflet towards the centre of the aorta [1].

The pulmonary valve, situated in the right ventricle, has a similar structure, except for the lack of coronaries. It connects the right ventricle to the pulmonary artery, which carries the blood to the lungs.

1.1.2.2 Atrioventricular valves

The two atrioventricular valves are both composed of four elements: the valve annulus, the leaflets, the papillary muscles and the chordae tendineae. The mitral valve’s annulus is attached to the atrial and ventricular walls and aortic root. From the annulus two thin membrane cusps of trapezoidal shape have origin. The leaflet’s margins are irregular because they are pulled by the chordae tendineae which originate from the papillary muscles on the ventricular walls [1]. The structure of the mitral valve is shown in Figure 1.4.

The tricuspid valve, situated in the right ventricle, is similar – it has three cusps instead of two.

![Mitral valve structure](image)
1.1.3 The aorta

The aorta is the great vessel at the beginning of the systemic circulation. It is composed by an ascending tract, an arch-shaped tract (the aortic arch) and a descending tract. In its origin, just downstream the aortic valve, it has three dilations representing sinuses of Valsalva. The length of the ascending tract of the aorta widens from 5 to 7 cm. The aortic arch has three branches (brachiocephalic trunk, left common carotid artery, left subclavian artery) which carry the blood to the superior part of the body. The descending portion of the aorta reaches the inferior part of the body.
1.2 The cardiac cycle

The cardiac cycle comprises all the events associated with the blood path inside the heart during a single beat. Every cardiac cycle begins with the appearance of an action potential into the sinoatrial node, situated in the superior wall of the right atrium. The electric activity translates into a mechanical one: the action potential propagates through the atria walls, which contract allowing the blood to flow inside the ventricles, and then through the ventricular walls, which contract allowing the blood to flow inside the arteries. A complete cardiac cycle includes both the contraction and the relaxation of the ventricle. Ventricular contraction phase is called systole; while ventricular filling phase is called diastole. The physiological heart rate is about 72 beats per minutes: that means that one cardiac cycle lasts about 0.8 seconds. The systolic time lasts about 0.3 seconds, hence about the 65% of the cycle is occupied by the diastole. The diastolic phase is slower because it allows the ventricle to be filled with blood.

1.2.1 Phases of the cardiac cycle

The cardiac cycle’s phases are the following:

A. Isovolumetric relaxation: at the beginning of the diastolic phase the ventricular myocardium is relaxed. All the valves are closed, so the volume of blood is constant.

B. Ventricular filling: the blood returns to the heart through the veins, it enters in the relaxed atria and, after that, inside the ventricles through the AV valves. The SL valves are closed because the pressure inside the ventricles is lower than the one in the aorta and pulmonary artery. The 70% of blood volume fills the ventricle in the first third of the phase, hence the first third of the phase is called rapid ventricular filling, the rest is called slow ventricular filling.

C. Atrial contraction: the atria contract and as a result of that more blood is pushed inside the ventricle.

D. Isovolumetric contraction: at the beginning of the systole ventricles start to contract and the pressure inside of them rises; when the ventricular pressure exceeds the atrial one, the AV valves close. The blood volume inside the ventricles remains constant.
E. *Ejection:* when the ventricular pressure exceeds the arterial one, the SL valves open and the blood is ejected inside the arteries. During this process the ventricular pressure reaches its peak and then it starts to decrease. The SL valves close again and that means that another diastolic phase occur.

Figure 1.6 shows a sketch of the five phases.

![Figure 1.6: Phases of the cardiac cycle.]

### 1.2.2 Pressures in the left ventricle and aorta

Figure 1.7 shows the Wiggers diagram that comprehends all the events that occurs in the left heart during the cardiac cycle in terms of atrial, ventricular and aortic pressure and ventricular volume.

![Figure 1.7: Wiggers diagram.]
During the diastole, blood does not enter the aorta because the aortic valve is closed. Once
the systole begins, the aortic valve is not open yet; when the ventricular pressure exceeds the
aortic one, the aortic valve opens and blood is ejected from the ventricle into the aorta. The
maximum pressure reached in the aorta is called *systolic pressure*. The minimum pressure is
called *diastolic pressure*. The passage between the systole to the diastole is marked by a
dicrotic notch, that can be associated to the aortic valve closing.

Not all the blood pumped into the aorta during systole immediately goes into systemic
circulation: a part of the blood distends the aortic walls, which are elastic, and another part
goes to the periphery. The amount of blood sent to the periphery is determined by the *total
peripheral resistance*. The peripheral resistance is the ratio between the difference of
pressure and the flow rate:

\[
R = \frac{\Delta p}{Q}
\]  

(1)

Where:

- \( \Delta p \) = pressure drop between two points;
- \( Q \) = flow rate as the product between the velocity of the fluid and the area of the
  vessel;

The compliance of the aortic wall is evaluated through the formula:

\[
C = \frac{\Delta V}{\Delta p}
\]  

(2)

Where:

- \( \Delta V \) = difference of volume;
- \( \Delta p \) = increase or decrease of pressure inside the vessel;

The fact that a part of the blood volume has distended the walls of the aorta allows the
pressure in the aorta, once the walls start to contract, to decrease at a rate which is lower than
the one inside the ventricle. This effect is called the *windkessel effect* (Figure 1.9). The result
of the windkessel effect is that, thanks to a compliant element, the large fluctuation of blood
pressure inside the ventricle is converted to a pressure wave with a higher mean value and a
smaller fluctuation in the aorta, as shown in Figure 1.8, and hence the perfusion of the organs is maintained while the heart ceases to eject blood.

![Figure 1.8: Blood pressure's changes in fluctuation from inside the left ventricle to the peripheral vessels.]

![Figure 1.9: The windkessel analogy explained. A pulsatile flow is transformed into a stationary one thanks to a compliant element. Credit: Wikimedia Commons.]

([2], [3], [4])
1.3 Pulmonary circulation

The right ventricle contracts and provides blood flow to the lungs. The blood, full of waste products and carbon dioxide, is ejected in the pulmonary artery though the pulmonary valve, and travels to the lungs to be oxygenated through gas exchange in the alveoli. Since the time-averaged flow rates pumped by the right and left ventricle, respectively, must be equal, and the pulmonary circulation is shorter in terms of distances travelled from the blood with respect to systemic circulation, with and internal diameter of the arteriole higher than the systemic circulation’s arteriole, the overall resistance is lower. That means that the pressure in the pulmonary artery is significantly lower with respect to the one in the aorta, because it is enough to maintain the same cardiac output. The pulmonary artery pressure has a shape which is similar to the aortic one, but it ranges from 8 to 22 mmHg.

1.4 Cardiovascular diseases

Cardiovascular diseases are one of the main causes of death in the western world. They are referred to all the changes and malfunctions that can occur to the heart, to the heart structures and to the vessels. They are usually due to age, poor habits such as smoking, or inflammatory disease. The incidence is predominant in the males. The most common diseases are valvular heart diseases, hypertension and atherosclerosis.

The valvular heart diseases can affect all four of the heart valves. They can be either congenital or resulting from the degeneration of the valvular structures due to aging, to inflammatory diseases such as endocarditis, or to rheumatic fever or altered calcium metabolism. The damage can lead to stenosis – reduced opening of the valve which lead to inadequate blood flow and higher difference of pressure within the valve, with the consequence of higher requested work from the heart – or insufficiency/regurgitation – incorrect closing of the valve which lead to the inability of prevent the backflow of blood. Sometimes both conditions can appear together. High blood pressure leads to higher stiffness and higher diameter (and consequent thinning) of arterial walls. It is a degenerating disease: the increasing of the peripheral resistance increases the load on the heart and the
high pressure apply higher stresses on the walls, which help the situation to get worse. The increased load can lead to left ventricular hypertrophy and higher risk of ischemia. The mechanical properties of the wall can degenerate to the point that the wall can rupture and cause an internal bleeding \( (aneurisms) \). **Atherosclerosis** is a disease that affects the internal wall of a vessel, with the accumulation of a fat plaque that reduces the diameter for the flow, leading to higher arterial pressure. The higher peripheral resistance requires more work from the heart, and a total occlusion of the vessel causes the lack of blood flow to the distal part of the tissue. In case of the coronaries, an infarct can lead to cardiac failure and death.

The **treatments** for these diseases are either pharmacological in the earlier stages of the diseases or surgical when the situation is critic. The surgery treatment can be to *fix* the interested structure or to *replace* it with an artificial cardiovascular device, such as heart valve prostheses, stents or vascular grafts.

The evaluation of the performance (i.e. how it affects pressures and blood flow) of an artificial cardiovascular device must be assessed in order to understand if the changes in pressure and flow are acceptable for the specific application of the device. Moreover, the contact between blood and an artificial material can lead to formation of thrombi and higher shear stresses lead to blood red cells haemolysis. For example, a bi-leaflet valve is a type of mechanical prosthetic heart valve. The bi-leaflet valve is characterized by a higher difference of pressure and higher backflow with respect to a natural, healthy valve. The materials in which it is made lead to blood coagulation and haemolysis, phenomena which are worsened by the creation of vortexes and high pressures and shear stresses in the blood flow. That is generally valid for each artificial cardiovascular device.
2. STATE OF THE ART AND DESIGN SPECIFICATIONS

2.1 Classical Mock circulation loops

When dealing with artificial cardiovascular devices, their performance must be considered in the testing phase in order to assess a proper functionality with respect to the application in which they are going to be used (patient’s age, gender, everyday activity, etc.). The evaluated parameters are used as an indicator of the expected clinical performance [5]. Therefore, the cardiovascular devices should be assessed under conditions which should replicate the physiological ones of the working environment in terms of pressures and flow rate.

The in vitro mock circulation loops are artificial laboratory devices which mimic the cardiovascular circulation by means of hydraulic elements. They are generally used for the testing of cardiovascular devices but also to study the cardiovascular system’s fluid dynamics. They are, ethically speaking, an alternative with respect to the use of animals or humans, with their main advantage being that they can provide highly controllable and reproducible results [6], and on the other hand their disadvantage being that they are, as artificial devices, less realistic than a natural organ.

Their use can be traced back to the 1970s, with a wide literature about the topic. The classical application of hydraulic mock loops is the testing of artificial cardiovascular devices such as artificial valve prostheses, while in the recent years their use was widened with the integration of ex-vivo excised sample or entire porcine hearts ([6];[7]).

2.1.1 Mock loops for prosthetic heart valves

Most of the mock loops addressed to the evaluation of an artificial valve’s performance are designed respecting the International Standard ISO 5840-1:2015 [8]. The ISO 5840-1:2015
accounts for tests in both stationary and pulsatile regimes, and it regulates the experimental conditions in which the parameters of interest are evaluated. The measured parameters are:

- In continuous flow, the difference of pressure across the valve and the amount of backflow
- In pulsatile flow, the pressure curve in correspondence of the valve and the effective orifice area.

The typical mock loop for pulsatile flow is a hydraulic circuit composed by a pumping system, a ventricle model that can be either artificial or animal derived, an afterload and a preload. The afterload purpose is to display a hydraulic impedance such that it guarantees a pressure waveform in the aorta phantom like the physiological one in the real aorta. Its construction is based on the windkessel effect (see Chapter 1). According to Sharp and Dharmalingam [9], the best compromise between accuracy and simplicity is to have a three-element model (RCR). The three-element model provides a reasonable correspondence between the physiological pressure waveform and the one obtained, with a relatively simple physical realization of the components ([9], [10]). The three elements are:

- **Characteristic resistance**: accounts for the characteristic impedance of the aortic branch;
- **Compliance**: accounts for the deformability of the great vessels;
- **Peripheral resistance**: accounts for the resistance of the peripheral circulatory system.

The electrical analogue is shown in Figure 2.1.

![Figure 2.1: Electrical analogue for the three element windkessel model. Rc: Characteristic resistance; Rp: Peripheral resistance. C: Compliance.](image_url)
The following is an example referred to the study of the fluid dynamic of an excised aortic valve.

### 2.1.2 Vismara’s mock loop for excised aortic valves

![Figure 2.2: Left: Schematic of the simulator. Right: Photograph of the complete setup.]

This mock loop by Vismara et al. [7] was designed in order to house whole natural ARFU (Aortic Root Functional Unit) samples for aortic surgery simulation. The goal was to allow the clinician to house and treat the ARFU sample in the mock loop with easiness and repeatability, and to study the fluid dynamics of the sample. The ARFU sample was subjected to physiologic-like mechanical conditions. The mock loop also provided accesses for video instrumentation.

The mock loop comprehends programmable pulse duplicator, adjustable hydraulic afterload, fluid-dynamic measurement systems and high-speed camera. More in details, letters a through e identify the main components of the simulator:

- **a) Sample holder**: composed of two parallel polymethylmethacrylate plates, whose distance is adjustable the fit to the ARFU sample length. The ARFU sample is sutured to an annular Dacron-reinforced silicone patch.

- **b) Main reservoir**: the ARFU sample is submerged in it in order for its outer surface to stay wet and at atmospheric pressure. Moreover, it is used as an atrial reservoir.

- **c) Ventricular chamber**: the main reservoir (b) is connected to it through a one-way service valve acting as the mitral valve. A polypropylene membrane separates the
working fluid (saline solution) from the service fluid (deionized water) of the pulsatile pumping device (d).

d) *Pulsatile pumping device* controlled by a driver, able to generate flow waves which are similar to the ones measured in vivo.

e) *Three element after-load*: to simulate the systemic hydraulic impedance. The peripheral resistance is adjustable.

The potentiality of the simulator in evaluating valvular hemodynamic was checked by means of experimental tests on fresh porcine ARFU samples with different diameter ranges and different hydrodynamic conditions. The simulator was equipped with piezo resistive pressure transducers and with an ultrasound flow meter for hydrodynamic measurements.

The behaviours shown in Figure 2.3 resemble the physiological ones except for the flow oscillations that take place at early diastole, which are due to the transient effect of the interaction between the inertia of the fluid downstream of the valve and the elastic nature of the ARFU walls.

![Figure 2.3: Example pressure tracing as measured at the inlet of the hydraulic afterload and corresponding flow rate course for a 21-mm untreated ARFU sample at f=70 bpm and mean flow rate Q=4 l/min.]

[Figure 2.3: Example pressure tracing as measured at the inlet of the hydraulic afterload and corresponding flow rate course for a 21-mm untreated ARFU sample at f=70 bpm and mean flow rate Q=4 l/min.]
2.2 Magnetic Resonance Imaging 4D flow

The Magnetic Resonance functioning is based on the measure of the precession of the protons spin when subjected to a magnetic field. The oscillating field, generated at an appropriate resonance frequency, excites the protons in tissues which contain water molecules. The protons emit a radio frequency signal measured by receiving coils [11]. In the clinical practice, the Magnetic Resonance Imaging (MRI) is commonly used as a tool in order to get morphological information for diagnosis and to assess patients’ response to surgical therapy. However, new technologies were developed through the years and allowed the distinction between moving and not-moving tissues, allowing the visualization not only of morphological structures but also of blood flow.

The PC-MRI technique consists in the visualization in a pre-selected plane of the blood flow in that plane. The main disadvantage is the difficulty of the choice of the plane, which depends on the operator’s ability.

Time-resolved PC-MRI – also called three-dimensional cine-phase contrast MRI or 4D-flow – is the evolution of PC-MRI: it can evaluate and visualize moving tissues, with information upon the velocity of blood flow along three directions and in the three-dimensional volume of interest, such as the heart and the aorta and the other large vessels. The 4D flow data can be reformatted in any plane orientation, to enable the visualization of complex hemodynamic pattern of blood flow as well as assessing the quantification of flow parameters such as peak pressure gradient, peak and mean velocities, net flow over one cardiac cycle, wall shear stress, pressure difference, turbulent kinetic energy, and others. Therefore, blood flow MRI can provide quantitative hemodynamic parameters, which complements the morphological assessment ([12]; [13]). This technology can provide additional information with respect to the morphological one about a pathology, especially when dealing with the cardiovascular system.

Echo particle image velocimetry is a technique which uses an ultrasound machine to generate instantaneous two-dimensional field of velocity. Echocardiography is a technique that makes use of this technology, and it is today the most widely available modality for the assessment of cardiac structure and function, with the advantages of being portable, of providing instant imaging and of having excellent temporal and spatial resolution. Its application in
hemodynamic include measures of peak and mean gradients of pressure and velocity. Its main disadvantage resides in the fact that it can provide information on a plane and not in a three-dimensional volume [14].

Today, Computation Fluid Dynamics (CFD) is considered the gold standard method for blood flow visualization, and for the evaluation of parameters such as wall shear stresses and flow energy loss. The advantages of using CFD instead of PC-MRI or echocardiography is that CFD allow the visualization of the flow in three-dimensional volume, that it can test the effects of isolated factors, and that it does not need a statistical study. The high spatial and temporal resolution allow the study of small volumes like small vessels. The disadvantages are that computational models such as the turbulence models must be appropriate to the computing subject. However, to not consider turbulence behaviour could lead to a large numerical error [11].

MRI 4D flow is a method that can visualize the 3D distribution of the blood vector field in vivo, so it could bridge the gap between CFD method and the other techniques such as PC-MRI and echocardiography.

Lately, the use of MRI 4D flow was used with in vitro flow systems. On the contrary to classical hydraulic mock loops, it enabled to provide more detailed information on the fluid dynamics parameters. Figures 2.4, 2.5, 2.6 shows some examples for the applications of MRI 4D flow in humans: Figure 2.4 shows the blood flow inside an aorta. The volume of interest shows the ascending aorta, the aortic branch and the descending aorta. The colour map provides information upon the blood velocity in every point of the volume, and the streamlines shows the regions with vortexes and recirculation [12]. The visualization of streamlines can be provided in a selected plane too, as shown in Figure 2.5. In such selected plane, the velocity-time curves can be provided too. The visualization of the fluid dynamics is useful not only for the diagnosis but also when dealing with post-operative follow-up such as after the replacement of a natural valve with a prosthetic one, as shown in Figure 2.6, to have a confrontation with a healthy volunteer.
[Figure 2.4: Example of a 4D Flow MRI: visualization of the blood flow inside an aortic vessel. The colour map shows the velocity of the flow in every point of the three-dimensional space of interest. [12]]

[Figure 2.5: Example of a fluid dynamics analysis with MRI 4D-Flow. Right, top: Plane of analysis. Left: Visualization of the streamlines of the flow in the plane of analysis. Right, bottom: velocity-time curves in the analysed section along the centre line. [15]]
In this part of the section, the focus will be brought on new MRI-compatible mock loops for different applications.

### 2.2.1 MRI compatible continuous flow system by Piatti et al.

In this work by Piatti [17], the INSPIRE 6 LPM module by Sorin, a real device which integrates an oxygenator (OXY) and a heat exchanger (HE), fabricated entirely with polymeric materials, was tested using the ad-hoc hydraulic mock loop sketched in Figure 2.7.

The circuit was filled with de-ionized water at room temperature with a centrifugal pump providing stationary 5 l/min flow rate. The flow was monitored through a transit-time flow meter downstream of the centrifugal pump. The water reservoir was positioned outside the MRI room as well as the centrifugal pump. The water was transported from outside the room to the device inside the scanner through a long silicone tube, passing through a previously made hole in the wall between the MR room and the acquisition room.
In Figures 2.8, 2.9 example of the results in the oxygenator flow by 4D-flow are shown, including the streamlines of flow and the computation of the wall shear stresses.
2.2.2 Pneumatic ventricle model

The aim of this paper by Jung et al. [18] is to study the alteration in the flow caused by the implantation of a continuous flow left Ventricular Assist Device (IVAD), a device used in patients with left heart failure, which allows to bypass the failing ventricle and to pump the blood directly into the aorta.

To visualize the changing in fluid-dynamics of the blood due to the presence of this device, an in vitro MRI-compatible model was built. The model replicated the aorta and the supra-aortic branches in synthetic resin to simulate the elastic properties of the human aorta. A ventricle model was represented by pneumatic driven IVAD which was placed inside the MRI scanner, while its driver was placed outside MRI room. Continuous flow IVAD (not MRI-compatible) was placed outside the MRI room and connected with the circuit by PVC tubes. The continuous VAD supplied the aorta with a retrograde flow through the brachiocephalic artery. Pre and afterloads were placed upstream and downstream the phantom, respectively. The afterload is composed only by resistances.
The results shown in Figure 2.11 comprehend flow-time curves for five different planes of selection, with correspondent evaluation of total and retrograde flow. Moreover, the 4D flow technology permitted the visualization of the streamlines (Figure 2.12).
The aorta phantom was accurate both from the morphological and the mechanical properties point of view. The main limitation of this work is that having a pneumatically driven device leads to no control on the flow waveforms.

### 2.2.3 MRI-compatible pulsatile pump

The purpose of this work from Urbina et al. [19] was to develop a MRI-compatible aortic phantom that simulates normal and aortic coarctation condition, to visualize the fluid dynamics through MRI 4D flow and then compare the results with the one from healthy and pathological volunteers.

The mock loop represents the aortic circulation. It is composed, as shown in Figure 2.13, by:

- A commercially available MRI-compatible pump (CardioFlow 500 MR, Shelley Medical Imaging Technologies, London, Canada);
- A commercially available realistic thoracic aortic model in flexible silicone;
- Two metres length connection tubes;
- A 20 litres reservoir.
Non-return valves were placed upstream and downstream the phantom to avoid negative pressures of the pump in diastolic phase. The afterload was composed by a shut-off valve and a compliance chamber in the descending aorta, while other shut off valves were placed downstream the supra-aortic vessels for the same purpose. Measures of pressure were taken through a catheterization unit, from which two catheters with transducers were placed in the ascending aorta and in the descending aorta. The pump and the phantom were placed upon the exam table.

The main limitation to this work was that the diastolic pressure had not a physiological form, likely due to lack of a compliance chamber downstream the supra-aortic branches. Moreover, being the phantom a commercial product and not made out by the same geometry of the aorta of one of the healthy volunteers, the accuracy of the data from 4D-flow could not be determined. Plus, while this set up was able to provide physiologic hemodynamic, there’s no guarantee that another configuration would be able to.
2.2.4 MRI-compatible pulsatile flow piston pump

The objective of the study by Jackson et al. [20] was to evaluate prosthetic mitral valve function within an MRI compatible pulsatile flow loop. The system was able to create controlled and reproducible pulsatile flow through a digital heartbeat simulator capable of replicating normal and pathologic cardiac flow conditions during systole and diastole, as well as to operate within the electromagnetic environment of the MRI scanner. The evaluated parameters were compared with one evaluated with Eco Doppler within the same conditions.

The flow loop was created without ferromagnetic components and placed inside MRI scanner, while the metallic servo-driven linear actuator and the heartbeat simulator were placed within the MRI room, outside the five Gauss line threshold of the magnet. This configuration required a long direct drive piston of about 4.5 m plus a system of support railings and linear motion pillow block bearings. The system could be disassembled and reassembled within the MRI room. The flow loop within the MRI scanner include an MRI-compatible pulsatile pump head, arterial resistance and compliance elements, a fill reservoir, and measurement instrumentation.

The main limitation of this work is that the mechanical valve area measurement demonstrated significant relative overestimation with respect to the Eco Doppler measures, likely due to the introduction of metallic image artefacts.
2.2.5 Pulsatile flow gear pump

This work’s [21] aim was to build a flow simulator capable of producing a range of repeatable, pulsatile flow waveforms similar to those found in various body areas, to be quick to assemble ad disassemble, and to have an integration of simultaneous monitoring system with flow simulation control to allow the synchronous temporal comparison of the waveform with the flow simulator waveforms through a LabView interface. The flow simulator was a bidirectional gear pump which generates aortic waveforms. The pump was connected to the phantom through 3.5 m long polybutylene tubing. The polybutylene is a stiff polymeric material: its stiffness was chosen to reduce waveform distortion. Snap-fit couplings allowed the system to be assembled in place. The accuracy of the waveform in the phantom is evaluated by the comparison between the gear pump waveform and the waveform in the phantom. The system was able to provide repeatable waveform of flow: the mean-normalized correlation between the waveform in the phantom and the reference one is 0.9978. The main limitation of this work was the lack of a proper afterload.

![Diagram of hydraulic circuit and data acquisition system (DAQ). Pot = potential divider. Right: example of an imposed aortic waveform.]

2.3 Analysis of the state of the art

The new cardiovascular devices must undergo a preclinical phase in which their performance must be assessed. The use of mock loops, integrating anatomically or functionally replicating phantoms or models, can provide reliable and repeatable results. In the recent years, strategies to integrate this type of studies using other technologies such as echocardiography or magnetic resonance imaging has paved the way for a fusion between experimental mock loops and the imaging field.

The analysis of the state of the art suggests that 4D-flow MRI can be used to provide additional information one cannot get from a classical hydraulic mock circulation loop only, such as the velocity field, wall shear stresses and pressure drops in any point of the volume of interest.

The main challenge when dealing with MRI is that the magnet generates an electro-magnetic field of 1.5 T or higher, depending on the machine model. All ferromagnetic materials would be subjected to the electro-magnetic force generated by the field and pulled into the magnet direction. A situation like that could lead to accidents and potential damaging of the objects and the machine itself. Moreover, metallic materials can introduce magnetic and radiofrequency interference and create image artefacts. Therefore, the instrumentations and computers are placed outside the room, at safety distance, in an area called control room. Since actuators and controllers are mostly made of ferromagnetic materials, proper modifications must be performed on a basic mock loop for it to be MRI-compatible.

Although the presented solutions to this problem are very different from one another, they generally condensed into two approaches:

- The actuator is MRI-compatible, and the controller is away from the magnet;
- The actuator as well as the controller are far away from the magnet, and the flow rate is delivered through long tubes or long transmission of movement.

The position of both the actuator and the controller are shown for every example in Table 2.2.
<table>
<thead>
<tr>
<th>Type of actuator</th>
<th>Controller’s position</th>
<th>Actuator’s position</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centrifugal pump</td>
<td>Control room</td>
<td>Control room</td>
<td>Continuous flow</td>
</tr>
<tr>
<td>Left VAD</td>
<td>Control room</td>
<td>MRI room, scanner table</td>
<td>Pulsatile pressure</td>
</tr>
<tr>
<td>MRI-compatible pump</td>
<td>Control room</td>
<td>MRI room, scanner table</td>
<td>Pulsatile flow</td>
</tr>
<tr>
<td>Long actuator</td>
<td>MRI room, 5-gauss line threshold</td>
<td>MRI room, scanner table</td>
<td>Pulsatile flow</td>
</tr>
<tr>
<td>Gear pump</td>
<td>MRI room, 5-gauss line threshold</td>
<td>MRI room, 5-gauss line threshold</td>
<td>Pulsatile flow</td>
</tr>
</tbody>
</table>

[Table 2.2: Differences between the topology of the elements of the different circuits.]

In the work from Piatti et al., the centrifugal pump and the instrumentations were left in the control room, as in this case there were no major fluid dynamics problems in having long distances between the phantom and the steady flow generator.

However, major of cardiovascular devices are subjected to pulsatile flow condition. Pulsatile flow applications face the dampening and distortion of the waveforms, hence having the phantom dislocated from the source of the flow is a potential challenge.

The works presented earlier achieved the goal of having physiological pulsatile flow, with some limitations:

- The control of the waveform: in the Jung’s work, a pulsatile VAD, MRI-compatible and pneumatically driven from outside was utilized, allowing the generation of flow waveform from the MRI table. However, a pneumatically driven device is not able to produce controlled and physiological flow waveforms;

- The difficult availability and replaceability of the flow generators, such as the long actuator, the MRI-compatible pump and the gear pump;
- The mechanical constraints of having a rigid transmission of the movement of a piston, such as in Jackson’s work, which requires control upon the movement of the piston and introduce metallic element in the scanner area;

- Moreover, the solutions which allowed some distance between the utilizer and the actuator relied on the possibility of placing the instrumentation behind the 5-gauss line, but to be still inside the MRI room. However, for safety reason, in hospital MRI scanners with diagnostic (and not research) purpose this is impracticable.

Do to these reasons, the set-up which is going to be designed in this work will use a pulsatile volumetric pump able to generate physiological flow rates. The pump will be placed in the control room in order for the mock loop to be utilizable in hospital MRI scanners. All the elements composing the hydraulic circuit will be easily available and replaceable. The layout of the set up will include polymeric tubing to carry the fluid from the control room to the scanner. This configuration leads to some challenges, mainly the dealing with the waveform distortion due to the large distances to be covered by the fluid, but also the filling volume and the overall management of the working set-up.

### 2.4 Design specifications

The goal of this thesis was to adopt the pulsatile flow mock circulation loop to be used in MRI scanner using lumped parameters modelling approach and its experimental verification. Specifically, the work was focused on designing the flow circuit to obtain representative pulsatile flow and pressure conditions in the test section, which is intended to be placed inside MRI scanner while the controller and actuator are placed in the control room. This way the setup could be used in diagnostic-oriented MRI scanners at local hospital, without the need for research-oriented MRI scanner.

As an example, the focus was put upon an aortic heart valve, but with some adjustments the mock loop can be adopted to study variety of cardiovascular diseases and other cardiovascular devices. In this work, a flow rate curve is considered physiological when it displays a peak in the systolic phase, and a zero-flow rate in the diastolic phase. The peak should be comparable with the one of the curve imposed by the pump, and the systole last
approximately one third of the whole cycle. The pressure is considered physiological if it displays a sphygmic shape, increasing in the systolic phase and slowly decreasing during diastole.

The **design specifications** are the following:

- The mock loop should be able to reproduce physiological pulsatile flow and pressure conditions in the test section regardless of imposed heart rate and stroke volume;
- The mock loop must be easily transported, and quickly assembled and disassembled;
- The components must be easily available and replaceable;
- The mock loop should be easy to be managed during the experiments.
3. MATERIALS AND METHODS

3.1 Adopted units of measurements

When dealing with subjects belonging to the biomechanical field, most of the units of measurements adopted are the ones from the medical field, such as millimetres of mercury (mmHg) for pressures, litres per minute (l/min) for flows, and beats per minute (bpm) for heart rate.

The units of measurements that will be used are shown in Table 3.1, as well as their conversion coefficients to the International System.

<table>
<thead>
<tr>
<th>Variable</th>
<th>S.I.</th>
<th>Adopted</th>
<th>Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure</td>
<td>Pa</td>
<td>mmHg</td>
<td>133,32 Pa = 1 mmHg</td>
</tr>
<tr>
<td>Flow</td>
<td>m^3/s</td>
<td>L/min</td>
<td>1 m^3/s = 60000 L/min</td>
</tr>
<tr>
<td>Heart rate</td>
<td>Hz</td>
<td>bpm</td>
<td>1 Hz = 60 bpm</td>
</tr>
<tr>
<td>Resistance</td>
<td>Pa*s/m^3</td>
<td>mmHg*s/L</td>
<td>133320 Pa<em>s/m^3 = 1 mmHg</em>s/L</td>
</tr>
<tr>
<td>Compliance</td>
<td>m^3/Pa</td>
<td>L/mmHg</td>
<td>1 m^3/Pa = 133320 L/mmHg</td>
</tr>
<tr>
<td>Inertance</td>
<td>Pa*s^2/m^3</td>
<td>mmHg*s^2/L</td>
<td>133320 Pa<em>s^2/m^3 = 1 mmHg</em>s^2/L</td>
</tr>
</tbody>
</table>

[Table 3.1: Adopted units of measurements and their conversion to International System.]

The pressures are measured in mmHg. The absolute atmospheric pressure (760 mmHg) is taken as a reference. Therefore, all pressure in this work are referred to the atmospheric pressure, which is considered as zero. For example, if a pressure is said to be 100 mmHg that means that it is 100 mmHg over the absolute atmospheric pressure, and hence 860 mmHg.
3.2 Initial circuit concept

Based on the design specifications, the circuit was composed by:

- A centrifugal pump to allow the initial filling and the de-bubbling of the circuit;
- A pulsatile volumetric pump, controlled by an external driver, that can provide the set flow waveform;
- Service valves, placed immediately after and before the volumetric pump, in order to obtain unidirectional fluid flow and avoid negative pressures downstream the pump;
- A phantom of the region of interest, consisting in an aorta phantom, placed inside the MRI scanner;
- A three-element afterload, simulating the impedance of the systemic circulation;
- Long delivery and returning tubes made out of polymeric material. The tubes carry the fluid from the pumping system to the test section inside the MRI scanner.

The circuit layout is shown in Figure 3.1.

[Figure 3.1: Schematic of the hydraulic circuit.]
In the following sections, the initial circuit concept’s hydraulic elements and the lumped parameter model used as a support during the design phase will be described, comprising a detailed description of all the elements composing it, as well as the parameter estimation and the choice of the proper model for every component.

Later, the final configuration of the mock loop, instrumentation and the testing protocol will be described.

### 3.3 Hydraulic circuit

The scheme of the circuit is shown in Figure 3.2. The pulsatile flow was imposed by a pulsatile pump (a) connected to a ventricular chamber (b). The ensemble withdrew fluid from a water reservoir (c), and pumped fluid inside the circuit through a service valve (d). Inside the reservoir there was a submersible centrifugal pump (e), which delivered continuous flow to the circuit during the preparation, in order to allow the filling of the long tubes and the de-bubbling the circuit. At the outlet of the pump, a PVC tube insert (f), 10 cm in length, was used to measure the flow rate through an ultrasound flowmeter. Connecting the pulsatile pump to the phantom, the delivery tube (g) was a 11 metres long silicone tube which allowed the fluid to be carried from the pump to the aorta phantom. The phantom of the aorta (i) was positioned just upstream a three element (RCR) afterload (l). The afterload allowed to obtain the pressure waveform similar to the physiological one. The compliance chamber of the afterload was connected to another close-to-air chamber (l3), placed distally from the afterload. Once the fluid exits the afterload, it was recollected inside the reservoir through another long silicone tube (m).
3.3.1 Fluid

The fluid utilized to carry out the experiments was water, which exhibits a density of 1000 kg/m^3 and a viscosity of 0.001 Pa*s. Generally, the mock circulation tests are carried out using a mixture of water and glycerine (70% water, 30% glycerine). The mixture exhibits a density of 1150 kg/m^3 and a viscosity of about 0.003 Pa*s, values which are similar to the blood’s properties.

The experiments were carried out using water to do the preliminary tests, while the use of water and glycerine was simulated. The results from simulations suggest that a higher viscosity and density helps the dampening of oscillations. However, that leads to higher pressures in the pump outlet.

3.3.2 Pumps

The centrifugal bilge pump is used during the preparation of the circuit. It provides a continuous flow. The pump fills the circuit and allows the operator to de-bubble it more easily. The volume of water needed to fill the circuit is approximately 12 litres. The centrifugal pump is a submersible pump, placed inside the same reservoir of the pulsatile pump.
Once the circuit is filled, the pulsatile pump is started and only after that the centrifugal pump is stopped and the tube connecting it to the circuit is clamped.

The **pulsatile pump**, previously shown in Figure 3.2, which 3D model is shown in Figure 3.3, is composed by a synchronous servo motor (MCS06C41, Lenze, Hameln, Germany) electrically controlled by a servo inverter (Servo 9322 EK, Lenze). The motor operates a worm screw that transforms the rotational movement of the motor in translational movement of a piston. Thanks to the electronic control system of the motor, a control software allows the setting of the piston displacement waveforms, corresponding to pump inflow and outflow waveforms and parameters, such as stroke volumes and heart rate, making it useful to simulate different work conditions. The use of this pump is hence justified by the fact that it is volumetric, and therefore guarantees controllable work conditions, that it can generate physiological pulsatile form and that it can be applied to different conditions through the set of parameters. During the diastole phase, the piston generates a flow waveform according to the analytical expression by Talukder and Reul (4) [22]; during the systole phase, the piston generates a flow waveform according to Swanson and Clark (3) [23].
The pump head has an elastomeric seal to ensure lack of fluid leakage in the interface. An 80 mm diameter flange allows the connection to other elements through four threaded rods. The piston chamber is connected to a ventricular chamber, which is connected to the reservoir. The ventricular chamber (Figures 3.4 and 3.5), already present in the μBS LAB, is put at the outlet of the pump. It is a cubic 60 x 60 x 60 mm chamber which can be connected to the pump, to a preload and to the circuit. A service valve (d) simulates the behaviour of a mitral valve: during the diastolic phase, when the piston moves backwards, the valve opens and the water is drawn into the chamber from the reservoir; during the systolic phase, when the piston moves forward, the valve closes and the flow is ejected into the systolic connector (a), which interface the circuit through another service valve. This configuration allows the flow entering the circuit to have the imposed wave form in the systolic phase and to be equal to zero in diastolic phase. This way of function is shown in detail in Figure 3.6.
[Figure 3.5: Comparison between the 3D model and the real picture of the ventricular chamber.]

[Figure 3.6: Pulsatile pump functionality. (a) Pulsatile pump and ventricular chamber ensemble. (b) Diastolic phase. (c) Systolic phase.]
Since the centrifugal and the pulsatile pump were connected to the same inlet, a three-way connector was needed (Figure 3.7). It is made in polymethylmethacrylate (PMMA), which is a rigid and transparent plastic material. The outer diameter is 25 mm, for the connection with the tubes. The inner diameter is 22 mm. The main tube has a hole made with a machine tool at 40 degrees with respect to its longitudinal axis, while the second tube was shaped in order to fit the hole shape and then glued to it. The lack of liquid leakage was tested and confirmed.

![Figure 3.7: Three ways connector. The two inlets are connected to two pumps, while the outlet is the same.]

3.3.3 Service valve

The service valve is a silicone valve anatomically representing the real aortic valve. A picture of the valve is shown in Figure 3.8. The valve, made by injection of silicone in a mould, presents three 0.6 mm thick leaflets (b) and the corresponding sinuses of Valsalva, as well as the left and right coronaries (c). The cusps form a 120° angle, while the annulus inner diameter is of 27 mm. The walls’ thickness is of 10 mm, while the inner diameter is of 20 mm. The two cylindrical parts upstream and downstream the leaflets (a), 10 mm thick and 20 mm inner diameter, are designed in order to facilitate the connection with the other mock loop components [24]: the choice of the valve relies on its flexibility, which makes it easier to connect the connection part of the ventricular chamber and the three-ways connector. The coronaries were used as an access to measure the pressure of the delivery tube.
The service valve’s purpose is to avoid having negative pressures downstream the pump, and preserving the correct functionality of the service valve inside the ventricular chamber.

### 3.3.4 Connection tubes

The tubing system’s purpose is to carry the fluid from the control room to the phantom inside the scanner, and then to carry the fluid from the phantom to the reservoir. Therefore, the tubes must be long, at least to cover the path from the control room table to the floor, and then again from the floor up to the scanner table. Moreover, redundancy of the length was taken into account due to safety reasons regarding the movement of the scanner table while the MRI machine is operating. Two 11 metres long tubes were chosen to satisfy these constraints. The tubes are made of flexible white silicone, with a 25 mm inner diameter and a 3.7 mm wall thickness.

Considerations were made upon the material of the delivery tube, whether it would be the best for the application, in Appendix C.

Two cylindrical straight PVC tubes were placed one at the outlet of the pump and one as a phantom for the aorta. Their length is approximately 10 cm, while their inner diameter is of 25 mm.
3.3.5 Phantom of the aorta

The phantom of the aorta is a cylindrical straight tube, made of flexible PVC, a polymeric material which permits the measure of flow through an ultrasound flowmeter. Its length is approximately 10 cm, while its diameter is of 25 mm.

3.3.6 After-load component

The afterload component, already available in the μBS Lab, was placed downstream the aorta phantom. It is the physical realization of a three element windkessel model, and its purpose is to impose a hydraulic impedance such that it provides a pressure waveform in the aorta phantom similar to the physiological. It is composed by, as shown in Figure 3.9, a characteristic resistance (c), a compliance chamber (d), and a peripheral resistance (e). The characteristic resistance’s value is fixed. The compliance can be adjusted by inserting or withdrawing air from the additional compliance chamber. The peripheral resistance is adjustable.

The compliance chamber is realized as a closed-to-atmosphere air reservoir, one incorporated into the afterload model and the other placed distally.

In order to reach a higher value of the peripheral resistance needed in order to have 100 mmHg of average aortic pressure in 70 mL stroke volume and 60 bpm heart rate conditions, an adjustable non-linear resistance was added downstream the afterload.
3.4 Lumped parameter model

The design phase was supported with a lumped parameter modelling approach. It was developed to study different configurations of the circuit and to assess the choice of the delivery’s tube material. The lumped parameter model’s layout is shown in Figure 3.10.
In general, circuit components properties can be described by three parameters, each of them accounting for a different behaviour:

- The resistance accounts for the pressure drops occurring in the element due to the viscosity of the fluid (energy dissipation);
- The inertance accounts for the changes in the fluid velocity. It is assumed that the fluid density and cross-sectional area of the pipe remain constant;
- The compliance accounts for the elastic behaviour of the walls, and therefore how the volume changes with respect to the changing pressure (energy storage).

The equations accounting for the lumped parameter model’s behaviour are shown in Appendix A.

Following paragraphs will introduce in more details each component of the circuit, the rationale behind their modelling approach and the lumped parameter estimation.
3.4.1 Imposed flow rate

During the diastole phase, the imposed flow rate is the analytical expression by Talukder and Reul (4) [22]; during the systole phase, the piston generates a flow waveform according to Swanson and Clark (3) [23].

\[
Q_{\text{imposed}} = \begin{cases} 
Q_{\text{sys}} & 0 < t < T_s \\
Q_{\text{dias}} & T_s < t < T_c 
\end{cases}
\]

\[
Q_{\text{sys}} = Q_a \left[0.924 \sin(A t) + 0.23 \sin(2A t) + 0.092 \sin(3A t)\right] \\
\text{(3)}
\]

\[
Q_{\text{dias}} = Q_d \left[0.52 \sin(B t) + 0.257 \sin(2B t) + 0.479 \sin(3B t)\right] \\
\text{(4)}
\]

\[
A = \frac{\pi}{T_s} \quad B = \frac{\pi}{T_c - T_s}
\]

\[
T_s = \sqrt{0.096T_c} \quad Q_a = 1.65Q_m \frac{T_c}{T_s} \quad Q_d = 2.32Q_m \frac{T_c}{T_c - T_s} \quad T_c = \frac{1}{f}
\]

Where:

- \(f\): heart rate;
- \(T_s\): systole time;
- \(T_c\): time of a cardiac cycle;
- \(Q_m\): average flow rate.
3.4.2 Service valve

The service valve at the outlet of the pump is a non-return valve, modelled as a variable resistance, with a value which is either zero when the valve is open or infinite when the valve is closed. The valve is either open or closed based on the value of the pressures upstream and downstream the valve:

\[ R_{\text{valve}} = \begin{cases} 0 & p_{\text{upstream}} \geq p_{\text{downstream}} \\ \infty & p_{\text{upstream}} < p_{\text{downstream}} \end{cases} \]

Since in the simulation the parameters’ values must be a finite number, a very high number was chosen in the place of infinite (10000).

The service valve at pump outlet is not rigid, being made from silicone. The viscoelastic properties were modelled with a compliance (whose value was already evaluated in Schiena’s work [24]) and a viscoelastic resistance, whose value was evaluated through a best-fit procedure.

3.4.3 Delivery tube

Tubes can be considered as a set of lumped parameters: a resistance, a compliance and an inertance, each one accounting for a different behaviour. The delivery tube, which is long
and flexible, was modelled as six T-models placed in series (see Figure 3.12) to account for the dynamic behaviours occurring in the tube. Each T-model consists of three parameters: resistance, compliance and inertance, which values are \(1/6\) of the total value assumed for the whole tube. The number of T-elements was estimated preliminary by fitting simplified experimental data to the simulation results. For further details see Appendix B.

![Figure 3.12: T-model.]

The parameter estimation was carried out in the following way:

The delivery tube’s \textbf{resistance} was modelled using the Poiseuille’s law:

\[
R = \frac{128\mu l}{\pi D^4}
\]  

Where:

- \(\mu\): fluid viscosity;
- \(l\): length of the tube;
- \(D\): diameter of the tube.

The \textbf{inertance} was evaluated through this definition:

\[
L = \frac{\rho l}{A}
\]  

Where:

- \(\rho\): fluid density;
- \(l\): length of the tube;
- \(A\): section of the tube.
The resulting values for R and L are 8.08 mmHg*s/l and 162.8 mmHg*s^2/l, respectively. Since the Poiseuille’s law (5) is valid under some hypothesis, such as stationary flow, rigid tube and circular cross-section, which in this case are not satisfied, the value for the resistance was likely underestimated in this work’s situation: in the simulations a value of 100 mmHg*s/l was used, to allow the data to best-fit the experimental curves.

The delivery tube compliance was evaluated through its operational definition, as the ratio between volume variation and difference of pressure:

\[ C = \frac{\Delta V}{\Delta p} \]  

(7)

The compliance value was estimated experimentally in a set-up sketched in Figure 3.13. A sample of the tube was filled with water and through a syringe, controlled volumes of water were added to the tube. Pressure was measured for every 1 ml of water injected.

As shown in Figure 3.14, the tube sample exhibited a compliance of 0.0121 mL/mmHg = 1.21 \times 10^{-5} L/mmHg.
To evaluate the total compliance of the delivery tube, the analytic formula for the estimation of the compliance (8) was taken into consideration.

\[
C = \frac{3}{2} \frac{\pi r^3 (1 - v^2)}{E t} l
\]  

(8)

Where:

- \( r \): tube radius;
- \( v \): Poisson’s ratio;
- \( E \): elastic modulus of the tube’s material;
- \( t \): wall thickness of the tube;
- \( l \): length of the tube.

The result from the experiment was hence normalized for the length of the sample and then multiplied by the length of the delivery tube, according to equation (8). The final value for the delivery tube’s compliance is the following:

\[
C_d = 1.21 \times 10^{-5} \times \frac{11 \text{ m}}{0.075 \text{ mmHg}} \frac{L}{\text{mmHg}} = 0.00177 \frac{L}{\text{mmHg}}
\]
3.4.4 Phantom of the aorta

The phantom of the aorta was considered as a series of a resistance and an inertance using equations (5) and (6), respectively. The compliant behaviour was considered negligible with respect to the one of the delivery tube, because the compliance of the delivery tube is very high with respect to the one of the aorta phantom. Moreover, a flowmeter probe was put around the aorta phantom, making it rigid.

3.4.5 Afterload

The afterload was modelled as a three-element windkessel model, composed by a characteristic resistance, a peripheral resistance and a compliance. The values were derived from the literature [25] and are reported in Table 3.2.

<table>
<thead>
<tr>
<th>Element</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic resistance</td>
<td>54 mmHg*s/L</td>
</tr>
<tr>
<td>Peripheral resistance</td>
<td>960 mmHg*s/L</td>
</tr>
<tr>
<td>Compliance</td>
<td>0.0036 L/mmHg</td>
</tr>
</tbody>
</table>

[Table 3.2: values from the literature for the three-element windkessel afterload.]

In order to reach an higher peripheral resistance, needed in the mock loop to reach an average aortic pressure of 100 mmHg*s/l with imposed 70 mL stroke volume and 60 bpm heart rate, an additional resistance was placed downstream the afterload. Therefore, the overall peripheral resistance has a value of 1367 mmHg*s/l instead of 960 mmHg*s/l.

3.4.6 Return tube

The return tube’s parameters were evaluated with the same protocol as the delivery tube, being made by the same material. However, the compliance of the tube was considered negligible. As a matter of fact, the returning flow is almost stationary, hence it does not exhibit dynamic behaviours. That means that, being that compliance and inertance accounts
for dynamic behaviours, as shown by their constitutive laws (9) and (10), in order not to further complicate the model the compliant behaviour was considered negligible. The inertance was taken into consideration for consistency with the writing of the equations.

\[ Q = C \frac{dp}{dt} \]  
\[ \Delta p = L \frac{dQ}{dt} \]  

### 3.4.7 Model parameters

Table 3.3 is a summary of all the parameters used in the model, their values in operating units of measurement, and their evaluation modality.

<table>
<thead>
<tr>
<th>Component</th>
<th>Parameter</th>
<th>Value</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Service valve</td>
<td>( R_{sv} )</td>
<td>300</td>
<td>Variable resistance</td>
</tr>
<tr>
<td></td>
<td>( R_{sve} )</td>
<td>300</td>
<td>Best-fit</td>
</tr>
<tr>
<td></td>
<td>( C_{sv} )</td>
<td>2.7 ( \times 10^{-5} )</td>
<td>Experiment</td>
</tr>
<tr>
<td>Delivery tube</td>
<td>( R_d )</td>
<td>100</td>
<td>Best-fit</td>
</tr>
<tr>
<td></td>
<td>( R_{dv} )</td>
<td>300</td>
<td>Best-fit</td>
</tr>
<tr>
<td></td>
<td>( L_d )</td>
<td>162.83</td>
<td>Inertance formula</td>
</tr>
<tr>
<td></td>
<td>( C_d )</td>
<td>0.001775</td>
<td>Experiment</td>
</tr>
<tr>
<td>Aorta phantom</td>
<td>( R_{ao} )</td>
<td>0.103</td>
<td>Poiseuille</td>
</tr>
<tr>
<td></td>
<td>( L_{ao} )</td>
<td>2.072</td>
<td>Inertance formula</td>
</tr>
<tr>
<td>Afterload</td>
<td>( R_c )</td>
<td>54</td>
<td>Literature</td>
</tr>
<tr>
<td></td>
<td>( R_p )</td>
<td>1367</td>
<td>Literature + additional R</td>
</tr>
<tr>
<td></td>
<td>( C )</td>
<td>0.036</td>
<td>Literature</td>
</tr>
<tr>
<td>Return tube</td>
<td>( R_r )</td>
<td>5.874</td>
<td>Poiseuille</td>
</tr>
<tr>
<td></td>
<td>( L_r )</td>
<td>118.423</td>
<td>Inertance formula</td>
</tr>
</tbody>
</table>

[Table 3.3: Model’s parameter’s values and their evaluation modality.]
3.5 Verification of the model

The initial experimental set-up was used to verify the lumped parameter model. The pressures and flows measured during the experiment were compared with the results obtained through the simulations, to check whether the model was detailed enough to explain the phenomena occurring in the delivery tube.

The model was verified qualitatively, by looking at the pressure and flow rate curves superimposed to the ones from the experimental set-up, and quantitatively by evaluating the determination coefficient for every variable of interest for every couple of heart rate and stroke volume imposed.

The determination coefficient \( R^2 \) provides a measure of how well observed outcomes are replicated by the model. Given a data set with \( n \) values \( y_i \), for \( i = 1, \ldots, n \), each one associated with a set of predicted values \( f_i \), for \( i = 1, \ldots, n \), the determination coefficient is evaluated as:

\[
R^2 = 1 - \frac{\sum_{i=1}^{n} (y_i - f_i)^2}{\sum_{i=1}^{n} (y_i - \bar{y})^2} \tag{11}
\]

Where:

- \( \sum_{i=1}^{n} (y_i - f_i)^2 \) is the sum of square of residuals;
- \( \sum_{i=1}^{n} (y_i - \bar{y})^2 \) is the total sum of squares;
- \( \bar{y} \) is the mean of the observed data,

\( R^2 \) is an index which can give information about the goodness of fit of a model. The \( R^2 \) index maximum value is 1. The more \( R^2 \) value is near to 1, the better is the model in fitting the experimental data.

3.6 Final configurations of the circuit

Once the model was verified, it was used to preliminary simulate variety of circuit configurations in order to get physiological flow rates and pressure in the test section.
Among these configurations, several promising configurations were chosen to be reproduced in the experimental set-up. Particularly, the simulations demonstrated that the best configurations were either the one with a valve in aortic position to avoid the backflow or the one with a higher resistance of the delivery tube to dampen the pressure and flow oscillations.

Due to this reasons, three configurations were tested and compared:

- Additional valve;
- Additional resistance in the delivery tube;
- Additional valve and additional resistance in the delivery tube.

Figures 3.15 and 3.16 show the layout of the last configuration and the corresponding lumped parameter model, respectively.

[Figure 3.15: Layout of the final configuration. (a) Pulsatile pump. (b) Ventricular chamber. (c) Fluid reservoir. (d) Service valve. (e) Centrifugal pump. (f) Input flow measure. (g) Delivery tube. (h) Aortic valve. (i) Aorta phantom. (l) Afterload: (l1) characteristic resistance; (l2) peripheral resistance; (l3) compliance. (m) Return tube. R: Additional resistance. Red arrows show the flow direction.]
3.6.1 Aortic valve

The aortic valve was, as the service valve, anatomically representing the real aortic valve, as shown in Figure 3.17. The structure is the same of the service valve, with leaflets and sinuses of Valsalva, without the coronaries. This is due to the fact that a custom-made rigid housing, 3D printed in Polylactic Acid (PLA), was made for the valve not to segregate too much volume of water in the distending of the walls. The flexibility of the connecting part allows the connection with the other rigid elements of the circuit.

[Figure 3.17: Aortic valve and rigid housing. (a) Rigid housing. (b) Connection with the circuit. (c) Leaflets.]
The aortic valve was modelled in the same way as the service valve. The compliance behaviour was not taken into account because the valve compliance effect can be considered negligible with respect to the effect of the tube. Moreover, the rigid housing prevents an excessive dilation of the walls, making it more rigid.

### 3.6.2 Additional resistance

In order to dampen the pressure and flow oscillations upstream the aortic valve, a resistance was placed at the end of the delivery tube. The values of the resistance was chosen through best fit seeing the results of the simulations. The best value for dampen the oscillation in case of 40 bpm heart rate and not changing the flow too much in the 60 and bpm cases, is 150 mmHg*s/l.

### 3.7 Preparation of the hydraulic circuit

The circuit was assembled simulating the displacement of the elements as in the MRI room. The pump was connected to the ventricular chamber, which was in turn connected to the reservoir and the service valve. The service valve was connected to the three ways connector. The other inlet of the connector was connected to the centrifugal pump. The centrifugal pump was placed inside the reservoir. In Figure 3.18 the first part of the circuit is shown. The pumping system was connected to the aortic valve and the aorta phantom through the delivery tube. The afterload was placed downstream the aorta phantom, and the connection was ensured between the flexible tube and the connector at the inlet of the afterload. The afterload’s compliance was connected to an external compliance chamber. The outlet of the afterload was connected to the return tube by means of a ½ inch to 1-inch connector. This second part of the circuit is shown in Figure 3.19. The connections were ensured through plastic cable ties. Figures 3.20, 3.21, 3.22 and 3.23 show pictures of the experimental set-up.
[Figure 3.18: Portion of the set up destined to the control room, that supply flow to the circuit. (a) Pulsatile pump; (b) Ventricular chamber; (c) Service valve; (d) Reservoir; (e) Three-ways connector.]

[Figure 3.19: Portion of the set-up destined to the scanner. (a) Delivery tube; (b) Aortic valve; (c) Aorta phantom; (d) Afterload; (e) Additional compliance.]
[Figure 3.20: Picture of the mock loop set-up.]

[Figure 3.21: Driver for imposing flow rate.]
Once the circuit was assembled, the centrifugal pump was started. The filling volume is about 12 litres. While the pump is running, the air bubbles are eliminated from the circuit. Once the circuit was filled with water, the pulsatile pump, previously connected to its driver, was started with a default setting of stroke volume and heart rate. The centrifugal pump was stopped only after the pulsatile pump is started in order to prevent emptying of the circuit elements with gravity.

3.8 Testing protocol

The mock loop was tested in order to check the flow and pressure waveforms in order to understand the behaviour of the mock loop in obtaining pulsatile flow and pressure in the test section.

The experiments were carried out in pulsatile flow regime, with changing heart rate between 40, 60 and 80 bpm and stroke volume between 30, 50 and 70 mL. This range of parameters
allowed to simulate different conditions: by changing the heart rate, different situations between rest and exercise can be simulated; by changing the stroke volume, different patient size, such as children or adults of different weights are simulated.

The initial experimental set-up was used to verify the lumped parameter model. The model goodness was checked through two configurations, A and B.

Once the model was verified, it was used to simulate different conditions and different adjustments to the initial circuit. Three other type of set-ups were considered:

- Inclusion of a second valve – Configuration C: the set-up was tested in order to assess the influence of the inclusion of a second valve in the aortic position.

- Inclusion of an additional resistance – Configuration D: the set-up was tested in order to assess the influence of an additional resistance at the end of the delivery tube on flow and pressure waveforms in the test section.

- Inclusion of a second valve and additional resistance – Configuration E.

The adjustable peripheral resistance of the afterload was set with reference to the situation of 70 ml and 60 bpm, in order to have an average aortic pressure of 100 mmHg.

In Table 3.4 and Figure 3.23 the different configurations for the tests are shown.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Pumping system and service valve</th>
<th>Length of delivery tube (m)</th>
<th>Resistance</th>
<th>Aortic valve</th>
<th>Phantom of the aorta, afterload and return tube</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>✔</td>
<td>11</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>✔</td>
<td>4</td>
<td></td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>✔</td>
<td>11</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>✔</td>
<td>11</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>✔</td>
<td>11</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

[Table 3.4: Different configurations for the tests.]
Figure 3.23: Different configurations for the tests.
Table 3.5 summarize the testing protocol, for every configuration, stroke volume and heart rate.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Stroke volume (mL)</th>
<th>Heart rate (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>A</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>B</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>C</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>D</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>E</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>40</td>
</tr>
</tbody>
</table>

[Table 3.5: Testing protocol. For every configuration nine tests were carried out, for different stroke volumes (30, 50, 70 mL) and heart rates (40, 60, 80 bpm).]
3.9 Mock loop’s instrumentation

3.9.1.1 One valve

[Figure 3.25: Accesses for measurements of pressures and flows. Pressures measured in the service valve’s position, upstream the aorta phantom and in the additional compliance position; flows measured downstream the service valve and in aortic position.]

During the experiments, four signals were measured in configurations A, B, E:

<table>
<thead>
<tr>
<th>Signal</th>
<th>Position</th>
<th>Name</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure</td>
<td>Immediately downstream the service valve</td>
<td>Delivery tube pressure</td>
<td>1</td>
</tr>
<tr>
<td>Pressure</td>
<td>Immediately downstream the aortic valve</td>
<td>Aortic pressure</td>
<td>2</td>
</tr>
<tr>
<td>Flow rate</td>
<td>Downstream the three-ways connector, upstream the delivery tube</td>
<td>Pump output</td>
<td>3</td>
</tr>
<tr>
<td>Flow rate</td>
<td>In the aorta phantom position</td>
<td>Aortic flow rate</td>
<td>4</td>
</tr>
</tbody>
</table>

[Table 3.6: Measured signals in the mock loop configurations A, B, E.]
3.9.1.2 Two valves

During the experiments, five signals were measured in configurations C, D, F:

<table>
<thead>
<tr>
<th>Signal</th>
<th>Position</th>
<th>Name</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pressure</strong></td>
<td>Immediately downstream the service valve</td>
<td>Delivery tube pressure</td>
<td>1</td>
</tr>
<tr>
<td><strong>Pressure</strong></td>
<td>Upstream the aortic valve</td>
<td>Upstream pressure</td>
<td>2</td>
</tr>
<tr>
<td><strong>Pressure</strong></td>
<td>Downstream the aortic valve</td>
<td>Aortic pressure</td>
<td>3</td>
</tr>
<tr>
<td><strong>Flow rate</strong></td>
<td>Downstream the three-ways connector, upstream the delivery tube</td>
<td>Pump output</td>
<td>4</td>
</tr>
<tr>
<td><strong>Flow rate</strong></td>
<td>In the aorta phantom position</td>
<td>Aortic flow rate</td>
<td>5</td>
</tr>
</tbody>
</table>

[Table 3.7:Measured signals in the mock loop configurations C, D.]
The pressures were measured through piezoresistive pressure transducers (143PC series, Honeywell Inc, New Jersey, USA) connected through Luer Locks. While connecting the transducer, it was made sure that no air bubble was interposed in between the access and the transducer. The pressure transducers were connected to an analog-digital converter (PCI-6042E, National Instruments, Austin, TX). The sampling was carried out at 200 Hz through a Lab-View Interface.

![Pressure transducer image](image)

[Figure 3.27: Pressure transducer.]

The flows were measured through an ultrasound flowmeter (HT110, Transonic System Inc, New York, USA) with a 25.4 mm probe.

![Flowmeter image](image)

[Figure 3.28: Left: Flowmeter. Right: Flowmeter probe.]
3.10 Evaluation the parameters

For configuration C, D and E several parameters were evaluated, for every SV and HR:

- Flow parameters:
  - Stroke volume – pump output: evaluated as the integral of the pump output during systole for 8 cycles and normalized for the number of cycles. The quantity is measured in mL. It is the measure of the volume of water entering in the delivery tube for every cycle.
  - Stroke volume – aortic flow rate: as for the previous parameter, the stroke volume in the aorta phantom, downstream the aortic valve, is evaluated to compare it to SV – pump output in order to check whether the accumulation of water in the delivery tube due to the presence of two valves is acceptable. It is measured in mL.
  - Backflow of aortic valve: evaluated as the integral in time of the negative flow rate in aortic position, it measures the amount of backflow of the aortic valve.
  - Average aortic flow rate: the average flow rate in aortic position, evaluated as the average of every value of the flow rate for 8 cycles.
  - Peak of systolic flow rate: evaluated from the curves, the peak of the aortic flow in systolic phase.
  - Systolic flow time: evaluated from the curve as the time interval between the beginning and the ending of the systole.

- Pressure parameters:
  - Peak delivery tube pressure: maximum of the pressure evaluated downstream the service valve. This pressure is considered as the maximum pressure occurring inside the circuit. It is evaluated for safety reasons, due to the presence of many connections in that point of the circuit.
- **Average aortic pressure**: as the average of all measuring points of the aortic pressure;

- **Systolic – diastolic pressure difference**: the difference between the systolic peak and the minimum value of the aortic pressure during systole.

- **Aortic valve average pressure drop**: average of the difference between the pressure upstream the aortic valve and downstream the aortic valve, only when the valve is open (hence if $p_{\text{upstream}} > p_{\text{aortic}}$)

The parameters are going to be presented, in the next chapter, for the best configuration chosen, and commented with respect to a qualitative evaluation of the pressures and flow curves.
4. RESULTS AND DISCUSSION

In this section, the results from the experimental testing and simulations of the previously presented configurations are showed. Configurations A and B were tested to verify the model. Configurations C, D and E were tested to check what configuration results the best for the application. In the last part, the hemodynamic assessment for the best configuration chosen is shown, with a discussion on the flow and pressure parameters.

4.1 Verification of the model

4.1.1 Configuration A

The comparison between the configuration A of the simulations and the experiments for 70 mL stroke volume is shown in Figure 4.1. The curves were superimposed by manually synchronizing the pump outputs from the simulations and the experiments, shifting the simulations track to have the time of beginning of the systole to match the one from the observed data.

The delivery tube pressure curve computed by the model fits the experimental data for the most part for 40 bpm and 60 bpm heart rate, showing that the dynamic phenomena of the waveforms are well predicted. However, the model fails to provide the pressure peak at the beginning of the systole in 60 bpm case. The peak is displayed but it is underestimated, being 50 mmHg lower with respect to the experimental one. When 80 bpm heart rate is imposed, the model curve of the pressure appears to be shifted of an offset of 50 mmHg. Moreover, the model shows some oscillations which are not present in the experimental data. The presence of oscillations and of a negative offset suggests an underestimation of the delivery tube resistance.
The imposed flow rate curve is well predicted for every heart rate, except for the backflow at the beginning of the diastolic phase. That is because the valve in the model is treated as an ideal valve, while the real valve does not close instantaneously. The oscillations at the beginning of the diastolic phase of the model’s curve of the imposed flow rate are not related to the backflow of the valve but they are due to the valve’s compliance. The systolic flow peak of the model is higher with respect to the experimental systolic flow peak, especially for 40 bpm and 60 bpm heart rates. This is likely due to a non-ideal behaviour of the valve, too. As a matter of fact, the leaflets may bounce back into the closed position for a few milliseconds during the ejection of fluid.

The aortic pressure presents the same average pressure and almost the same systolic peak pressure in the 60-bpm heart rate case, while the peak is overestimated in the 40-bpm heart rate case. In the 80-bpm heart rate case, the pressure appears shifted of an offset of 50 mmHg difference of pressure, consistently with the delivery tube’s pressure. The pressure curve appears phase-shifted in time for every bpm.

The aortic flow rate computed by the model in the systolic phase for 40-bpm and 60-bpm heart rate is almost superimposed to the experimental data. However, in the diastole, the model underestimates the backflow. That could be due to the fact that in the lumped parameter model the valve was modelled as an ideal valve with no backflow. In the 80-bpm heart rate case, the flow appears phase-shifted in time of -0.2 seconds.

The results shown are just for 70-mL stroke volume. The curves for lower stroke volumes show similar patterns, and the same considerations drawn for the 70-mL case apply.
For a deeper analysis of the similarity of the curves, the determination coefficient for every couple (model/experiment) of curves was evaluated. The determination coefficients of the simulations with respect to the experimental data is shown in Table 4.1, for 70-mL stroke volume.
In the 40-bpm case, the aortic pressure presented an offset of -5 mmHg, which was eliminated to study the goodness of the curve. In the 60-bpm case, the service valve pressure has an offset of -11 mmHg. In the 80-bpm case, the imposed flow rate has an offset of 51.64 mmHg. The aortic pressure has an offset of 40 mmHg. The aortic flow rate displayed a phase shift of -0.27 s.

<table>
<thead>
<tr>
<th>R²</th>
<th>HR (bpm)</th>
<th>Aortic pressure</th>
<th>Aortic flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40</td>
<td>0.9977*</td>
<td>0.9292</td>
</tr>
<tr>
<td>SV=70 mL</td>
<td>60</td>
<td>0.9955</td>
<td>0.9547</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>0.7779*</td>
<td>0.9259**</td>
</tr>
</tbody>
</table>

[Table 4.1: Determination coefficients (R²) of the lumped parameter model for SV=70 mL and different HR, configuration A. (*) The R² is computed without the offset. (**) The R² is computed without the phase.]

The R² index is evaluated considering the fact that the pump output of the model and the experiment are different, because the service valve is modelled as an ideal valve.

The offset and phase shift cases are explainable in two ways:

- **Offset**: the value of resistances of the components were considered linear, without taking into account the non-linear resistances present in the connections of the components.

- **Phase shift**: the access for the measure of pressure and the point in which the pressure was evaluated in the model may not coincide.

### 4.1.2 Configuration B

In configuration B, the model provides result which are coherent with the one found for configuration A. The peaks for the delivery tube pressure are underestimated. Moreover, the pressures are phase-shifted in time, as well as the aortic flow. The peaks for the aortic pressures are overestimated. The dynamic behaviours are well-predicted, except for the aortic flow in the 80-bpm case.
Figure 4.2: Delivery tube pressure (blue), pump output (yellow), aortic pressure (orange) and aortic flow rate (green) from the experimental data (test) and model (simu) for 70 mL SV and different HR, Configuration B.
<table>
<thead>
<tr>
<th>R²</th>
<th>HR (bpm)</th>
<th>Aortic pressure</th>
<th>Aortic flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40</td>
<td>0.7015*</td>
<td>0.9292**</td>
</tr>
<tr>
<td>SV=70 mL</td>
<td>60</td>
<td>0.9127*</td>
<td>0.7823**</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>0.8512</td>
<td>0.6605**</td>
</tr>
</tbody>
</table>

[Table 4.1: Determination coefficients (R²) of the lumped parameter model for SV=70 mL and different HR, configuration B. (*) The R² is computed without the offset. (**) The R² is computed without the phase.]

### 4.1.3 Considerations on the initial circuit and model verification

Figure 4.1 shows that the curves of flow rate and pressure in the aortic position are not physiological, especially for the 40-bpm case, in which the aortic flow presents a high backflow. Particularly, peaks at different frequencies seem to translate and superimpose, therefore the negative peak in the 40-bpm heart rate case is concealed in the 60-bpm case. Hence, the circuit as it is does not comply with the design specifications.

In general, the model fitted the data well in terms of dynamic behaviour for both configurations A and B, for lower heart rates (40 bpm), while for 60 bpm it fails to catch some dynamic peaks occurring at the inlet of the circuit. The aortic pressure and aortic flow rate waveforms are well fitted, except the under/overestimation of the peaks. At 80-bpm the model fails to describe the aortic pressure curve in terms of average pressure, and the curve of the aortic flow rate is similar but phase-shifted in time, likely due to the fact that the model parameters may be dependent on the imposed heart rate. However, for the purpose of this work, the model shows promising results in order to check different configurations for the wanted transmission of waveforms, which will be done in the next sections.
4.2 Simulations

In this paragraph the results from the simulations of the three configurations are shown for the three configurations chose as a possible solution to the problem. In the next paragraph, the experimental results of the three configurations are going to be showed and discussed.

4.2.1 Additional valve

In Figure 4.3 the results for the addition of a second valve in the aortic position are shown. The valve seems to avoid the backflow in the aortic position, previously seen in Figure 4.1, and as a consequence to allow the pressure and flow rate in aortic position to be physiologically accurate in shape.

[Figure 4.3: Aortic pressure (top, orange) and flow rate (bottom) due to the simulation of the inclusion of an aortic valve upstream the aorta phantom for 70 mL SV and different HR.]
4.2.2 Additional resistance

In Figure 4.4 the results from the inclusion of an additional resistance in the model are shown. Overall, the waveform distortion is reduced, and the oscillations are dampened. The delivery tube’s pressure is higher with respect to the configuration C. The aortic pressure and flow rate seem almost-physiological in 60 bpm and 80 bpm heart rate cases, while for 40 bpm the aortic flow still presents some backflow. That suggests that a higher value for the resistance should be tested when in 40 bpm heart rate condition.

4.2.3 Additional valve and resistance

The results of the simulation are shown in Figure 4.5. The valve seems to avoid the backflow in the 40-bpm case with respect to configuration C. However, in 60 and especially 80 bpm case, the aortic flow rate in diastolic phase exhibits a value which is not zero. These results suggest that probably the value of the resistance should be changed with respect to the heart
rate imposed, being higher when the heart rate is lower and lower when the heart rate is higher. That means that an adjustable resistance should be included in the mock loop as a hydraulic element.

[Figure 4.5: Aortic pressure (top) and flow rate (bottom) due to the simulation of the inclusion of an aortic valve upstream the aorta phantom and of an additional resistance at the distal part of the delivery tube for 70 mL SV and different HR.]
4.3 Choice of the best configuration

The three configurations were tested experimentally. In this paragraph the results from the experimental tests are shown, including an analysis of the three layouts behaviour and the reasons of the choice of one of them as the best for the application.

4.3.1 Influence of an additional valve

The results for the inclusion of an additional valve in the aortic position are shown in Figure 4.6, for 70 mL stroke volume and every heart rate.

The waveforms of the aortic flow are almost physiological. The addition of an aortic valve to the circuit avoids the backflow in the aorta phantom position, which was observed in configuration A (reported in Figure 4.1). Hence the flow rate in diastolic phase in aortic position stays around zero with some oscillations. In Figure 4.6 the visual comparison between the pump output and aortic flow rate is shown: the aortic flow rate presents a phase shift of almost 0.4 seconds with respect to the pump output, for every SV and HR. That is the effect of the propagation of the wave in the delivery tube due to its high inertance and compliance. Moreover, the peak of the aortic flow in systolic phase results higher with respect to the pump output for 40 bpm HRs, and lower for 60 and 80 bpm HRs.

The aortic pressure’s waveform is almost physiological (see Vismara’s mock loop results in Figure 2.4), except for the presence of a marked dicrotic notch and some oscillations in the diastole phase. The dicrotic notch can be due to the valve’s behaviour, since it is a compliant valve with a time of closure which is not instantaneous, and its magnitude is related to the backflow present in the aortic flow at the beginning of the systolic phase; the pressure oscillations during the diastole reflect the oscillations of the aortic flow during diastole. The oscillations are likely due to the valve’s compliance. The systolic-diastolic difference is about 20 mmHg, and not 40 mmHg as physiological, maybe due to the fact that the compliance during the experiments was set at a too high value.

The peak delivery tube pressures for SV=70 mL and every heart rate are reported in Table 4.2. As expected, the higher is the heart rate, the higher is the pressure in the delivery tube.
Figure 4.6: Aortic pressure (top, orange) and aortic flow rate (bottom, green) for $SV=70\ mL$ and different $HR$ in Configuration C.

Figure 4.7: Comparison between pump output (yellow) and aortic flow rate (green) for 70 mL $SV$ and different $HR$, Configuration C.

<table>
<thead>
<tr>
<th>Heart rate (bpm)</th>
<th>40</th>
<th>60</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak delivery tube pressure (mmHg)</td>
<td>173</td>
<td>236</td>
<td>338</td>
</tr>
</tbody>
</table>

Table 4.2: Peak delivery tube pressures for 70 mL $SV$ and different $HR$, Configuration C.
4.3.2 Influence of an additional resistance

The results for configuration D are shown in Figure 4.8.

The **aortic flow** presents a physiological waveform only in the 60 bpm case. The flow in 40 bpm presents a backflow reaching -2 L/min, as expected from the simulations. For 80 bpm, we see a backflow in the early-diastole, and a peak in the end diastole phase. The situation is not acceptable except for 60 bpm. Also for that heart rate and for 80 bpm, the systolic peak is lower with respect to the pump output, as shown in Figure 4.9.

The **aortic pressure** presents an almost-physiological form, but with a systolic-diastolic difference which is not physiological. The systolic-diastolic difference is about 15 mmHg in 70 mL stroke volume - 60 bpm heart rate case.

The **pressure peaks**, in Table 4.3, are higher than the previous situation. That should be avoided because it could lead to failure of the connections between the pump and the delivery tube.

![Figure 4.8: Aortic pressure (top, orange) and aortic flow rate (bottom, green) for SV=70 mL and different HR in Configuration D.](image-url)
4.3.3 Influence of two valves and an additional resistance

The results in Figure 4.10 show no improvement with respect to the previous configurations, except in 60 bpm heart rate case, which displays physiological waveforms with no backflow and negligible oscillations in the pressure.

The experimental set-up does not behave as predicted in 40-bpm case. As a matter of fact, the pressure upstream the valve is higher than the downstream pressure (see Figure 4.12), hence the valve does not close during diastole, leading to backflow, and making the configuration to behave as the configuration D for 40-bpm heart rate. This results suggest that this is a case in which the over-underestimation of the parameters due to model simplifications matters, and therefore it should be fixed.
[Figure 4.10: Aortic pressure (top, orange) and aortic flow rate (bottom, green) for $SV=70 \text{ mL}$ and different $HR$ in Configuration E.]

[Figure 4.11: Comparison between pump output (yellow) and aortic flow rate (green) for $70 \text{ mL SV}$ and different $HR$, Configuration E.]

<table>
<thead>
<tr>
<th>Heart rate (bpm)</th>
<th>40</th>
<th>60</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak delivery tube pressure (mmHg)</td>
<td>206</td>
<td>250</td>
<td>377</td>
</tr>
</tbody>
</table>

[Table 4.4: Peak delivery tube pressures for $70 \text{ mL SV}$ and different $HR$, Configuration E.]
4.3.4 Considerations on the best configuration for the application

In the previous paragraphs, the three configurations were showed. Configuration C displays almost physiological flow rate and pressure waveforms in aortic position. The term physiological means that the curve should have some characteristic, as stated in paragraph 2.4, Design specifications: a flow rate curve is considered physiological when it displays a peak in the systolic phase, and a zero-flow rate in the diastolic phase; the pressure is considered physiological if it displays a sphygmic shape, increasing in the systolic phase and slowly decreasing during diastole. The aortic pressure in the diastole phase shows some oscillations, and a marked dicrotic notch due to the high amount of backflow of the valve. Configuration D showed that the presence of a resistance dampens the oscillations, which were present in configuration C; however, the waveforms were not physiological. The inclusion of both elements in configuration E led to the lack of closure of the valve during the diastole for some heart rates, which stresses the need of an adjustable resistance.

The mock loop is intended to be used in MRI rooms, which require versatile and easily manageable set-ups; therefore, having an adjustable resistance, to be adjusted every time the pumping conditions are changed, does not comply with this design specification. Moreover, the system was thought for the testing of aortic valve applications, so, as shown from Configuration E, a resistance upstream the valve could corrupt the correct behaviour of a prosthetic valve. Finally, both in configurations D and E, the pressures in the delivery tube are higher with respect to configuration C, which leads to safety problems.
For those reasons, the best configuration out of the three cases in terms of flow and pressure curves is configuration C. In the following section the hemodynamic assessment is shown for configuration C.
4.4 Hemodynamic assessment

In this paragraph, the hemodynamic assessment for configuration C is shown. The pressure and flow-related parameters are shown and discussed.

5.1.1 Flow and pressure-related parameters

In the following Figure 4.13 the results for aortic flow rate and pressure in configuration C are shown.

[Figure 4.13: Aortic pressures (orange) and flow rates (green) in configuration C, for the imposed heart rates of 40, 60, and 80 bpm, and for the different stroke volumes of 30, 50, 70 mL.]

5.1.1.1 Flow rates

In the Table 4.5, all flow-related parameters are shown. The stroke volumes of the imposed flow rate and the aorta phantom are comparable. The average aortic flow is coherent with the physiological one.
<table>
<thead>
<tr>
<th>Imposed stroke volume (mL)</th>
<th>Imposed heart rate (bpm)</th>
<th>SV – pump output (mL)</th>
<th>SV – aorta phantom (mL)</th>
<th>Backflow of aortic valve (mL)</th>
<th>Average aortic flow (mL)</th>
<th>Peak of systolic aortic flow (L/min)</th>
<th>Systolic aortic flow time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>40</td>
<td>25.8</td>
<td>26.9</td>
<td>-2.97</td>
<td>1.79</td>
<td>6.64</td>
<td>0.51</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>26.7</td>
<td>28.7</td>
<td>-2.11</td>
<td>2.87</td>
<td>7.81</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>26.9</td>
<td>29.2</td>
<td>-1.65</td>
<td>3.89</td>
<td>10.6</td>
<td>0.31</td>
</tr>
<tr>
<td>50</td>
<td>40</td>
<td>45.5</td>
<td>44.6</td>
<td>-4.78</td>
<td>3.06</td>
<td>10.6</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>45.4</td>
<td>48.4</td>
<td>-2.23</td>
<td>4.85</td>
<td>12.8</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>46.00</td>
<td>47.3</td>
<td>-3.18</td>
<td>6.31</td>
<td>17.3</td>
<td>0.32</td>
</tr>
<tr>
<td>70</td>
<td>40</td>
<td>61.3</td>
<td>65.2</td>
<td>-5.21</td>
<td>4.03</td>
<td>15.1</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>65.9</td>
<td>63.6</td>
<td>-6.15</td>
<td>6.32</td>
<td>17.5</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>66.0</td>
<td>65.2</td>
<td>-4.79</td>
<td>8.69</td>
<td>23.9</td>
<td>0.32</td>
</tr>
</tbody>
</table>

[Table 4.5: Evaluated flow parameters for different HRs and SVs.]

In Figure 4.14 the comparison between the waveforms of the pump output and the aortic flow rate is shown for every heart rate and stroke volume. The systolic peak of the aortic flow is higher than the peak of the pump output in 40-bpm case, while it is lower in 60-bpm and 80-bpm heart rates. That is likely due to the way peaks at different frequencies are transmitted inside the delivery tube.
In Figure 4.15 the amount of backflow across the aortic valve is shown. The backflow is substantial in the case of 70 mL. In general, the higher the stroke volume, the higher the backflow; while the opposite is true for the heart rate. Since the backflow is evaluated as the integral of the negative aortic flow in diastolic phase, and since the diastolic phase is quicker
the higher is the heart rate, the volume of backflow is lower. The high backflow is likely due to the valve’s performance.

In Figure 4.16 the systolic time for different heart rates and stroke volumes is shown, in comparison with the systolic time of the pump output. In Figure 4.7 the peak of systolic flow rate with respect to the peak of imposed flow rate is shown. The systolic peak rises with rising SVs and HRs, while the systolic time decreases, which is physiologically accurate. The systolic time stays almost the same for different SV and the same HR.
[Figure 4.16: Comparison of systolic times of aortic and pump output for different HR and SV.]

[Figure 4.17: Comparison between systolic peaks of aortic flow rate and pump output for different HR and SV.]
The aortic flow displays less high frequency oscillations with respect to the pump output. As a matter of fact, the delivery tube acts as a low-pass filter, as the Bode diagram in Figure 4.18 shows.

![Bode Diagram](image)

[Figure 4.18: Bode diagram of the delivery tube. The magnitude in dB, the phase is in radians. The frequency axis units of measurement is in Hz, in a logarithmic scale.]

The problem with having two valves in a circuit upstream and downstream a compliant element such as the delivery tube, respectively, is that some volume of water may be accumulated in the tube. As a matter of facts, the stroke volumes are not equal (Figure 4.19): however, their difference can be considered negligible and can be due to errors from the measurements.
The average flow rate (Figure 4.20) is almost the same between imposed flow rate and aortic flow rate, as expected.
5.1.1.2 Pressures

The pressure-related parameters are shown in Table 4.6.

<table>
<thead>
<tr>
<th>Imposed stroke volume (mL)</th>
<th>Imposed heart rate (bpm)</th>
<th>Peak delivery tube pressure (mmHg)</th>
<th>Average aortic pressure (mmHg)</th>
<th>Systolic-diastolic pressure difference (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>40</td>
<td>102</td>
<td>49.5</td>
<td>6.62</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>146</td>
<td>45.1</td>
<td>9.07</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>195</td>
<td>64.2</td>
<td>12.0</td>
</tr>
<tr>
<td>50</td>
<td>40</td>
<td>143</td>
<td>72.2</td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>172</td>
<td>82.8</td>
<td>13.7</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>260</td>
<td>97.2</td>
<td>19.4</td>
</tr>
<tr>
<td>70</td>
<td>40</td>
<td>173</td>
<td>79.6</td>
<td>17.9</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>236</td>
<td>103</td>
<td>19.6</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>338</td>
<td>132</td>
<td>27.9</td>
</tr>
</tbody>
</table>

[Table 4.6: Pressure parameters in configuration C.]

The higher the heart rate/stroke volume, the higher are the average pressures and systolic-diastolic pressure difference. This is coherent with the real situation.

The **systolic-diastolic pressure difference** never reaches the physiological value of 40 mmHg. The not-physiological systolic-diastolic pressure difference is probably due to two reasons: the high value of the compliance set during the experiment, which does not allow the diastolic pressure to decrease, and the high pressure drop across the aortic valve.

The **average aortic pressure** is physiological in 70 mL stroke volume and 60 bpm.

The **peak pressure in the delivery tube**, measured just downstream the service valve, increased with growing heart rates and stroke volumes, as expected. The higher value (338 mmHg) is measured with 70 ml stroke volume and 80 bpm heart rate. For that reason, having a stroke volume higher than 70 ml or a heart rate higher than 80 bpm may be a risky situation regarding the connections downstream the pulsatile pump; due to safety reasons, no SV higher than 70 mL and HR higher than 80 bpm were tested.
5.1.2 Comparison with simulations

In the following figure, the pressure and flow rate curves computed by the model are shown for SV=70 mL, HR=60 bpm as an example.

The flow curves are well predicted. The dynamic backflow of the aortic valve is missing in the model because the valve is treated as an ideal variable resistance, while the real valve’s leaflets take some time to close properly. The peak of the aortic flow was overestimated of around 3 L/min, while the pressures averages were underestimated by 10 mmHg, consistently with the results found in section 4.1.

![Comparison between pressure and flow rate curves computed by the model and the one observed during the experiment.](image)
5.1.3 Final considerations

The model was used in order to understand if the inclusion of a valve in aortic position could lead to improvement in the pressure and flow rate curves. The backflow previously seen in the configuration A of the circuit for the different heart rates is totally avoided by the valve’s presence. The aortic pressure presents an almost physiological curve, while it does not reach the proper 40 mmHg systolic-diastolic difference.
5. CONCLUSIONS AND FUTURE DEVELOPMENTS

5.2 Conclusions

The aim of this work was to design an MRI-compatible mock loop for aortic-valve applications, with easily available and replaceable materials, easy to assemble and disassemble and manageable during its functioning.

The challenges resided in the compatibility of the mock loop’s elements with the electromagnetic field generated by the MRI scanner, which led to constraints on the placement of the pulsatile pumping system and the control system, mostly made by non-MRI-compatible materials. After an analysis of the state of the art, the decision was to design the mock loop with the intention of placing the pumping and control systems in the control room, while the test section was intended to be placed inside the scanner. This way the mock loop could be used also in non-research-oriented hospitals. The pumping system was set in order to provide a physiological systolic waveform, thanks to a service valve, to avoid having negative pressures at the outlet of the pump. The distance between the pumping system and the test section was covered by tubes made of silicone rubber, carrying the fluid in and out the MRI-room. The tube’s material was chosen both for its MRI-compatibility and in order not to have too high pressures at the outlet of the pump, for safety reasons.

The behaviour of the circuit in its preliminary form did not comply with the design specification of providing physiological flow rates and pressures in the test section. Particularly, the flow rate in the test section appeared different for different heart rates, and the waveforms were not physiological in most conditions, due to the distortion of the waveform in the tube as a consequence of the tube’s high compliance and inertance. The aortic pressure exhibited the same behaviour, with non-physiological oscillations and distortion. Hence, different elements were added to the mock loop for it to comply to the
design specifications. The inclusion of these elements was simulated with the aid of a lumped parameter model.

The model was first verified through experimental verification, and then used to assess three different configurations, which corresponded with the inclusion of an additional valve in the test section (configuration C), the inclusion of a resistance in the distal part of the delivery tube (configuration D) and, finally, the inclusion of both the elements (configuration E). These configurations were later tested. Among the three configurations, configuration C was chosen as the best for the application. For this configuration, the fluid-dynamic parameters were evaluated with respect to a physiological reference.

Overall, the lumped-parameter model seemed to provide good results in terms of predicting the dynamic behaviours of pressure and flow rates. It did not predict with high accuracy parameters such as peak or average flow and pressure, which were often under- or overestimated. This is likely due to the simplifications used in the lumped parameters model. Nonetheless, the model was detailed enough to predict different circuit configurations, except for one case.

With the addition of a second valve, the backflow which was systematically present in the initial configuration of the circuit for the different heart rates was totally avoided by the valve’s presence, and the flow rate in the test section could be considered close to a physiological behaviour. The differences in the flow parameters with respect to the pump output’s parameters were negligible, except for an accumulation of fluid in the delivery tube in time computed by the differences between the stroke volume in the inlet and at the outlet of the tube. However, the difference for few millimetres was negligible and likely related to measurements errors. At 60 bpm heart rate and 70 mL stroke volume, the aortic pressure presented an almost physiologically-shaped curve with mean value of 100 mmHg and systolic-diastolic difference of 20 mmHg, which can be considered acceptable. The aortic pressure showed some oscillations likely due to the presence of the compliant valve.

The presence of an additional resistance allowed the dampening of unwanted oscillation and a reduction of the distortion of the waveforms. However, the flow rate was considered to have a physiological waveform only for 60 bpm heart rate. Moreover, the pressures at the outlet of the pump resulted up to almost 400 mmHg, 50 mmHg higher than the configuration with just the additional valve. A too high pressure could lead to a failure of the connections
between the pump and the tube. The addition of the second valve in aortic position to this configuration provided some advantages regarding the backflow, but for some heart rates the valve did not close properly during diastole.

For every configuration, the pressure upstream the aortic valve did not show a physiological waveform due to the presence of the service valve.

The results from configuration D and E suggest that probably an adjustable resistance with respect to the imposed heart rate would be needed, in addition to the second valve, in order for the circuit to work at its best with every heart rate. The mock loop is intended to be used in MRI-rooms, which require versatile and easily manageable set-ups; therefore, having an adjustable resistance, to be adjusted every time the pumping conditions are changed, does not comply with this design specification. Moreover, the system was thought for the testing of aortic valve applications, so, as shown from Configuration E, a resistance upstream the valve could interfere with the correct behaviour of a prosthetic valve.

In conclusion, the configuration C layout apparently complies with the design specifications, as it displays almost-physiological waveforms in the aorta phantom position, the components are easily available and replaceable, and the circuit can be easily assembled, disassembled, and managed during the acquisitions. The mock loop can be used to assess the fluid velocity field due to the presence of a prosthetic valve, and with some adjustments to the afterload it could be used for pulmonary circulation too.

5.3 Future developments

The lumped parameter model should be more detailed, in terms of the choice of the parameters, and include the presence of the non-linear behaviour of the elements and connections. Moreover, a non-ideal valve behaviour should be considered to account for the backflow. As a possible alternative approach to the one adopted in this work, a reverse-engineering approach might be tried, by using the transfer function of the delivery tube to compute the wanted pump input in order to have the wanted flow output in the test section, using the model developed on Simulink®.
Since the adding of a resistance in the distal part of the delivery tube seems to inhibit the valve’s closing behaviour during diastole in certain conditions, the use of such solution should be further analysed. A possible solution might be including the resistance in other positions of the delivery tube.

Moreover, a commercial valve should be tested instead of the aortic valve used in this work, and the tests should be carried out with a mixture of glycerine and water as a fluid, to simulate the blood’s behaviour. Future works on the mock loop should include a phantom of the aorta anatomically representing the real geometry of the vessel.

Some elements of the circuit part intended to be placed inside the MRI-scanner are made of metallic materials, such as the afterload screws. These elements should be substituted with MRI-compatible elements. The mock loop should be tested in the MRI-room, and MRI-acquisitions should be analysed in comparison with CFD simulations.
BIBLIOGRAPHY


APPENDIX A

The lumped parameter model was implemented on Simulink® (The MathWorks, Inc.). In the following figures, the block diagram of the model is shown. Later, the model equations are shown.

Input flow – cardiac cycle
Service valve

Delivery tube (and additional resistance)
Aortic valve

Afterload
Model equations

\[
\begin{align*}
\frac{dp_{v,in}}{dt} &= \frac{Q_s - Q_{in}}{C_s} \\
\frac{dp_{vd,1}}{dt} &= \frac{Q_{in} - Q_{d,1}}{C_d/6} \\
\frac{dp_{vd,2}}{dt} &= \frac{Q_{d,1} - Q_{d,2}}{C_d/6} \\
\frac{dp_{vd,3}}{dt} &= \frac{Q_{d,2} - Q_{d,3}}{C_d/6} \\
\frac{dp_{vd,4}}{dt} &= \frac{Q_{d,3} - Q_{d,4}}{C_d/6} \\
\frac{dp_{vd,5}}{dt} &= \frac{Q_{d,4} - Q_{d,5}}{C_d/6} \\
\frac{dp_{vd,ao}}{dt} &= \frac{Q_{d,5} - Q_{ao}}{C_d/6} \\
\frac{dp_c}{dt} &= \frac{Q_{ao} - Q_c}{C} \\
\frac{dp_{v,ao}}{dt} &= \frac{Q_{d,3} - Q_{d,4}}{C_d/6} \\
p_{vd,1} &= p_{vd,1} + \frac{R_{vd}}{6} (Q_{d,3} - Q_{d,4}) \\
p_{vd,2} &= p_{vd,2} + \frac{R_{vd}}{6} (Q_{d,4} - Q_{d,5}) \\
p_{vd,3} &= p_{vd,3} + \frac{R_{vd}}{6} (Q_{d,5} - Q_{d,6}) \\
p_{vd,4} &= p_{vd,4} + \frac{R_{vd}}{6} (Q_{d,6} - Q_{d,7}) \\
p_{vd,5} &= p_{vd,5} + \frac{R_{vd}}{6} (Q_{d,7} - Q_{d,8}) \\
p_{ao} &= p_{v,ao} + \frac{R_{vd}}{6} (Q_{d,8} - Q_{d,9}) \\
dQ_{in} &= \left(p_{in} - p_{d,1} - \left(\frac{R_{d}}{12} * Q_{in}\right)\right)/(L_d/12) \\
dQ_{d,1} &= \left(p_{d,1} - p_{d,2} - \left(\frac{R_{d}}{6} * Q_{d,1}\right)\right)/(L_d/6) \\
dQ_{d,2} &= \left(p_{d,2} - p_{d,3} - \left(\frac{R_{d}}{6} * Q_{d,2}\right)\right)/(L_d/6) \\
dQ_{d,3} &= \left(p_{d,3} - p_{d,4} - \left(\frac{R_{d}}{6} * Q_{d,3}\right)\right)/(L_d/6) \\
dQ_{d,4} &= \left(p_{d,4} - p_{d,5} - \left(\frac{R_{d}}{6} * Q_{d,4}\right)\right)/(L_d/6) \\
dQ_{d,5} &= \left(p_{d,5} - p_{d,6} - \left(\frac{R_{d}}{6} * Q_{d,5}\right)\right)/(L_d/6) \\
dQ_{v,ao} &= \left(p_{v,ao} - p_{c} - \left(\frac{R_{d} + R_{vd} + R_{vd,ao} + R_{c}}{12} * Q_{ao}\right)\right) \\
&\quad /((L_d/12 + L_{ao})/L_r) \\
dQ_r &= \left(p_{c} - (R_{p} + R_{r}) * Q_{r}\right)/L_r 
\end{align*}
\]
APPENDIX B

The model of the delivery tube was chosen taking as a reference the experimental results from the configuration A of the circuit.

The circuit was tested in order to evaluate the accuracy of the model in simulating the dynamic behaviours occurring in the tube.

The earlier simulations with either one T-model or one π-model (shown in Figure B.1) as model for the delivery tube suggested that the tube is too long for the single T- or π-model to be able to describe all the dynamic behaviours and changing of the waveforms that happen within it, so a strict lumped parameter model is not detailed enough. The idea is to treat the delivery tube as if it is composed by a series of a number of shorter tubes. In other words, the tube can be interpreted not as one lumped set of resistance, inertance and compliance but as a series of a different number of models. Since resistance, inertance and compliance values are directly proportional to the length of the tube, the models put in series should exhibit parameters normalized from the length.

Since:

\[ L_{element} = \frac{L_{tube}}{n} \]

Where \( n \) is the number of elements, then:

\[ R \propto l \rightarrow R_{element} = \frac{R_{tube}}{n} \]

\[ L \propto l \rightarrow L_{element} = \frac{L_{tube}}{n} \]

\[ C \propto l \rightarrow C_{element} = \frac{C_{tube}}{n} \]

The resulting model which fit the experimental results in the best way is composed by six T-models in series. The T-model is preferable with respect to the π-model because it shows the
dynamic peak due to the inertance in the inlet branch, even though the overall difference is minimum.

[Figure B.1: Left: T-model. Right: π-model.]
APPENDIX C

As a matter of fact, the starting point of the work was to be in the situation of Piatti et al. [17], hence the same silicone tubes were adopted to provide the pulsatile flow and cover the distance between the instrumentation and the aorta phantom. Simulations were carried out to assess if maybe it was worth the idea of taking into consideration other materials.

Since the length of the tube is fixed, the degrees of freedom in the choice of the tube were its diameter and its material in terms of elastic modulus. The diameter was set to 25 mm in order to facilitate the connections to the other elements of the circuit.

Three values of compliance were evaluated: the one evaluated through the experiments, and the remainder one order of magnitude higher and lower, respectively.

The presence of a compliant element such as the delivery tube downstream the pump have consequences on the waveforms and the medium values of the imposed flow rate, which may differ from the one imposed from the volumetric pump, since a part of the fluid entering the tube is not rigidly transported through the tube but it is used to deform elastically the wall of the tube. Hence having a rigid tube means that the waveforms are less distorted [21]. However, when simulating a lower compliance, the inlet pressure reaches a peak of 500 mmHg.
Even though having rigid tubes allow the rigid transportation of the fluid, while compliances introduce oscillations in the waveform, having a rigid tube was not taken into consideration for two reasons:

- The first is the easiness of disassemble the circuit. Once the experiment is over, the circuit must be emptied from the fluid. Approximately 12 litres of water are needed to fill the whole circuit, and the most part of this volume is segregated into the delivery and return tubes. The more the tubes are rigid, the more difficult is to empty them. Moreover, the flexibility of the tube allows the clamping of it in case it is needed.

- The inlet pressure, at the outlet of the pump, is around 200 mmHg. With a compliance of one higher order of magnitude, the maximum value is three times that. That is, for safety reason, not convenient, because it rises the risk for leakage or failing of the connections between elements.

On the other hand, simulations with a more flexible tube suggests that the dampening of the flow waveform would be too high, with the resulting waveform in the aortic phantom being almost stationary, as shown in Figure C.2.
Once the order of magnitude of the compliance was assessed, a way of proceeding would be to find the exact value, in the same order of magnitude, for the elastic modulus that exhibits the best behaviour for the application. However, when dealing with polymers, their mechanical properties depend on the way they are made and what type of transformation they have been subjected to, so for the same material they may vary or may not even be available. That means that even if a proper compliance value was found, there is no guarantee that it would correspond to a particular tube on the market.

The results show that there is no sufficient proof to justify the use of another tube.