Influence of Outlet Boundary Conditions on Cerebrovascular Aneurysm Hemodynamics

by

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David F. Katz

Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Department of
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2016
ABSTRACT

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Abstract

Computational fluid dynamic (CFD) studies of blood flow in cerebrovascular aneurysms have potential to improve patient treatment planning by enabling clinicians and engineers to model patient-specific geometries and compute predictors and risks prior to neurovascular intervention. However, the use of patient-specific computational models in clinical settings is unfeasible due to their complexity, computationally intensive and time-consuming nature. An important factor contributing to this challenge is the choice of outlet boundary conditions, which often involves a trade-off between physiological accuracy, patient-specificity, simplicity and speed. In this study, we analyze how resistance and impedance outlet boundary conditions affect blood flow velocities, wall shear stresses and pressure distributions in a patient-specific model of a cerebrovascular aneurysm. We also use geometrical manipulation techniques to obtain a model of the patient’s vasculature prior to aneurysm development, and study how forces and stresses may have been involved in the initiation of aneurysm growth. Our CFD results show that the nature of the prescribed outlet boundary conditions is not as important as the relative distributions of blood flow through each outlet branch. As long as the appropriate parameters are chosen to keep these flow distributions consistent with physiology, resistance boundary conditions, which are simpler, easier to use and more practical than their impedance counterparts, are sufficient to study aneurysm
pathophysiology, since they predict very similar wall shear stresses, time-averaged wall shear stresses, time-averaged pressures, and blood flow patterns and velocities. The only situations where the use of impedance boundary conditions should be prioritized is if pressure waveforms are being analyzed, or if local pressure distributions are being evaluated at specific time points, especially at peak systole, where the use of resistance boundary conditions leads to unnaturally large pressure pulses. In addition, we show that in this specific patient, the region of the blood vessel where the neck of the aneurysm developed was subject to abnormally high wall shear stresses, and that regions surrounding blebs on the aneurysmal surface were subject to low, oscillatory wall shear stresses. Computational models using resistance outlet boundary conditions may be suitable to study patient-specific aneurysm progression in a clinical setting, although several other challenges must be addressed before these tools can be applied clinically.
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1. Introduction

Cerebral aneurysms are abnormal dilatation of arterial blood vessel walls due to pathological weakness (1). When left untreated, aneurysms continue to grow, leading to further wall weakness and a high chance of rupture, an event that causes hemorrhagic stroke and has a mortality rate of 40%. The fact that two of every three people who survive an aneurysmal rupture suffer from neurological deficits or disabilities is equally as concerning (2).

Several factors may contribute to aneurysm progression and rupture, including vascular cell biology, genetics, and hemodynamics (3). The latter is a central reason that is poorly understood; with very little scientific agreement on how abnormal biomechanical forces, pressures and stresses applied by incident blood flow may drive cellular or tissue-level responses that cause initial aneurysmal growth, enlargement and rupture. Elucidating the role of biofluid mechanics in vascular remodeling and aneurysm pathophysiology is of critical importance, as it could drive the development of computational tools that can help improve clinical decisions based on estimated hemodynamic parameters. As such, computational studies of blood flow in patient-specific geometries can be valuable tools to evaluate patient condition, assess risks, and predict the outcome of neurovascular intervention before a procedure is performed. These studies may also provide a foundation for the development of more effective minimally invasive devices for neurovascular intervention.
One of the main difficulties of using computational fluid mechanics in a clinical setting is the feasibility of running these simulations at the point of care. Two critical limitations include the computational power required to perform these simulations within a reasonable time frame, as well as the need for patient-specific measurements. These issues are prevalent when choosing boundary conditions to impose at the outlets. For example, using patient-specific flow rates, pressure waveforms or velocity profiles at the outlets would be impractical in a clinical setting due to the need for additional patient-specific measurements.

The choice of which boundary conditions to prescribe at the outlets is largely dependent on physiological accuracy, practicality and speed of solution convergence. Several studies in the past have imposed constant pressures (zero-traction) at the outlets (4-8). More recently, resistance and impedance models have become increasingly popular (9-10). Although the accuracy of constant pressure, resistance and impedance boundary conditions has been studied in the past for various vascular geometries (9), there are no studies evaluating how these boundary conditions may affect hemodynamic parameters relevant to the aneurysm growth, progression, and risk of rupture. Here, we apply two different resistance boundary conditions and a simple first-order Windkessel impedance model to assess how the choice of outlet boundary conditions may affect parameters relevant to aneurysm pathophysiology. We focus on a patient-specific Internal Carotid Artery (ICA) saccular aneurysm in close proximity to the Anterior Cerebral Artery
(ACA) and Middle Cerebral Artery (MCA) bifurcation. We test two different resistance boundary conditions: one that assumes equal resistances through the ACA and the MCA (50/50 resistance), and another that forces a 60%/40% flow rate distribution through the MCA and the ACA respectively (60/40 resistance), consistent with previous reports in the literature (11-12). Using this method, we evaluate how outlet flow distributions affect wall shear stresses, pressures and blood flow velocities. For the impedance boundary condition, we also use parameters that force a 60%/40% flow rate distribution through the MCA and the ACA in order to make a fair comparison and assess how the nature of the boundary condition (resistance or impedance), affects hemodynamic parameters relevant to aneurysm pathophysiology.

1.1 Hemodynamic Parameters

1.1.1 Wall Shear Stress

One of the most important hemodynamic parameters in our understanding of aneurysm pathophysiology is wall shear stress. Studies in the past have shown that endothelial cells are sensitive to wall shear stresses and may lead to vascular remodeling through various mechanotransduction pathways. For example, elevated wall shear stresses are associated with overproduction of vasoactive molecules such as nitric oxide (NO) as part of a negative feedback loop that increases blood vessel diameter to effectively reduce wall shear stresses back to normal physiological values. Overexpression of NO results in reduced vascular wall tone and thickness via apoptosis of smooth muscle cells (13).
Abnormally high wall shear stresses at local regions may also physically damage the internal elastic lamina of blood vessels by over-stretching collagen and elastin fibers, forcing them to experience elevated internal stresses and abnormally high mechanical loading throughout each cardiac cycle (3), and potentially resulting in the formation of blebs which have been associated with an increased risk of rupture (14). High wall shear stress may also stimulate overproduction of matrix metalloproteinases, leading to further destructive remodeling of the internal elastic lamina (15-17). Ultimately, high local wall shear stresses may weaken the structure of the blood vessel wall and be conducive to the initiation of aneurysm growth and an increased risk of aneurysmal rupture.

It is also known that uniform wall shear stress, within normal physiological limits, stabilizes and limits cell proliferation and apoptosis, whereas low wall shear stress may lead to neointimal hyperplasia (18) and blood vessel regression via endothelial cell apoptosis (17,19). Low shear stresses also result in reduced production of NO, resulting in endothelial cell dysfunction (3). Moreover, endothelial cells may also be sensitive to directional variations in wall shear stress. Laminar wall shear stresses cause endothelial cell alignment, whereas low, oscillatory stresses result in irregular morphologies that may cause pathological weakness (18). Directional changes in wall shear stresses are measured quantitatively by the oscillatory shear index (OSI), a dimensionless parameter ranging from 0 to 0.5 that computes the magnitude of wall shear stress fluctuations (20).
In combination with low blood flow velocities, oscillatory wall shear stresses and non-uniform endothelial cell alignments may cause stagnation of red blood cells, platelets and leukocytes along the vessel surface. The presence and infiltration of white blood cells leads to an inflammation cascade that ultimately releases enzymes that digest extracellular proteins and weaken the structural integrity of the blood vessel wall (21). The spatial derivative of the wall shear stress in the direction of flow is often also considered as a potential risk factor for aneurysm initiation and progression. However, its effect on vascular biology is not well understood and its correlation with aneurysm rupture is not robust, with some studies finding that there is a strong correlation (8, 22), and others finding minimal to no correlation (23).

There is some controversy as to whether high wall shear stress or low wall shear stresses result in aneurysm enlargement and rupture. However, evidence suggests that the aneurysmal initiation phase is driven by high wall shear stress, and subsequent progression continues due to two possible pathways, the first involving low wall shear stresses at the bleb of aneurysms, resulting in inflammatory processes that weaken the blood vessel wall, and the other involving high wall shear stresses driven by high speed impinging flow at small, focal areas (24). Either way, it is clear that wall shear stresses play a fundamental role in aneurysm pathophysiology, and that studying their
distribution throughout the surface of aneurysms and adjacent blood vessels is critical to evaluating aneurysm development and rupture risk. Wall shear stress and the oscillatory shear index are computed and analyzed in this study.

1.1.2 Blood Velocity Patterns and Impinging Jet Flow

Blood velocity profiles are responsible for applied wall shear stresses and pressures, and are therefore also involved in aneurysm pathophysiology. Some factors that have been associated with aneurysm progression and rupture include flow complexity, with complex flows consisting of multiple vortices or recirculation zones, flow stability, with instability being measured by variations in flow patterns and vortex structures over a single cardiac cycle, and the flow impingement zone, described as the region on the aneurysm wall that is hit by the inflow stream (21). If the inflow jet has a narrow impingement zone, the area of impingement is less than 50% of the total aneurysmal area. On average, flow in healthy vessels is steady and stable, with only transient vortices, if any. However, in aneurysms there is a higher incidence of blood flow recirculation zones that persist throughout the cardiac cycle. Computational studies suggest that ruptured aneurysms are more likely to have complex and unstable flows with narrow impingement regions (21, 25-26). In this study, we analyze flow patterns in terms of complexity, stability and impingement zone qualitatively, as part of a comparison between the different prescribed outlet boundary conditions.
1.1.3 Blood Pressure and Local Pressures at the Aneurysmal Surface

It is widely known that systemic hypertension is a risk factor for aneurysmal growth and rupture. Hypertension leads to higher impinging flow velocities and mechanical stresses, resulting in physical damage to the aneurysm wall as well as overproduction of matrix metalloproteinases that cause destructive vascular remodeling. High systemic blood pressure may also affect the behavior of the renin-angiotensin hormone system, causing vascular inflammation and further remodeling (27). Although the correlation between systemic hypertension and aneurysm pathophysiology is well understood, the role of local pressures incident on the walls of aneurysms has not been studied extensively. This is partially due to the limitations of computational studies with regard to the boundary conditions prescribed at the outlets. The most popular outlet boundary condition, constant pressure, results in unrealistic pressure fields throughout the vasculature, limiting the reliability of studies that attempt to correlate local pressures with risk for aneurysmal rupture (9). A previous study by Shojima et al. reported elevated local pressures at regions of flow impingement, accompanied by high wall shear stresses distal to the region of elevated pressure (28). This study did not find any correlation between elevated local pressures and risk for rupture, based on how low the magnitudes of local pressures were with respect to systemic blood pressures. However, this correlation may become more prevalent in studies with improved outlet boundary conditions that estimate local pressures within physiological ranges. In this study, we
use resistance and impedance boundary conditions at the outlets to constrain pressure distributions within physiological ranges throughout the entire vasculature.

**1.2 Outlet Boundary Conditions**

**1.2.1 Resistance Boundary Condition**

Resistance is one of the simplest outlet boundary conditions available for cardiovascular simulations, other than the constant pressure boundary condition. It works under the assumption that there is a linear relationship between mean pressure and flow rate given by \( P = QR \), with pressure being spatially constant over the cross-sectional area of the inlet and outlet boundaries. However, pressure is not temporally constrained (9).

The resistance boundary condition improves upon the constant-pressure or traction-free boundary condition by providing a means of controlling flow distributions through each outlet based on downstream resistances. Applying a constant-pressure boundary condition forces flow to be distributed through each outlet branch depending entirely on the geometry of the simulation domain. However, the resistance of downstream vasculature is a dominant factor determining the flow rate distribution across each outlet branch, and the resistance boundary condition gives the ability to account for this using a single parameter. In contrast to traction-free outlets, this boundary condition partially accounts for wave reflection from the downstream vascular system (29).

The constant pressure boundary condition also results in abnormally small pressure pulses with incorrect phase. In contrast, the resistance boundary condition overestimates
the magnitude of the pressure pulse and forces pressure and flow to be in phase, a condition that is also not physiologically accurate (9). However, applying a constant resistance at the outlet results in more realistic pressure fields without sacrificing practicality, as this boundary condition does not require additional patient-specific measurements of flows or pressures. Therefore, despite the disadvantages of the resistance boundary condition, its superior accuracy compared to the traction-free boundary condition and its simplicity make it an attractive option for hemodynamic simulations of blood flow in aneurysms. In this study, we investigate the effects of using resistance boundary conditions on hemodynamic parameters relevant to aneurysm pathophysiology, including wall shear stresses, pressure fields and velocity patterns.

1.2.2 Impedance Boundary Condition

Impedance boundary conditions improve upon the resistance boundary condition by allowing the model to account for the compliance of downstream vasculature, often quantified as a capacitance by electric analogs. Much like the resistance boundary condition, it also gives the ability to control flow distributions through each outlet based on impedance magnitudes, but it has the additional advantage of applying a phase to force pressure to lag behind flow, leading to more physiologically relevant models (9).

Although there are many different types of impedance boundary conditions, one of the most popular, and perhaps the simplest one, is the RCR Windkessel model, a first-order impedance model that reduces the effects of downstream vasculature into three
parameters based on an electric analog: a proximal resistance (Rp), a distal resistance (Rd), and a capacitance (C) as shown in Figure 1 (10).

The RCR boundary condition accounts for the magnitude and arrival time of wave reflection phenomena (29). In addition, previous studies show that pressure waveforms calculated using this boundary condition are similar to physiological curves (9, 30).

![Figure 1: RCR boundary condition](image)

Although the improved accuracy of impedance boundary conditions has been verified based on pressure and flow waveforms at inlets and outlets in various vascular models, its impact on local pressure fields, flow patterns and wall shear stresses as relevant to initiation of aneurysm growth, progression and rupture has not been reported. Moreover, impedance boundary conditions are more complex, require higher computational power and take more cycles to allow flow to stabilize. As such, despite being more accurate, the use of impedance boundary conditions may be undesirable on
patient-specific simulations in a clinical setting. Here, we evaluate if the improved accuracy of the RCR Windkessel impedance boundary condition is significant enough to warrant its use for hemodynamic studies of aneurysm pathophysiology.
2. Methods

2.1 Constructing aneurysm and blood vessel solid models:

The geometry of a giant, ICA aneurysm in a 49 year old, female patient was obtained via 3D rotational angiography, using a contrast injection of 20cm³ over a 5 second period (Figure 1). The reconstructed 3D geometry included the terminal section of the ICA and the initial segments of the ACA and the MCA branches. This model was imported into the open source software MeshLab (31) and MeshMixer (32) for manipulation. More specifically, non-manifold vertices and edges were removed, and the geometry was smoothed out to eliminate visible irregularities arising from measurement and 3D reconstruction errors, which may otherwise introduce non-physiological artifacts in our simulation results. Only segments of the outlet blood vessels proximal to the aneurysm were included to reduce computational power. Finally, planar surfaces were interpolated at the inlet and outlets to close in the volume (Figure 2). We superimposed the original and the final geometry to ensure geometrical similarity and check that all the main curvatures were conserved (Figure 3).

The geometry of the healthy vasculature excluding the aneurysm was obtained using MeshMixer. This process involved removing the aneurysmal volume, bending the outward-facing edges at the neck so that they faced each other, and interpolating a curved surface to close in the gap. Finally, smoothing was done to ensure curvature continuity at the interface between the blood vessel geometry and the curved,
interpolated surface (Figure 4). The final geometry with the aneurysm had 65,738 faces, whereas that of the blood vessels excluding the aneurysm had 54,638 faces. The files were imported as solid models into the open source software package SimVascular (33), which uses TetGen (34) to generate meshes with tetrahedral elements.

Figure 2: Angiogram of patient-specific ICA saccular aneurysm used in our model.
Figure 3: Solid models of diseased vasculature. A- Solid model of aneurysm after manipulation in MeshLab and MeshMixer. B- Manipulated geometry (light grey) superimposed over original 3D geometry obtained via 3D rotational angiography (dark grey).

Figure 4: Solid model of vasculature with the aneurysm removed (in grey). The initial geometry including the aneurysm is shown in pink for comparison.
2.2 Generating mesh geometries

The mesh elements for all geometries were generated with TetGen within SimVascular. The final meshes consisted of 14,441 and 925,097 tetrahedral elements for the geometries excluding the aneurysm and including it respectively (Figure 4).

![Meshes](image)

Figure 5: Left: Mesh of healthy vasculature (excluding aneurysm). Right - Mesh of vasculature including the aneurysm.

2.3 Boundary Conditions

The inlet boundary condition was set as the flow rate at the ICA. Due to lack of patient-specific measurements, we used a generic ICA volumetric flow rate reported in a previous study, obtained by averaging measurements from multiple healthy human
subjects (Figure 5) (35). Womersley velocity profiles were generated from this flow rate using a Fourier series decomposition of 30 modes (see Appendix A).

Figure 6: Inlet boundary condition set as the flow rate at the ICA.

Resistance and RCR boundary conditions were used at the outlets. The resistance values were set to provide a physiologically relevant pressure range at the inlet (70-80/110-120mmHg), with an average pressure of roughly 70mmHg (9). Two different resistance conditions were tested. The first assumed equal resistances at both the ACA and the MCA, a condition that may not be physiologically accurate but is used on occasion if the exact flow distribution is not known. In addition, this assumption results in similar hemodynamic behavior to constant pressure boundary conditions, where the
distribution of blood flowing through each outlet is determined entirely by the geometry of the modeled domain and ignores the influence of the downstream vasculature, which is generally a dominant factor. The parameters for the second resistance boundary condition were chosen to force a flow distribution of 60% through the MCA and 40% through the ACA, consistent with previous physiological observations in healthy humans (11-12).

The impedance boundary condition consisted of the Windkessel RCR model. The parameters chosen for the ACA were adapted from values used previously by Coogan et al. (36), scaled down so that the sum of the proximal and distal resistances was equivalent to the resistance that we prescribed at the ACA for the 60/40-resistance boundary condition. The capacitance was scaled to keep the phase unchanged. The parameters used for the RCR model at the MCA were calculated to keep a blood flow distribution at 60/40 through the MCA and ACA respectively, in order to enable a reliable comparison with the resistance boundary condition. More specifically, the sum of the proximal and distal resistances was made equivalent to the resistance that was prescribed at the MCA in the 60/40-resistance case. For simplicity, the ratio $\alpha = \frac{R_p}{R_p + R_d}$ was assumed to be the same for both outlets. The capacitance at the MCA was adjusted to ensure physiological ranges of blood pressure in this branch. The final parameters for all boundary conditions are shown in Table 1.
Table 1: Outlet boundary condition parameter values

<table>
<thead>
<tr>
<th>Outlet Boundary condition</th>
<th>MCA</th>
<th>ACA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rp  (10^3 dyn s/cm^5)</td>
<td>Rd (10^5 cm^3/dynes)</td>
</tr>
<tr>
<td>50/50 Resistance</td>
<td>-</td>
<td>30.0</td>
</tr>
<tr>
<td>60/40 Resistance</td>
<td>-</td>
<td>24.6</td>
</tr>
<tr>
<td>RCR</td>
<td>2.44</td>
<td>22.2</td>
</tr>
</tbody>
</table>

The units for resistance are 10^3 dyn s/cm^5, while those for capacitance are 10^5 cm^3/dynes.

2.4 Simulations in SimVascular

Simulations were done in the finite element, Navier-Stokes solver svSolver, which is a module of the open source software package SimVascular (37-41). Walls were assumed to be rigid and impermeable, with the no-slip condition applied at the boundaries. Blood was assumed to be homogenous, incompressible and Newtonian, with a viscosity of 0.04 g / (cm s) and a density of 1.06 g/cm^3. For the geometry of the healthy blood vessels, simulations were run for 4 full cardiac cycles with a time step of 2ms for the models with resistance boundary conditions prescribed at the outlets, and for 8 full cardiac cycles with a time step of 1ms for the RCR outlet boundary condition case. For the geometry of the blood vessels containing the aneurysm, a time step of 1ms was used for 4 full cardiac cycles and 8 cardiac cycles for the resistance and RCR outlet boundary conditions respectively. In all cases, we checked for mass conservation at the outlets to ensure that the time step used in each simulation was appropriate. In order to guarantee that our mesh was suitable and our results were accurate, we also constructed less refined tetrahedral meshes, computed the average flow rates at the inlet and outlets, and
compared these values with those obtained using our final mesh to make sure that these values did not change by more than 0.5%. The flow rate and pressure waveforms at the inlet and outlets, as well as their average values, were examined and compared between cardiac cycles to make sure that flow was stable and fully developed. The results of the last simulated cardiac cycle were used in all of our analyses.
3. Results

3.1 Flow Rate and Pressure Waveforms

The flow rate (Figure 7) at the inlet and outlets over a full cardiac cycle was computed for the healthy and diseased states given all relevant outlet boundary conditions. The inlet flow rate remained unchanged regardless of the boundary conditions prescribed at the outlets. As expected, the 50/50 resistance boundary condition showed similar flow rates through both the ACA and the MCA, with an average difference of only 6% between these branches in the healthy geometry and 4% in the diseased, aneurysm model. These differences originate from the geometry of the modeled domain and its intrinsic influence in diverting blood flow through each outlet. The flow rate through the ACA and the MCA for the RCR and 60/40 resistance outlet boundary condition models were virtually identical in both the healthy and diseased cases, constrained to 60% and 40% through the MCA and ACA respectively. This fact confirmed that the parameters used for the RCR model conserved the 60/40-blood flow distribution as intended. The presence of the aneurysm resulted in a minimal change in the flow rate distribution (approximately 1%) for each outlet, regardless of the prescribed outlet boundary conditions (Table 2).

In contrast, the choice of outlet boundary condition did affect the pressure waveform at the ICA, especially at peak systole (Figure 8). In the healthy model, the pressure at peak systole was approximately 140mmHg using the 50/50 resistance outlet boundary
condition, with this pressure decreasing to 135mmHg (3.6% lower) when using 60/40 boundary condition and 100mmHg for the RCR case (28.5% lower). Changes in pressure at peak systole were also observed at the outlets depending on the prescribed outlet boundary condition. At the ACA, the pressure at peak systole was 86.7mmHg using the 60/40 resistance boundary condition and 54.2mmHg when prescribing RCR boundary condition. On the other hand, at the MCA, the pressure at peak systole decreased from 94.6mmHg to 58.4mmHg when changing the boundary condition from 60/40-resistance to the RCR model respectively. Interestingly, the presence of the aneurysm also influenced the peak systolic pressure at the inlet and outlets, with the largest difference being a reduction of up to 15% at the ICA for all prescribed outlet boundary conditions. However, the choice of boundary condition had very little impact on the average pressure at the inlet and outlets over the full cardiac cycle (Table 2). The only substantial change occurred at the MCA, with the average pressure decreasing by 7.5% between the 50/50 case and the 60/40 and RCR cases. The presence of the aneurysm also affected the average pressures at the ICA, MCA and ACA, although its impact was small when compared to its influence on peak systolic pressures. The effect was largest at the ICA, where the average pressure decreased by 5-6% for all boundary conditions between the healthy and diseased models.
Figure 7: Flow rate through the ICA, ACA and MCA given different boundary conditions. Plots a - c show the flow rates in the healthy blood vessels, whereas d - f display the flow rates in the diseased vasculature containing the aneurysm
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50/50 resistance boundary condition  60/40 resistance boundary condition  RCR boundary condition

Figure 8: Average pressure at the ICA, ACA and MCA given different boundary conditions. Plots a - c show the pressure in healthy blood vessels, whereas d - f display the pressure in the diseased vasculature containing the aneurysm.
Table 2: Average flow rate and pressure at ICA, ACA and MCA given different conditions.

<table>
<thead>
<tr>
<th>Resistance</th>
<th>Average Flow Rate (ml/s)</th>
<th>Average Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICA</td>
<td>ACA</td>
</tr>
<tr>
<td>Healthy Vasculature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50/50</td>
<td>4.80</td>
<td>2.25 (47%)</td>
</tr>
<tr>
<td>60/40</td>
<td>4.80</td>
<td>1.92 (40%)</td>
</tr>
<tr>
<td>RCR</td>
<td>4.80</td>
<td>1.92 (40%)</td>
</tr>
<tr>
<td>Diseased Vasculature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50/50</td>
<td>4.80</td>
<td>2.31 (48%)</td>
</tr>
<tr>
<td>60/40</td>
<td>4.80</td>
<td>1.96 (41%)</td>
</tr>
<tr>
<td>RCR</td>
<td>4.80</td>
<td>1.97 (41%)</td>
</tr>
</tbody>
</table>

3.2 Blood Velocity - Patterns and Streamlines

Blood velocity streamlines and velocity heat-maps at cross-sections throughout the geometry were plotted in Figures 9 and 10 for the healthy and diseased models respectively. In the healthy vasculature, the choice of boundary condition had very little influence on blood velocity throughout the cardiac cycle, as was expected from our previous flow rate analysis at the inlet and outlets. Visibly, there was a small increase in
the maximum blood flow velocity at the MCA between the 50/50 and the 60/40 cases, accompanied by an attenuation of blood velocity at the ACA. However, between the 60/40 resistance and the RCR cases, blood flow velocities were very similar at peak systole and peak diastole. Similar trends were observed in the aneurysm model (Figure 10). The choice of using a 50/50 or a 60/40-resistance boundary condition only affected blood flow velocities at small distances away from the outlets. In addition, any velocity differences between the case with prescribed 60/40-resistance outlet boundary conditions and the RCR model were small enough to be negligible at peak systole, peak diastole and throughout the cardiac cycle in general.

Blood flow through the healthy vasculature was laminar, had no vortices or recirculation zones, indicating low complexity, and was highly stable throughout the cardiac cycle. There was no indication of jet flow impinging on the region where the neck of the aneurysm originated. In the aneurysm model, blood flow was also laminar and had a single recirculation vortex that persisted throughout the cardiac cycle, suggesting simple, stable flow (Figure 11). However, the blood flow pattern inside the aneurysmal domain at peak systole showed indications of a narrow inflow jet impingement zone on the aneurysmal surface (Figure 10).
Figure 9: Blood flow velocity (cm/s) in healthy vasculature at peak systole and diastole.
Figure 10: Blood flow velocity (cm/s) streamlines and cross-sections in aneurysm model at peak systole and diastole. Jet inflow from the ICA impinges on a fairly small area of the aneurysmal surface, highlighted with a red arrow.
**Figure 11**: Posterior view of blood flow velocity (cm/s) streamlines in aneurysm model at peak systole.
3.3 Wall Shear Stresses and OSI

Wall shear stresses in the healthy vasculature were particularly high on three regions throughout the cardiac cycle: at the MCA outlet, at the junction between the ICA and the MCA, and at a curved section of the ICA that corresponds to the location of the aneurysmal neck (Figure 12). The only section of high wall shear stress that was affected by the nature of the prescribed outlet boundary condition was the first, at the MCA. In this zone, the maximum wall shear stress was lower and the total area affected by high wall shear stress (>366 dyn/cm² at peak systole) was smaller when using the 50/50 resistance boundary condition compared to the 60/40 and RCR cases. The remaining two regions of high wall shear stress in the healthy vasculature were virtually identical for all prescribed outlet boundary conditions. On the region corresponding to the aneurysmal neck, the maximum shear stress at peak systole was 450 dyn/cm² regardless of the boundary conditions that were imposed at the outlets.

A similar trend was observed when analyzing the time-averaged wall shear stress (TAWSS) over a full cardiac cycle in the healthy vasculature (Figure 13). Regardless of the prescribed boundary conditions at the outlets, 3 main regions of high TAWSS were observed (highlighted in red in Figure 13): adjacent to the outlet at the MCA (region 1), at the ICA-MCA junction (region 2), and at a location on the ICA that coincides with the aneurysmal neck in the diseased model (region 3). The choice of outlet boundary condition did not affect the TAWSS distribution in regions 2 and 3. However, using a
50/50 resistance boundary condition resulted in an underestimation of the maximum TAWSS in region 1, accompanied by a reduction in the area of this zone affected by high wall shear stress. All boundary condition cases predicted a maximum TAWSS of approximately 250dyn/cm² in region 3.

In the diseased model, once again, we only observed a difference in wall shear stresses close to the outlets between the 50/50 and the 60/40 resistance boundary condition cases (Figure 14). There was no difference between the 60/40 and the RCR cases either at peak systole or at peak diastole. We also observed high wall shear stresses at the outlets and at the curved portion of the ICA leading to the ACA/MCA bifurcation. The bulk of the aneurysm, however, was dominated by low wall shear stresses at peak systole and diastole, with only relatively higher wall shear stresses on the regions of the walls where jet inflow impinged.

The TAWSS in the diseased model (Figure 15) also showed similar results to what was observed at peak systole and peak diastole. Only the shear stresses on regions close to the outlets were affected by the choice of outlet boundary conditions. Interestingly, for the 60/40 and RCR boundary condition cases, the presence of the aneurysm increased the average TAWSS around the ACA by roughly 30% when compared to that in the healthy geometry. This percentage was even greater for the 50/50 case (close to 40%). In contrast, at the MCA, the presence of the aneurysm reduced the spatially averaged TAWSS by 15-20% for all cases. The TAWSS analysis also revealed three regions of very
low wall shear stress (< 2 dyn/cm²) on the aneurysm, two surrounding the superior bleb, (Figure 16, top row), and one on the inferior bleb (Figure 16, bottom row). These regions of low wall shear stress correlated reasonably well with regions of high OSI on the aneurysmal surface.
Figure 12: Wall shear stress distribution on healthy vasculature at peak systole and diastole. The aneurysm model is superimposed in grey.
Figure 13: Time-averaged wall shear stress (TAWSS) over a full cardiac cycle in the healthy vasculature, focusing on the outlets (top row), and the neck of the aneurysm (bottom row). Regions of high TAWSS (> 210 dyn/cm²) are highlighted by arrows in red.
Figure 14: Wall shear stresses in aneurysm model at peak systole and diastole.
Figure 15: Time-averaged wall shear stress (TAWSS) over a full cardiac cycle in the aneurysm model: frontal view (top row) and posterior view (bottom row).
Figure 16: Time-averaged wall shear stress (TAWSS) (left) and OSI (right) in aneurysm model given the 60/40-outlet resistance boundary condition. The top row shows a posterior view of the aneurysm, focusing on the superior bleb, and the bottom row exhibits a frontal view, focusing on the inferior bleb. Regions of very low wall shear stress (< 2dyn/cm²) are highlighted by arrows in red. The OSI plots for the models using the other outlet boundary conditions are not included, but they show very similar results to the plots shown here.
3.4 Local Pressures

On the healthy vasculature, local pressures were highest at the inlet and decreased along the length of the vasculature (Figure 17). Regardless of the outlet boundary conditions that were prescribed, the pressure at the MCA was consistently higher than the pressure at the ACA. However, the pressure at the MCA was higher for the 50/50 case than for the 60/40-resistance model. Similarly, the pressure at the ICA was also slightly higher for the former than for the latter at peak systole and peak diastole. The pressure at the ACA was approximately the same in all cases. These observations were anticipated, as they matched with our analysis in Table 2. In addition, the peak systolic pressure along the vasculature was considerably lower for the RCR case relative to that for the 50/50 and 60/40 resistance models. Although this trend was also observed at peak diastole, it was not as pronounced. Elevated pressures were also observed at the zone of flow impingement at the bifurcation between the two outlets.

Despite the significantly lower pressures at peak systole and peak diastole when using the RCR boundary condition, the time-average pressure (TAP) over the full cardiac cycle was identical for the RCR outlet boundary condition and the 60/40-resistance case. In contrast, the TAP distribution when using the 50/50 boundary condition was slightly higher throughout the geometry compared to the other cases, especially at the inlet and the MCA branch.
For the diseased model, the pressure distribution was slightly more complex, although similar trends were observed (Figure 19). Pressure decreased along the length of the geometry, with peaks occurring at the zones of jet inflow impingement on the aneurysmal wall and at the bifurcation between the two outlets, with these pressures being distinctively larger on the 50/50 resistance model. Overall, pressures were higher for the 50/50 case than they were for the 60/40-resistance condition at peak systole and peak diastole. In addition, the pressure at the MCA was visibly lower when using the 60/40-resistance boundary condition. The pressure distribution at peak systole for the RCR case was substantially lower when compared to the other boundary condition cases. This was also observed at peak diastole, but the difference was smaller, analogous to what was observed for the model of healthy vasculature and matching our waveform analysis in Figure 8. Once again, despite these sharp differences at peak systole and diastole, the TAP distributions displayed negligible difference between the RCR and 60/40 cases. For the 50/50 case, the overall pressures were slightly higher when compared to the other two cases.
Figure 17: Local pressures in healthy vasculature at peak systole and diastole.
Figure 18: Time-averaged pressure (TAP) over a full cardiac cycle in healthy vasculature: frontal view (top row) and posterior view (bottom row).
Figure 19: Local pressures in aneurysm model at peak systole and diastole.
Figure 20: Time-averaged pressure (TAP) over a full cardiac cycle in aneurysm model – frontal view.
4. Discussion

In this study, we analyzed hemodynamics in a patient-specific aneurysmal model after prescribing three different boundary conditions at the outlets: resistance boundary conditions imposing identical resistances at the ACA and the MCA (50/50 resistance), resistance boundary conditions forcing 60% of flow to go through the MCA and 40% through the ACA (60/40 resistance), and an RCR model that also forces a 60/40 flow distribution through the MCA and the ACA respectively, but adds an additional phase lag between pressure and flow. We also manipulated the patient-specific geometry in Meshmixer to remove the bulk of the aneurysm and model the patient’s vasculature prior to aneurysmal development. We ran our analysis with the various outlet boundary conditions on this geometry to obtain insights on how hemodynamic forces and stresses may have contributed to the initiation of aneurysm growth. We concentrated on evaluating spatiotemporal and time-averaged distributions of blood flow velocities, wall shear stresses, and pressures at peak systole, peak diastole and throughout the entire cardiac cycle. Overall, our results show that the flow rate distribution ratio \( R = \frac{Q_{ACA}}{Q_{MCA}} \) is an important factor influencing the magnitude of several hemodynamic parameters, particularly in the vicinity of the outlets. However, as long as this ratio is kept constant, the choice of resistance or RCR boundary conditions through each outlet has no substantial effect on computed wall shear stresses, time-averaged pressures, and blood flow velocities. Using this knowledge, we then examined the
hemodynamic properties of blood flow in the cerebral arteries of this particular patient, and used this to predict and infer important information about aneurysm progression. We observed normal blood flow patterns and pressure distributions throughout the geometry of the healthy blood vessels, but abnormally high wall shear stresses on the region where the neck of the aneurysm ultimately developed. It is possible that elevated wall shear stresses contributed to the initiation of aneurysmal growth in this patient by inducing abnormal endothelial behavior and damaging the constitution of the blood vessel wall. We also observed regions of low wall shear stresses and high OSI proximal to blebs on the aneurysmal surface, indicating zones with low blood flow velocities that may be correlated with severe vascular wall weakness due to leukocyte accumulation and inflammation.

In order to validate our results, we checked for conservation of mass at the outlets and compared the flow rate and pressure waveforms between subsequent cardiac cycles to make sure that flow was steady and fully developed. We also compared the average flow rates at the inlet and outlets with those obtained from less refined meshes, in order to confirm that the mesh design was appropriate and that it was not influencing our analysis. However, there are still limitations to our model that must be addressed, including the assumption of rigid, impermeable, vascular walls and the length of the outlet branches, which may not have been sufficiently long to accurately capture
physiological hemodynamics through the ACA and the MCA. These issues are discussed in section 4.3.

4.1 Implications of Boundary Condition Comparison

Blood flow patterns were not severely affected by the choice of boundary condition, as long as the flow rate distribution ratio through the outlet branches was kept constant. Flow streamlines were slightly different depending on whether a resistance or RCR boundary condition was used, but overall, all boundary condition models predicted stable and non-complex flow with similar vorticity in both the healthy and diseased geometries. Blood flow velocities throughout the cardiac cycle between the 60/40-resistance case and the RCR model were also very similar. On the other hand, blood flow velocities through the MCA and ACA branches for the 50/50 resistance case were different relative to the 60/40 and RCR cases, with slower flow through the MCA, and faster flow through the ACA. This was anticipated, since the 50/50 resistance boundary condition assumes that the vasculature downstream of the ACA and the MCA impose equivalent resistances, and so flow is distributed more evenly through these branches, with irregularities arising entirely due to the geometry of the modeled domain. These results are corroborated by our flow rate waveform analysis (Figure 7), which revealed that flow rate through the ICA, ACA and MCA for the RCR and the 60/40 resistance boundary conditions are approximately the same, since both of these models force 60% of the total flow to go through the MCA and 40% to go through the ACA, whereas for
the 50/50 resistance case, flow rates through the MCA and the ACA are more balanced and only differ by 6% (Table 2).

Similarly, our analysis also revealed that wall shear stresses were not affected by the nature of the boundary conditions prescribed at the outlets, as long as the flow distributions through the outlet branches were conserved. We observed differences in wall shear stresses between the 50/50 resistance and the 60/40 resistance cases, since these boundary conditions resulted in differing outlet flow rate waveforms. However, wall shear stresses were only substantially different at close proximity from the outlets, and remained roughly the same throughout the remaining geometry, including on the region of the healthy vasculature where the neck of the aneurysm developed and on the bulk of the aneurysm itself. In contrast, we did not observe any differences in wall shear stress distributions between the 60/40 resistance case and the RCR model, since both of these conditions conserved the same 60%/40% flow distribution through the MCA and the ACA respectively. These results indicate that the choice of using an RCR model over resistance as a boundary condition has no effect on wall shear stresses as long as the flow distribution ratio is conserved.

On the other hand, we did observe large differences in pressure pulse waveforms at the ICA, MCA and ACA between the various boundary conditions, especially when applying RCR boundary conditions at the outlets (Figure 8). The pressure waveforms that were obtained for the resistance and RCR boundary conditions at the outlets
resembled waveforms in previous studies, and supported assertions by Vignon-Clementel et al. suggesting that prescribing resistance boundary conditions at the outlets leads to abnormally large pressure amplitudes at peak systole and no phase difference between pressure and flow, whereas using RCR boundary conditions leads to more natural pressure waveforms that lag behind flow and resemble physiological pressure pulses (9, 35, 42). These observations are supported by the lower pressure distributions that were computed at peak systole when applying RCR boundary conditions at the outlets compared to those when using resistance boundary conditions (Figures 17 and 19). Similar relationships were observed at peak diastole and at different points throughout the cardiac cycle, although the differences in pressure distributions were not as acute as they were at peak systole. However, the TAP over the full cardiac cycle for the 60/40-resistance case and the RCR model were identical, with the 50/50 resistance case predicting slightly different local pressures. This means that although local pressures may be different at specific time points throughout the cardiac cycle, the average pressures over a full cardiac cycle are equivalent regardless of whether resistance or RCR boundary conditions were imposed at the outlets, as long as the flow distribution through the outlet branches is kept constant.

If computational studies of this nature are being performed for the purpose of treatment planning and clinical decision support, it is important to use methods that are fast, accurate, efficient, and practical. Impedance boundary conditions lead to physiologically
accurate results, but their speed and practicality may not be suitable for these types of applications. On the other hand, resistance boundary conditions are simple and easy to use, but their accuracy and reliability has been subject of concern since they force pressure and flow to be in phase and they predict unnaturally large pressures pulses. In our study, we have shown that resistance and RCR impedance boundary conditions lead to similar computations of wall shear stress, time-averaged pressure, and flow velocities, provided that the flow rate distribution through the outlet branches remains unchanged. Local pressure distributions at specific time points, such as at peak systole or peak diastole, are drastically different between resistance and RCR boundary conditions. Therefore, if pressure-dependent parameters correlated to aneurysm progression and rupture are calculated at peak systole (or at any other specific time point throughout the cardiac cycle) with the purpose of assisting clinical treatment planning, it may be necessary to use impedance boundary conditions. However, if these parameters are calculated as time-averages over the entire cardiac cycle, then using resistance boundary conditions at the outlets may be sufficient. Similarly, if hemodynamic parameters associated with wall shear stresses or blood flow velocity patterns are used to analyze aneurysm progression in a clinical setting, resistance boundary conditions may also be suitable.

Using resistance boundary conditions over RCR variants does not lead to any significant sacrifice in accuracy when calculating wall shear stresses, time-averaged pressures or
flow velocities, and provides additional advantages in terms of simplicity, speed and practically, especially since they do not require any additional patient-specific measurements or prior knowledge of the downstream vasculature. We recommend the use of resistance boundary conditions at the outlets for future studies seeking to use computational biofluid mechanics as tools for clinical treatment planning.

4.2 Implications of Hemodynamic Analysis on Aneurysm Progression

Our analysis of hemodynamics in the healthy vasculature revealed that over a full cardiac cycle, there is a region of high time-averaged wall shear stress (>210 dyn/cm²) that coincides with the region where the neck of the aneurysm develops (Figure 13). In healthy cardiovascular physiology, endothelial cells are usually subjected to wall shear stresses on the order of 10 to 30 dyn/cm² (43-44), an order of magnitude lower than what was calculated. However, wall shear stresses exceed this physiological range almost throughout the entire modeled geometry other than at the ICA and the area adjacent to the ACA-MCA bifurcation. Assuming rigid vascular walls may have been partially responsible for this overestimation. Regardless, the increase in wall shear stress at the region of aneurysm development relative to the stresses on rest of the geometry is still significant in our analysis, and it ultimately supports the hypothesis that high wall shear stress is correlated with the initiation of aneurysm growth.

Our model also predicted regions of high wall shear stress at the MCA (region 1) and at the junction between the ICA and the MCA (region 2). In region 1, the TAWSS was, on
average, higher to what was calculated at the region that develops into the aneurysmal neck. We anticipate that this patch of high wall shear stress is at least partially artificial in nature, arising due the short length of the MCA in the modeled domain which may not have provided enough space for flow to fully develop along this branch. Simulations on geometries that include greater lengths of each outlet branch may be necessary in future studies to confirm this hypothesis and provide more robustness to the model. In region 2, the zone with high shear stresses at the ICA-MCA junction, the TAWSS was, on average, lower than what was calculated in the region coinciding with the aneurysmal neck. However, it was still considerably elevated relative to stresses on the vasculature as a whole. This suggests that analyzing wall shear stresses in isolation may be insufficient to evaluate risks for aneurysmal development, since they may give false positives. Other biological factors that are not commonly evaluated in fluid mechanical studies may play a significant role.

The influence of local pressures on the initiation of aneurysm development is not well understood. In our analysis of the geometry prior to aneurysm growth, pressure decreased linearly along the length of the vasculature, and though we observed a slight elevation at the ICA-ACA bifurcation relative to local pressures in the vicinity, there was no indication of higher pressures in the region that ultimately developed into the aneurysmal neck (Figures 17 and 18). This suggests that local pressures, in this particular case, were not involved in aneurysm growth initiation. However, the magnitude of local
intravascular pressures is several times larger than the magnitude of applied wall shear stresses, and so their influence in aneurysmal progression should still be carefully considered. It is possible that aneurysmal growth initiation occurs via two pathways: the first originating from abnormal wall shear stresses leading to unnatural vascular remodeling via mechanotransduction, and the other arising from high focal blood pressures impinging on vascular walls and leading to physical damage and inflammation.

On the other hand, our model of the diseased vasculature predicted non-complex and stable blood flow patterns within the aneurysmal domain. There was, however, a narrow impingement zone, visualized by elevated local pressures on a small area within the aneurysmal surface that directly faced jet inflow from the ICA (Figures 19 and 20). The pressure in this region was not elevated by a substantial margin, but it may have been sufficient to further weaken the thin aneurysmal wall. It seems more likely, however, that low wall shear stresses had a more fundamental role in aneurysm progression, and that they may be better correlated with an elevated risk for aneurysmal rupture in this particular patient. Our study revealed three main regions with very low wall shear stresses, below normal physiological ranges. Incidentally, these three regions were either located on aneurysmal blebs or were directly adjacent to them, and they correlated well with areas on the aneurysmal surface with high OSI. As expected, these regions were also characterized by slow blood flow velocities. Based on these
observations, it is highly likely that this particular aneurysm had a very high risk of rupture based on the hypothesis that low, oscillating shear stresses and low blood flow velocities lead to local stagnation of leukocytes, which generates a highly inflammatory and pro-oxidative environment that damages the vascular wall. Moreover, these low, oscillating shear stresses may cause abnormal endothelial cell behavior via mechanotransduction pathways, causing further weakness by destructive vascular remodeling.

Ultimately, our results suggest in this particular geometry, high wall shear stresses are correlated with the initiation of aneurysmal growth, whereas low wall shear stresses and high OSI may be associated with further enlargement and a high risk of rupture.

4.3 Limitations, Challenges and Future Directions

In order to construct our model, several assumptions were made, including that of rigid vessel walls. Several studies in the past have shown that this assumption leads to a large overestimation of wall shear stress magnitudes (45), which explains why our model predicted abnormally high wall shear stresses throughout most of the modeled vasculature. However, accounting for flexible, elastic walls may require additional patient-specific measurements of vascular wall material properties and lead to computationally intensive simulations that take a much longer time to converge. As a result, these types of studies may be impractical for use in a clinical setting. Future sensitivity analyses comparing normalized wall shear stress distributions in rigid wall
and flexible wall models may be necessary to evaluate the importance of accounting for vascular wall properties for these types of simulations.

Wall shear stresses in our model were elevated in the region where the neck of the aneurysm develops, as well as on the vicinity of the MCA outlet and at the ICA-MCA junction. The presence of high wall shear stresses at the MCA may be partially due to the short length of the MCA branch in the modeled domain, which may be insufficient to accurately capture physiological hemodynamics. We recommend that future studies include longer segments of the outlet branches in their simulations to avoid these issues from arising. In addition, the presence of high wall shear stresses at the ICA-MCA junction suggests that analyzing wall shear stresses in isolation may lead to false positive predictions of aneurysmal development. Indeed, computational fluid dynamic studies only account for fluid-solid interactions and the mechanical aspects of vascular disease, but they do not consider important biological phenomena such as cellular response to mechanical loading, including endothelial cell alignment and cell-mediated turnover of extracellular matrix, both of which are largely responsible for lesion growth, variations in vascular wall material properties, and likelihood of aneurysm growth and rupture (45). Models that incorporate biological parameters and account for biological phenomena may lead to the development of more accurate predictors of aneurysm pathophysiology.
Finally, our results suggest that high wall shear stress is associated with the initiation of aneurysm growth, and low wall shear stresses and high OSI are associated with further enlargement and risk of aneurysmal rupture. However, we have only run simulations on the geometry of a single aneurysm model. It is likely that there are other pathways that are correlated with aneurysm progression, for example via high focal pressures impinging on the vascular walls. Large-scale studies on several patient-specific geometries are essential to develop accurate predictors and to assess if the relationships found here hold true elsewhere. For this purpose, manipulation of patient-specific models via computer-aided design (CAD) is an extremely valuable tool that enables the reconstruction of blood vessel geometries prior to aneurysmal development, in order to study the initial stages of aneurysmal growth. Future investigations should not only study hemodynamics in aneurysm models, but also on models of vasculature prior to aneurysm growth via retrospective, geometrical-manipulation techniques.
5. Conclusions

In conclusion, we have shown that flow distribution through outlet branches is an important factor affecting wall shear stresses, pressures and blood flow velocities in the near vicinity of the outlets. However, as long as this distribution is conserved, prescribing RCR impedance boundary conditions at the outlets holds no significant advantage over using the more practical and simple resistance boundary conditions. As such, resistance boundary conditions may be more suitable for use in a clinical setting, where computational simulations of blood flow must be computationally inexpensive, practical, simple and fast to support patient-specific treatment planning. In addition, we have shown that retrospective modeling of healthy vasculature prior to aneurysm growth can elucidate important mechanisms in initiation of aneurysm growth. In our particular patient-specific model, hemodynamic analysis suggests that high wall shear stresses were associated with aneurysm development, and low wall shear stresses and high OSI were correlated with aneurysm enlargement and risk of rupture. Elevated local pressures on the aneurysmal surface may have also contributed to these mechanisms. Larger-scale studies of a similar nature are necessary to establish more robust correlations.
Appendix A: Flow Rate Fourier-Series Decomposition

In order to ensure periodicity and to obtain Womersley velocity profiles from the flow rate at the inlet, SimVascular automatically makes a Fourier series fit of the prescribed flow rate. In our case, we selected $n = 30$ total modes, with values shown below.

\[
a_0 = 9.5919 \\
a_1 = -0.1684 \quad b_1 = 1.4297 \\
a_2 = -0.2887 \quad b_2 = 0.8117 \\
a_3 = -0.5546 \quad b_3 = 0.2839 \\
a_4 = -0.2654 \quad b_4 = 0.1768 \\
a_5 = -0.4722 \quad b_5 = 0.0454 \\
a_6 = -0.2641 \quad b_6 = -0.2473 \\
a_7 = -0.0720 \quad b_7 = -0.1812 \\
a_8 = -0.0286 \quad b_8 = -0.1619 \\
a_9 = 0.0505, \quad b_9 = -0.1261 \\
a_{10} = 0.0629 \quad b_{10} = -0.0643 \\
a_{11} = 0.0760 \quad b_{11} = -0.0338 \\
a_{12} = 0.0595 \quad b_{12} = 0.0093 \\
a_{13} = 0.0371 \quad b_{13} = 0.0271 \\
a_{14} = 0.0155 \quad b_{14} = 0.0297 \\
a_{15} = 0.0015 \quad b_{15} = 0.0281 \\
a_{16} = -0.0105 \quad b_{16} = 0.0220 \\
a_{17} = -0.0167 \quad b_{17} = 0.0132 \\
a_{18} = -0.0187 \quad b_{18} = 0.0025 \\
a_{19} = -0.0151 \quad b_{19} = -0.0059 \\
a_{20} = -0.0095 \quad b_{20} = -0.0107 \\
a_{21} = -0.0029 \quad b_{21} = -0.0122 \\
a_{22} = 0.0024 \quad b_{22} = -0.0109 \\
a_{23} = 0.0065 \quad b_{23} = -0.0072 \\
a_{24} = 0.0071 \quad b_{24} = -0.0029 \\
a_{25} = 0.0070 \quad b_{25} = 0.0003 \\
a_{26} = 0.0050 \quad b_{26} = 0.0029 \\
a_{27} = 0.0027 \quad b_{27} = 0.0040 \\
a_{28} = 0.0004 \quad b_{28} = 0.0042 \\
a_{29} = -0.0013 \quad b_{29} = 0.0036 \\
a_{30} = -0.0027 \quad b_{30} = 0.0024
\]

The Fourier series fit is given by: $Q = \frac{a_0}{2} + \sum_{k=1}^{n} \left( a_k \cos \frac{2\pi kt}{T} + b_k \sin \frac{2\pi kt}{T} \right)$
References


