Computational Biomechanics

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Abstract

CompBioM aims to validate FlowPhys' (FPS) computational tools in cardiovascular settings. Specifically, the FPS 3D Computational Fluid Dynamics (CFD) solver and FPS 1D pipe network solver will be used to create 3D CFD and 1D models of coronary artery disease to evaluate the accuracy and reliability of the software in analysing blood flow dynamics. To this end, clinically relevant parameters such as Fractional Flow Reserve are to be calculated. This initiative is in response to the European Union's EU4Health research directives to enable a public health system resilient to illnesses. To this end, CompBioM will develop a hybrid rheological model to approximate blood flow, implement relevant boundary conditions for CFD and 1D models, and investigate the feasibility of using 1D models via a comparison of results between 1D and 3D. The objective of CompBioM is to showcase a competent and valid 3D and 1D simulation in blood flow using FPS software and draw clinical conclusions. The project aims to provide added value to FPS through increased credibility for partnerships with potential research collaborators in Horizon Europe projects.

1. Introduction

The project aim is to verify the computational tools developed by FlowPhys AS (FPS) for coronary artery disease in 3D and 1D to evaluate the software's potential to contribute to clinical decision support systems. FPS has invested in this project as an initial drive into the development of computational tools to assist clinical decision support procedures in the cardiovascular sciences. The initiative is a response to the EU policy EU2021/522. This program has direct synergy with the Horizon Europe research program, of which FPS is an active member. Consequently, the company seeks to develop biomechanical models that demonstrate the capacity of its software in this area.

1.1 Literature Review

1.1.1 Burden of the Disease

Coronary artery disease (CAD) is a cardiovascular disease that is responsible as it's the leading cause of death in developed and developing countries (Mohsen et al., 2015). It's characterised by the atherosclerosis arising from the inflammation of the coronary vessel walls with approximately 6 million deaths were attributed to it in 2015 (Lloyd-Jones et al., 2009). By 2030, World Health Organisation (WHO) projects that 15% of male deaths will be attributed to this

disease (World Health Organization, 2011). The pathogenesis of CAD from a conventional medical description is when the endothelial wall (arterial vessel wall) is damaged, and atherosclerosis – also termed stenosis once developed, begins due to the accumulation of lipoprotein droplets in the intima of the coronary vessels (Badimon et al., 2012). The result is the production of extracellular matrix, which in turn grows into fibrous plaques, causing flow constriction and initiating cardiac ischemia. It has been theorised that abnormal Wall Shear Stress (WSS) may alter the endothelial cell signalling, and kick start the above pathogenesis (Dhawan et al., 2010).

Coronary artery disease is typically diagnosed by two types of parameters: anatomic (diameter of stenosis), or functional (impaired myocardial function from ischemia due to restricted blood flow). There are non-invasive tests for myocardial functions, which are relatively accurate on a per-patient basis. They're less successful in quantifying the severity of individual coronary territory ischemia (Zhong et al., 2018). The clinically relevant parameter is the Fractional Flow Reserve (FFR) (Zhong, 2018) – which is a ratio of pressure difference between the proximal (upstream) and distal (downstream) region of the stenosis. This is measured during invasive coronary angiography (ICA) under adenosine-induced hyperaemia.

1.1.2 Computational FFR

Patient specific CFD modelling coupled with Computed Tomography (CT) has emerged as a promising tool to non-invasively determine FFR. This is derived from CT generated patient specific models, to which a computational mesh is generated, and Navier Stokes' equations are solved via either scale resolving, or Reynolds averaged form to obtain the flow field for the fluid domain.

Boundary conditions:

To obtain a valid cardiovascular simulation, appropriate boundary conditions are paramount, but difficult to obtain (Zhong et al., 2018). Cardiovascular flow has a transient pulsatile nature, which cannot be replicated from a steady-state simulation (Freidoonimehr et al., 2020). To this end, Freidoonimehr et al. (2020) suggests a pulse flow waveform should be implemented at the inlet, and vascular resistance should be considered at the outlet.

Rheological models:

Blood have been investigated by Fedosov et al. (2011), and Flormann et al. (2017) with both agreeing it to be a shear thinning non-Newtonian fluid. This manifests itself via red blood cell aggregation at low shear rates, which significantly increases blood viscosity. For CFD simulation of the coronaries, the Carreau and the Carreau-Yasuda (CY) models were found to have produced acceptable results (Carvalho et al., 2021) .

Flow structures in a stenosed artery:

Transitional and turbulent flow have been investigated in a stenosed artery (Freidoonimehr et al., 2020) and it was shown that there is a significant increase in turbulent kinetic energy (TKE) 5D (pipe diameter) distal from the stenosis, propagating until 10D, where the flow re-laminarises. The authors have concluded that formation of turbulent vortices associated with the higher WSS may assist cardiologists to determine the enlargement of the existing stenosis,

or formation of a distal secondary stenosis. A combination of pulse flow, accounting for turbulence, and coupling to a non-Newtonian blood model should yield interesting results.

1.1.3 Computational Tools and Workflow:

Typically, tetrahedral, hexahedral or a hybrid of both meshes are used to discretise the simulation domain. For tetrahedral, the meshing process can be easily automated, while hexahedral suffers from long model development time for complex geometries. Nevertheless, hexahedral elements are preferred where possible due to a reduction in mesh error, smaller element counts, and improved reliability over its tetrahedral counterparts (Shepherd & Johnson, 2008). Since ideal geometries are considered in this project, hexahedral elements are chosen for the mesh.

Turbulence modelling is a necessary step in CFD workflows and in this project, the type of model chosen will significantly affect the results of the analysis. Large Eddy Simulation (LES) is to be investigated as a potential method to model blood flows. The Dynamic Smagorinsky Sub-grid-scale model proposed by Germano et al. (1991) is to be used due to its ability to model transition to turbulence (Sayadi & Moin, 2011).

1D models:

3D CFD is computationally expensive and time consuming compared to their 1D counterparts. 1D models are actively being investigated to calculate FFR in a steady, Newtonian setting by Blanco et al., (2018). The authors concluded that the 1D model provided good approximation towards 3D. This project aims to go a step beyond their work, with the prospect of comparisons of 3D and 1D transient analysis with non-Newtonian flow and against steady and Newtonian flow. The Non-Newtonian models can be integrated as a pipe friction factor term within the 1D transport equation (Krivovichev, 2021). This project will utilise the CY model as derived by the author for the 1D analysis.

2. Project Objectives and Methodology

The aim of CompBioM is to investigate the flow phenomenon associated with CAD in 3D and 1D using the FlowPhys software suite. The hypothesis is that CFD is time consuming and challenging to implement for inexperienced users, thus a 1D model may be a good compromise between accuracy, speed, and ease of access. The hypothesis is specific to feasible clinical implementation of such software. The specific objectives are:

1 To develop a hybrid Newtonian and Non-Newtonian rheological model to better approximate the real nature of blood flow.
2 To implement a pulsatile inlet condition, and vascular resistance on the outlet.
3 To verify Eddy Viscosity Models for LES.
4 To create a CFD models with the above conditions, analyse results, and compare with literature.
5 To adapt the hybrid rheological model to 1D.
6 To compare the accuracy of 1D Non-Newtonian CAD models vs its 3D counterpart.

2.1 Methodology

2.1.1 Geometry and Mesh:

The geometry to be studied in this project is an ideal case with 5 regions: inlet length, contraction region, stenosis length, expanding region, and outlet length. To incorporate turbulent eddy transport, outlet length is set to be 10D post stenosis. With D = 3.3mm, this project will consider two cases of stenosis, from 33% to 60% reduction of D, to be compared with Mohammadi & Bahramian (2009). An example of the model is shown below, sourced from the same author.

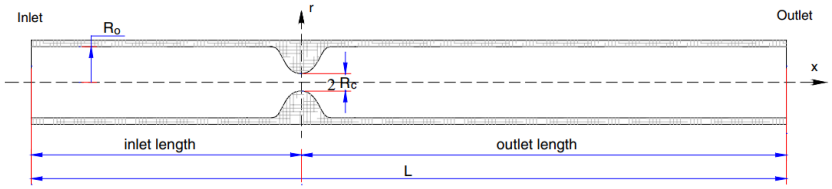

Figure 1 Example of an ideal stenosis model.

A full parametric hexahedral mesh is to be used. This is achieved by creating a 2D circle with an annulus. The circle center has free hex mesh, while the annulus has structured prism meshes. This is then extruded along the z-axis using FPS custom mesh generator, and the length and the diameter of the stenosis is chosen.

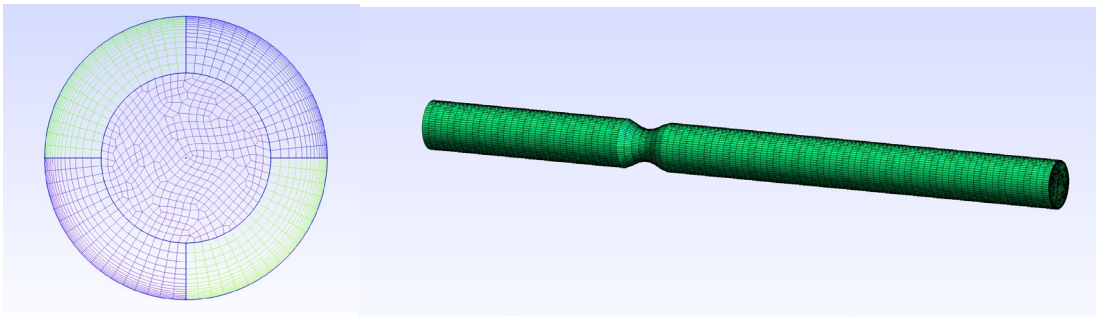

Figure 2 Generated mesh for 33% stenosis.

2.1.2 Rheological model:

A hybrid model encompassing non-Newtonian CY model and Newtonian model based on shear rate is applied for which a smoothing region of shear rate $150 < \dot{\gamma} < 250$ based on investigations by Fedosov et al. (2011). The hybrid model is as follows:

$$\mu_{CY} = 0.0035 + (0.16 - 0.0035)[1 + (8.2 * \dot{\gamma})^{0.64}]^{\frac{0.2128-1}{0.64}}, \quad \dot{\gamma} < 150 \qquad [1]$$

$$\mu_{hybrid} = y * \mu_{CY} + (1 - y) * \mu_N, y = \frac{250}{100} - \frac{\dot{\gamma}}{100}, \quad 150 < \dot{\gamma} < 250 \qquad [2]$$

$$\mu_N = 0.0035, \quad \dot{\gamma} > 250 \qquad [3]$$

2.1.3 Boundary Conditions:

As discussed above, the inlet flow wave form was obtained from Freidoonimehr et al. (2020) and is shown below. The velocity axis represents the bulk flow.

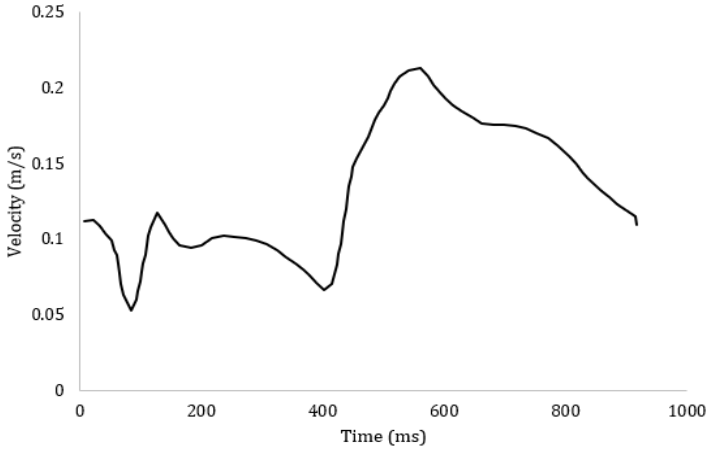

Figure 3 Non patient specific time varying flow rate at the coronary arteries for a single cardiac. cycle.

The above curve is to be discretised into timesteps with linear interpolation carried out at each timestep to approximate the final wave form. The inlet flow profile will be obtained at the outlet of a 10D straight pipe using the above wave form. For the outlet, initial simulations will be carried out with zero gauge pressure at the outlet at steady state to obtain the pressure waves (Xie et al., 2018). The pressure is then re-used to implement vascular resistance with the following equation:

$$R = \frac{\Delta P}{Q} \quad [4]$$

Specific microvascular resistance is to be obtained from Xie et al. (2018)

2.1.3 Turbulence model:

FPS 3D will be used as the solver of choice for this study. Here, a priori DNS simulation will be conducted to verify the LES solver for a test case. Specific variables of interest are: WSS, OSI, and contours of velocity and pressure. The formulation of the Dynamic Smagorinsky LES is as follows (Germano et al., 1991):

$$\frac{\partial \widetilde{\overline{u}_i}}{\partial t} + \frac{\partial \widetilde{\overline{u}_i}\widetilde{\overline{u}_j}}{\partial x_j} = -\frac{1}{\rho}\frac{\partial \tilde{\bar{p}}}{\partial x_i} + \mu\frac{\partial^2 \widetilde{\overline{u}_i}}{\partial x_j x_j} + \frac{\partial}{\partial x_j}T_{ij} \quad [5]$$

Note that “bar” represents grid filter, and “tilde” test filter. The Smagorinsky constant is calculated as follows:

$$C = \frac{M_{ij}\zeta_{ij}}{M_{ij}M_{ij}} \quad [6]$$

The FPS solver uses a semi-implicit fractional step Finite Element Method, with a 4-stage Runge-Kutta explicit algorithm for convection terms and implicit Crank-Nicholson algorithm for the diffusive terms. Pressure is solved implicitly through a Poisson’s equation. For further information, see Kjellgren (1997).

3. Conclusions and Future Work

The most immediate work is to compete the 3D calculation of 33% and 60% stenosis, carry out Grid Convergence analysis, and compare with literature. Then the 3D boundary conditions are to be adapted to 1D, as well as the rheological models. The FPS 1D solver is to be modified with the new additions. Calculation is to be performed on 1D, and then FFR calculated from 3D and 1D is compared.

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