

Article

Three-Dimensional Modeling of the Behavior of a Blood Clot Using Different Mechanical Properties of a Blood Vessel

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Abstract: In this work, the behavior of a 3D blood clot located inside a vein under the influence of the mechanical effect of blood flow was analyzed. It has been observed that the mechanical properties of the blood vessel play an important role in the behavior of a blood clot. When the blood vessel changes its shape and/or diameter over time, the position and orientation of the clot in space and time is not constant, and consequently, it influences the blood flow. Moreover, the changed lumen of the blood vessel has a direct impact on the blood velocity, and thus the pressure is exerted not only on the blood vessel wall but also on the thrombus itself. Under these different conditions, it is important to understand the behavior of the blood clot, where each factor with a mechanical influence could potentially lead to clot detachment. Therefore, several variants of numerical simulations were analyzed, including models with different blood vessel properties, considering when the blood vessel wall has (flexible) or does not have (fixed) elastic properties. The results show the blood flow velocity, vessel wall, and blood clot deformations and/or stresses using different vessel wall rigidity levels as well as different blood clot viscoelasticity parameters.

Keywords: thrombus; vein; numerical analysis; modelling; deformation; vessel elasticity

MSC: 37M05; 37M10; 37N15; 70K40; 74H15; 92B05; 92C05; 92C10



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1. Introduction

Thrombus. In vivo and in vitro. *Mechanics implementation.* An overview of the modelling and mechanical testing of a material of thrombus for vascular implant and the structure of the device is given by Johnson et al. [1]. They investigated the use of different constitutive and computing models for modeling material behavior and the formation of a blood clot. The measurement of the influence of thrombosis, the maturation of a thrombus and thrombolysis on the mechanical properties of a clot in the in vitro model is given by Dwivedi et al. [2]. They mentioned the meaning of thrombolysis and its effect on the mechanical properties of the clot by reducing its rigidity. The modeling of the growth and the formation of a blood clot is given by Hosseinzadegan and Tafti [3]. Their review gives beneficial strategies for predicting the growth and formation of a blood clot.

Vessel elasticity. *Mechanics implementation.* In vitro and computational. A computational method for estimating unloaded configurations and the in vivo stresses of patient's blood vessels was investigated by Bols et al. [4]. They mentioned that as it includes in vivo

stress in the arteries' numerical model, it is necessary to correctly assess displacement and stress across a range of physiological blood pressures. Garbye et al. [5] introduced a multi-scale computational framework for understanding vascular adaptation. They propose this framework of vascular adaptation for the development of a bridge between experimental observation and theory, as well as to ensure the systematic testing of appropriate clinical hypotheses. An alternative formulation of the mechanics of blood vessels and the meaning of the property *in vivo* are given by Brossollet and Vito [6]. They mentioned that their experimental results show that the value of total force in *in vivo* scenarios were able to be reliably measured during the biomechanical experiments or the corresponding relevant range.

Types of analysis of the thrombus from different perspectives. A visualization of thrombosis to improve the resolution of the thrombus is given by Weisel and Litvinov [7]. They analyzed recent studies that describe the qualitative and quantitative morphologic characteristics of venous and arterial blood clots that relate to pathogenesis, diagnosis, prophylaxis, and thrombosis treatment. Current methods, diagnostic pitfalls, and spectra of results are presented by Leach et al. [8]. They noted that unenhanced time-of-flight MR venography, magnetic resonance (MR) imaging, contrast material-enhanced MR venography, and CT venography unenhanced computed tomography (CT) are particularly useful methods for detecting changes in the brain parenchyma and cerebral veins that may be associated with thrombosis. Implications for a deep vein thrombosis diagnosis and changes in the lower limb venous anatomy are given by Quinlan et al. [9]. They performed a retrospective analysis of bilateral thrombus-free venograms and assessed the frequency and types of changes observed in the venous anatomy.

Numerical simulation: what is applicable, software, and places where the thrombus is mainly analyzed. A computational model of thromboembolism and thrombosis induced by device is presented by Goodman et al. [10]. They noted that in areas of flow disturbance, thrombus growth can be enhanced due to a higher convective flux and shear stress. A general shear-dependent thrombus formation model was proposed by Yazdani et al. [11]. They offer a general numerical model that covers a wide range of hemodynamics conditions in arteries and veins, with individual platelets included in the model. A review of methods for macroscopic thrombus modeling is presented by Cito et al. [12]. They systematically examine the state of the art in computational fluid dynamics methods and macroscopic computational fluid dynamics for modeling thrombus formations, highlighting their weaknesses and strengths.

Current and future directions. Achievements in the understanding of thrombosis are given by Satoh et al. [13]. The purpose of this review is to cover new studies on thrombosis in the field of vascular medicine. A review of the general models of thrombosis *in vivo* and *in vitro* is given by Ayyoub et al. [14]. They mentioned that it is vital to switch attention to the standardization of thrombosis models for each specific use, since there are a large number of studies developing thrombosis models without using specific and well-prepared characteristics of the generated thrombus. Nanomedicine for thrombosis, a treatment strategy, and an accurate diagnosis are given by Su et al. [15]. They emphasized that a diagnostic system based on imaging nanoprobe and biomarkers may enable the early detection of thrombosis.

2. Problem Formulations

The detachment of a blood clot (embolization) is a known life-threatening process; therefore, the relevance of studying a clot's behavior remains of utmost importance. In the first stage, it is important to know the effect of blood on the deformation of the thrombus and the vessel itself.

Each year, cardiovascular diseases (CVDs) lead to 3.9 million deaths in Europe, representing 45% of all fatalities, according to Wilkins et al. [16]. Currently, there are two primary methods for thrombus removal in stroke patients: (i) pharmacological thrombolysis using recombinant tissue plasminogen activator (rt-PA), which is accessible to fewer than 15% of patients in most European countries, and (ii) mechanical thrombus removal through endovascular thrombectomy (EVT), which fails to successfully remove the thrombus in up to 20% of the patients, as stated by Staessens et al. [17]. In the field of mechanics, the majority of recent scientific articles focus on uncovering certain mechanical parameters or the most suitable model (e.g., viscoelasticity, hyperelasticity, visco-poro-elasticity) [18–21]. But there always are the fundamental questions: how a blood clot interacts with the blood flow and the vein; what forces appear there; and how a clot influences the blood flow. Therefore, in this study, we aim to look at the issue of the clot through the application of numerical analysis in order to understand what external influences the clot is exposed to and how it changes the flow afterwards. All this is necessary for the prediction of its behavior, even more so for its separation, which we plan to analyze in the future steps.

In previous studies, we examined the behavior of a 2D clot. In this work, the task is made more difficult and the problem is formulated as a solution/implementation of a three-dimensional problem. The three-dimensional problem involves drawing a blood clot inside a vessel, while specifying the properties from known scientific articles of the corresponding fluid. Another issue is associated with the blood vessel wall. The deformation of the wall caused by the blood flow (geometry change) affects both the movement of the blood itself and its mechanical properties (pressure, flow rate), as well as the behavior of the clot, its position in time and space, and the pressure caused by the movement of the fluid. All this is important for implementing a numerical simulation using COMSOL Multiphysics software (software version 6.2; developer location: 100 District Avenue, Burlington, MA 01803, USA).

In our study, blood clots are treated as homogeneous, and intracellular (such as platelet and RBC) interactions are not considered. This approach ensures the feasibility of numerical analysis, as current computational resources are insufficient for modeling the mechanical interactions of millions of individual cells. Due to this, in our model, the porosity is not applied directly (as the mechanical parameters of blood clot are taken from known physical experiments). It is important to note that our analysis is limited to a specific segment of the vein and focuses on a particular moment in time (three heartbeats). Furthermore, vein valve deformations are not represented in this section, but their influence is considered via a certain pulsatility. This choice aligns with the scope of our study, which focuses on the deformation of the vein itself. Considering the computational resources required, extending the analysis to a longer vein segment that includes valve deformations could be the next step of our future work. It should be noted that when describing the behavior of the clot, one of the tasks is the assignment of the elastic properties of the clot; the selection of hyperelastic and viscoelastic properties is distinguished in the work.

3. Methodology

From in vivo and in vitro experiments on blood clot geometry [7,22–26], a single 3D blood clot was created and modeled using Siemens NX (software version 1973; developer location: 5800 Granite Parkway, Suite 600, Plano, TX 75024, USA) and then imported into COMSOL Multiphysics.

The vessel was modeled as a vein with an inner diameter of 6 mm and a length of 60 mm [27]. The visualization of the blood clot inside the vein is shown in Figure 1. The thickness of vein wall is 0.25 mm. The blood clot is approximately 9 mm long, with a maximum height of about 3 mm and peaks reaching around 3.2 mm.

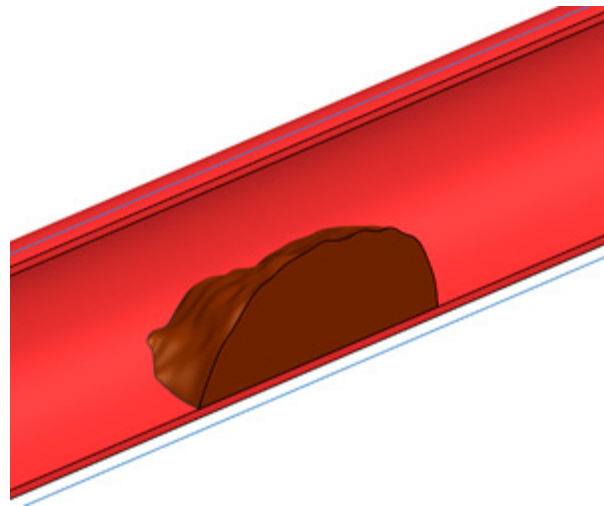


Figure 1. Initial parameters. Visualization: cross section of blood clot and part of the vessel, created using Siemens NX.

The principal blood flow graph of the vein is presented in Figure 2, with reference to the literature [28,29]. We would like to mention that we do not exclude the possibility that other blood flow pulsatility scenarios are possible. A duration of 0.8 s was used to simulate the typical human heartbeat (75 bpm). Inlet blood pressure gradient values in mmHg were set to ensure that the blood flowed at a normal velocity for a vein of this diameter, estimated to be between 2 and 30 cm/s, depending on the lumen size, until it encounters an obstacle, which in this case is a blood clot. This simulation includes three complete heartbeats.

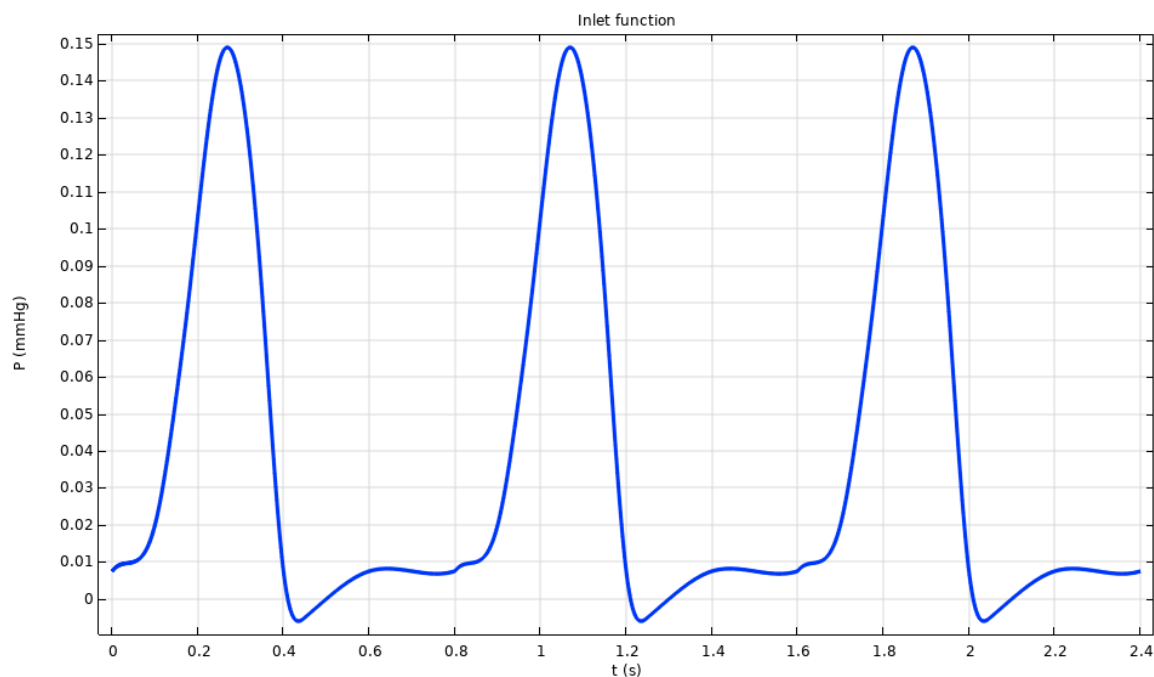


Figure 2. Initial parameters. The graphic of the principal blood flow, created using COMSOL Multiphysics.

For all simulations, the following boundary conditions and assumptions were established: fluid structure interaction (FSI) with fully coupled interfaces; laminar flow with incompressible fluid properties; non-suppressed backflow at the inlet and outlet; no-slip boundary conditions of the wall and the blood clot; pressure boundary conditions at the inlet and the outlet; the blood clot is treated as incompressible; deforming domain and

Yeoh mesh adaption method with smoothing factor $C_2 = 10$; viscoelasticity is considered using generalized Maxwell model; the used solver method is PARDISO; and the implicit solver method is used with a time step of 0.01 s, following the generalized alpha model.

The boundary condition for inlet and outlet is pressure. For both the inlet and outlet, this option allows us to obtain the normal stress, which in most cases is approximately equal to the pressure. Also, for the outlet, the tangential stress component is set to zero. If the reference pressure, defined at the physics interface level, is equal to 0, the value of the pressure p_0 , at the boundary, is the absolute pressure. Otherwise, p_0 is the relative pressure at the boundary. The suppress backflow option adjusts the inlet pressure locally in order to prevent fluid from exiting the domain through the boundary. Considering we used the non-suppressed backflow option, the inlet boundary could become an outlet depending on the pressure field in the rest of the domain.

In all simulations, the main parameters of blood, blood vessel, and blood clot are considered as follows [19,30–32]. Blood: dynamic viscosity 4 cP; density 1060 kg/m³. Blood clot: density 1100 kg/m³; Mooney–Rivlin $C_{01} = 1.8 \times 10^{-3}$ kPa and $C_{10} = 8.38 \times 10^{-6}$ kPa. Vessel wall: Young's modulus 5000 Pa; Poisson's ratio 0.47; density 1060 kg/m³. Viscoelasticity expressed using generalized Maxwell model with values shown in Table 1. The first set of viscoelasticity parameters used in simulations are Fixed Vein Wall 3 (FixVW3) and Flexible Vein Wall 3 (FlexVW3), while the second set of viscoelasticity parameters used in simulations are Fixed Vein Wall 4 (FixVW4) and Flexible Vein Wall 4 (FlexVW4).

Table 1. Viscoelasticity parameters using generalized Maxwell model. g_i is the normalized shear modulus for i th spring; τ_i is the time scale for the i th viscoelastic dissipation.

Parameter	First Set of Parameters [19]	Second Set of Parameters [20]
g_1	0.058	0.316
g_2	0.062	0.10
g_3	0.431	0.116
g_4	-	0.0987
τ_1 (s)	2.14	0.0104
τ_2 (s)	45.73	0.0214
τ_3 (s)	205.77	0.298
τ_4 (s)	-	14.6

All domains are meshed using finite element method inside the COMSOL software, with 32,502 elements. The geometry, size, and distribution of finite elements can be seen in Figure 3.

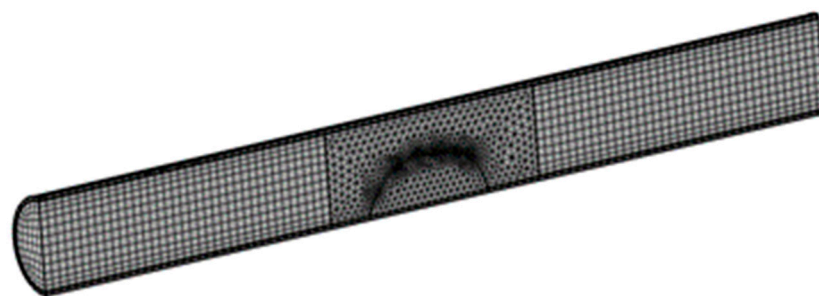


Figure 3. Meshed domains, created using COMSOL Multiphysics [33].

Given the equation of the Navier–Stokes [33], the equations of motion for a single-phase fluid are the continuity Equation (1) and the momentum Equation (2):

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{u}) = 0 \quad (1)$$

Here, ρ is the density of the mass (fluid), t is time, $\nabla \cdot$ is the divergence, and $\mathbf{u}$ is the flow velocity.

$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \nabla \cdot \left(\mu \left(\nabla \mathbf{u} + (\nabla \mathbf{u})^T \right) - \frac{2}{3} \mu (\nabla \cdot \mathbf{u}) \mathbf{I} \right) + \mathbf{F} \quad (2)$$

Here, p is the pressure of the fluid, μ is the dynamic viscosity of the fluid, and $\mathbf{I}$ is the identity tensor.

When the temperature variations in the flow are small, a single-phase fluid can often be assumed incompressible; that is, ρ is constant or nearly constant. Therefore, for constant ρ , Equation (1) is reduced to:

$$\rho \nabla \cdot \mathbf{u} = 0 \quad (3)$$

And the Navier–Stokes Equation (2) becomes:

$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho (\mathbf{u} \cdot \nabla) \mathbf{u} = \nabla \cdot \left[-p \mathbf{I} + \mu \left(\nabla \mathbf{u} + (\nabla \mathbf{u})^T \right) \right] + \mathbf{F} \quad (4)$$

The numerical simulation uses the hyperelastic material model [33]. A hyperelastic material is defined by its elastic strain energy density W_s , which is a function of the elastic strain state. It is often referred to as the *energy density*. The hyperelastic formulation normally gives a nonlinear relation between stress and strain, as opposed to Hooke's law of linear elasticity.

Once the strain energy density is defined, the second Piola–Kirchhoff stress in the local coordinate system is computed as:

$$\mathbf{S} = 2 \frac{\partial W_s}{\partial \mathbf{C}} \quad (5)$$

where $\mathbf{C}$ is the Cauchy–Green deformation tensor.

In this general case, the expression for energy W_s is symbolically evaluated down to the components of $\mathbf{C}$ using the invariants definitions prior to the calculations of the components of the second Piola–Kirchhoff stress tensor. The differentiation is performed in components on the local coordinate system.

Generally, for nearly incompressible and incompressible materials, the total strain energy density W_s is split into two parts:

$$W_s = W_{iso} + W_{vol} \quad (6)$$

where W_{iso} is the isochoric strain energy density and W_{vol} is the volumetric strain energy density.

The volumetric strain energy density W_{vol} can only be defined as an expression of the elastic volumetric deformation J_{el} . The quadratic volumetric strain energy density is defined as:

$$W_{vol}(J_{el}) = \frac{1}{2} \kappa (J_{el} - 1)^2 \quad (7)$$

where κ is the bulk modulus.

For incompressible material, a weak constraint is added to account for the incompressibility condition:

$$J_{el} = 1 \quad (8)$$

The auxiliary variable p_w acts as a Lagrange multiplier to enforce the constraint $J_{el} = 1$; this variable is then used as the pressure when computing stresses.

Because of Equations (7) and (8), the strain energy density W_s consists only of the isochoric strain energy density W_{iso} contribution:

$$W_s = W_{iso} \quad (9)$$

Then, the second Piola–Kirchhoff stress is given as:

$$S = p_w J C^{-1} + 2 \frac{\partial W_{iso}}{\partial C} \quad (10)$$

And the Cauchy stress tensor as:

$$\sigma = J^{-1} F S F^T = -p_w I + 2 J^{-1} F \frac{\partial W_{iso}}{\partial C} F^T \quad (11)$$

Hyperelasticity model based on Mooney–Rivlin using two parameters; therefore, the isochoric strain energy density is written in terms of the two isochoric invariants of the elastic right Cauchy–Green deformation tensors $I_1(\bar{C}_{el})$ and $I_2(\bar{C}_{el})$:

$$W_{iso} = C_{10}(\bar{I}_1 - 3) + C_{01}(\bar{I}_2 - 3) \quad (12)$$

The material parameters C_{10} and C_{01} are related to the Lamé parameter (shear modulus):

$$\mu = 2(C_{10} + C_{01}) \quad (13)$$

The formulas are presented in their general form to illustrate models used during the simulation.

4. Results

The numerical experiments were performed using COMSOL Multiphysics. The main focus was to evaluate the difference when analyzing a blood clot inside a vein with flexible vein wall compared to the commonly used fixed vein wall. Also, as mentioned in the methodology section, two sets of different generalized Maxwell viscoelasticity parameters were found in the scientific literature that seemed drastically different from one another; therefore, we wanted to analyze the simulations using both sets. Consequently, four main simulation variants were calculated, and their results are shown. In graphs, their names are Fixed Vein Wall 3 (FixVW3); Flexible Vein Wall 3 (FlexVW3); Fixed Vein Wall 4 (FixVW4); and Flexible Vein Wall 4 (FlexVW4), where the numbers 3 and 4 indicate the viscoelasticity parameter set used.

GIF files of each simulation version containing both velocity and deformation analysis are included with the article, in order to show simulation results through pictures. For this, certain time steps were chosen: 1.03 s; 1.16 s; 1.31 s; and 1.45 s. This allows us to preliminarily illustrate the processes that occur during the blood flow. Here, it is important to note that the time steps were chosen from the second heartbeat (from 0.8 s to 1.6 s) in order to evaluate the process, which is continuous in in vivo situations.

In order to provide a minimum number of separate figures, the results were grouped. In Figure 4a–e,h, the following simulation variants are shown (top to bottom): FixVW3; FixVW4; FlexVW3; FlexVW4. In Figure 4f,i, the following simulation variants are shown

(top to bottom): FixVW3; FixVW4. In Figure 4g,j, the following simulation variants are shown (top to bottom): FlexVW3; FlexVW4.

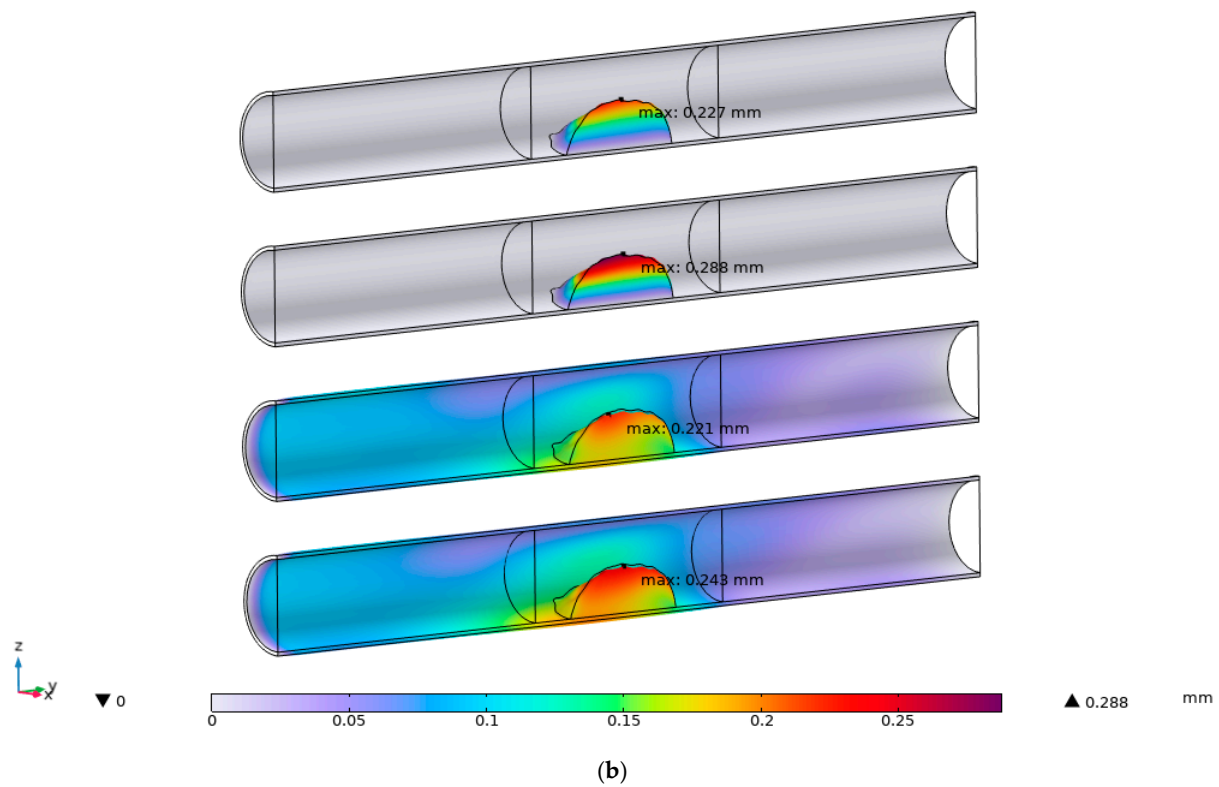
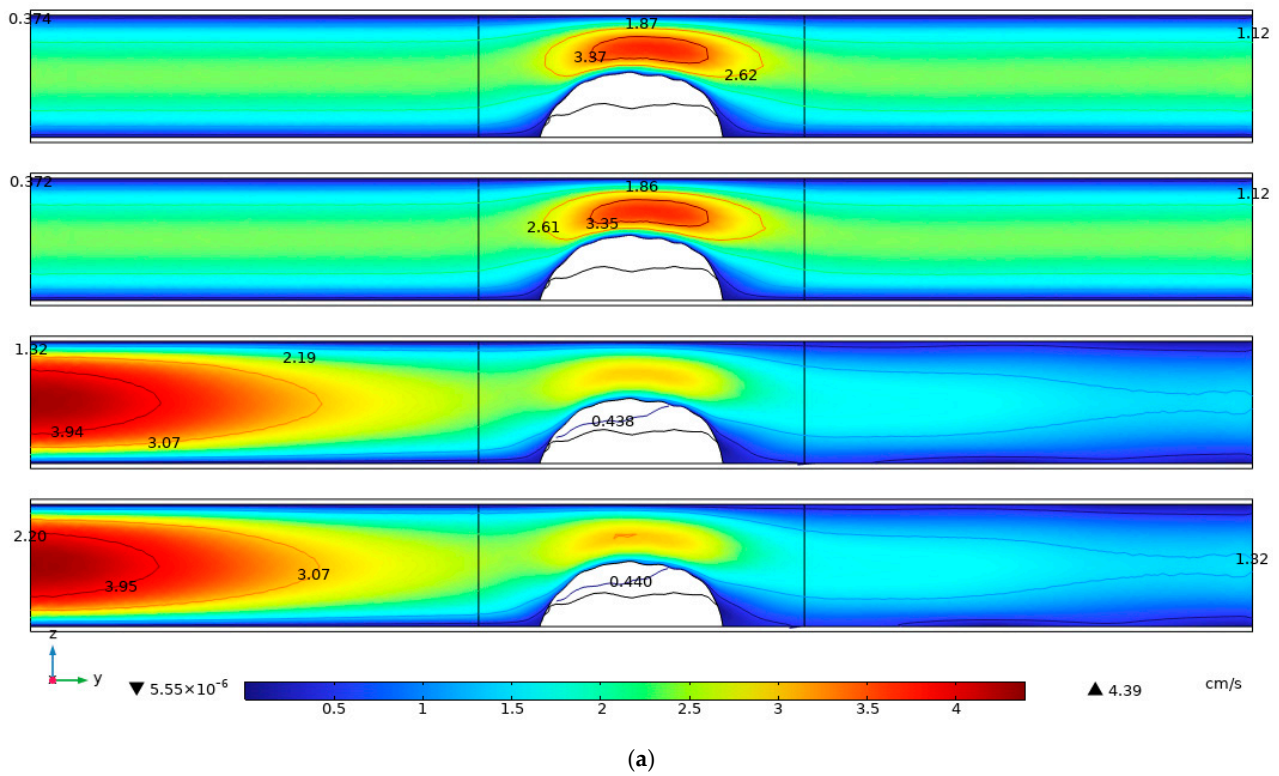


Figure 4. Cont.

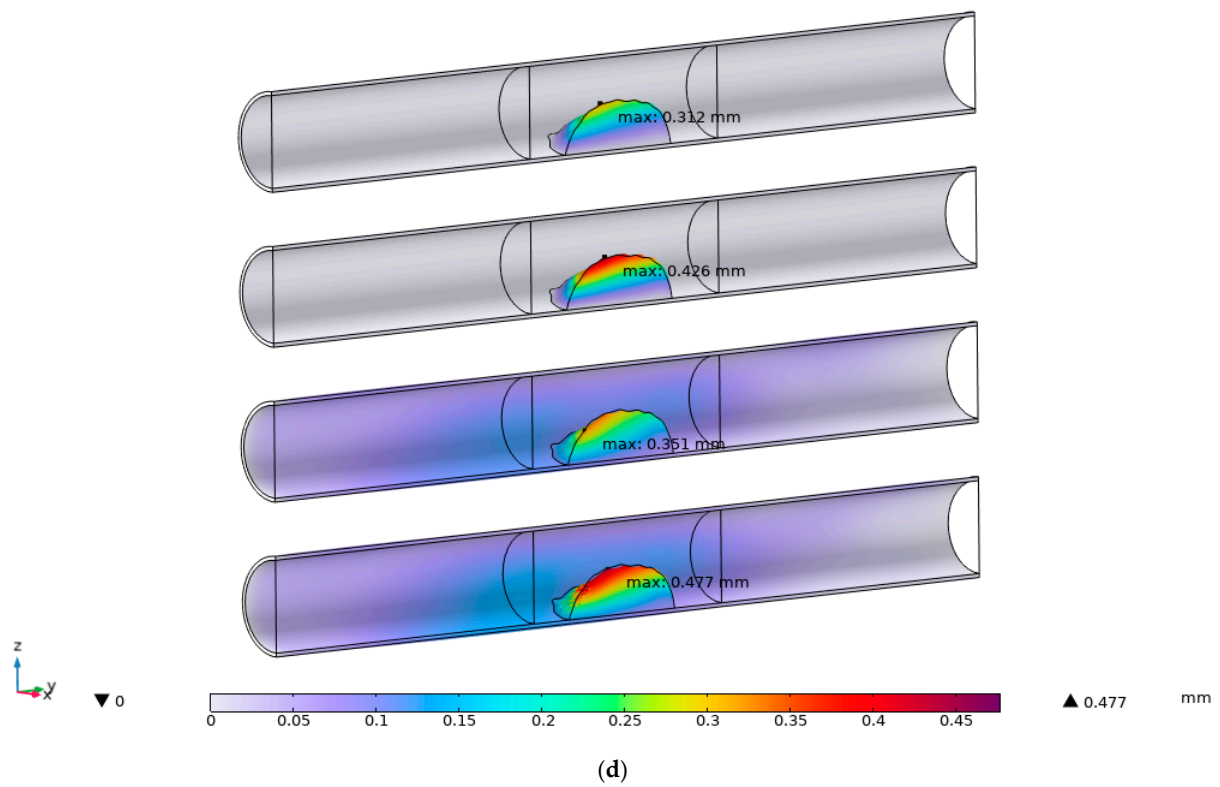
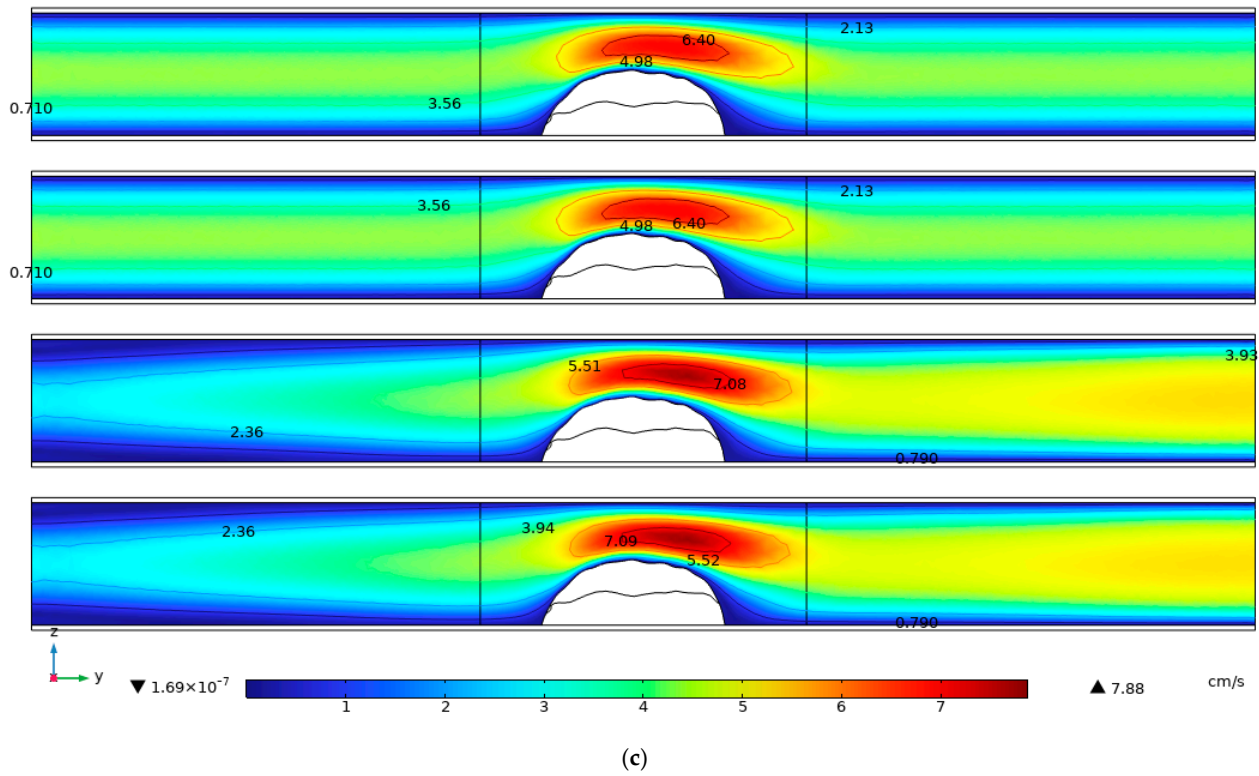


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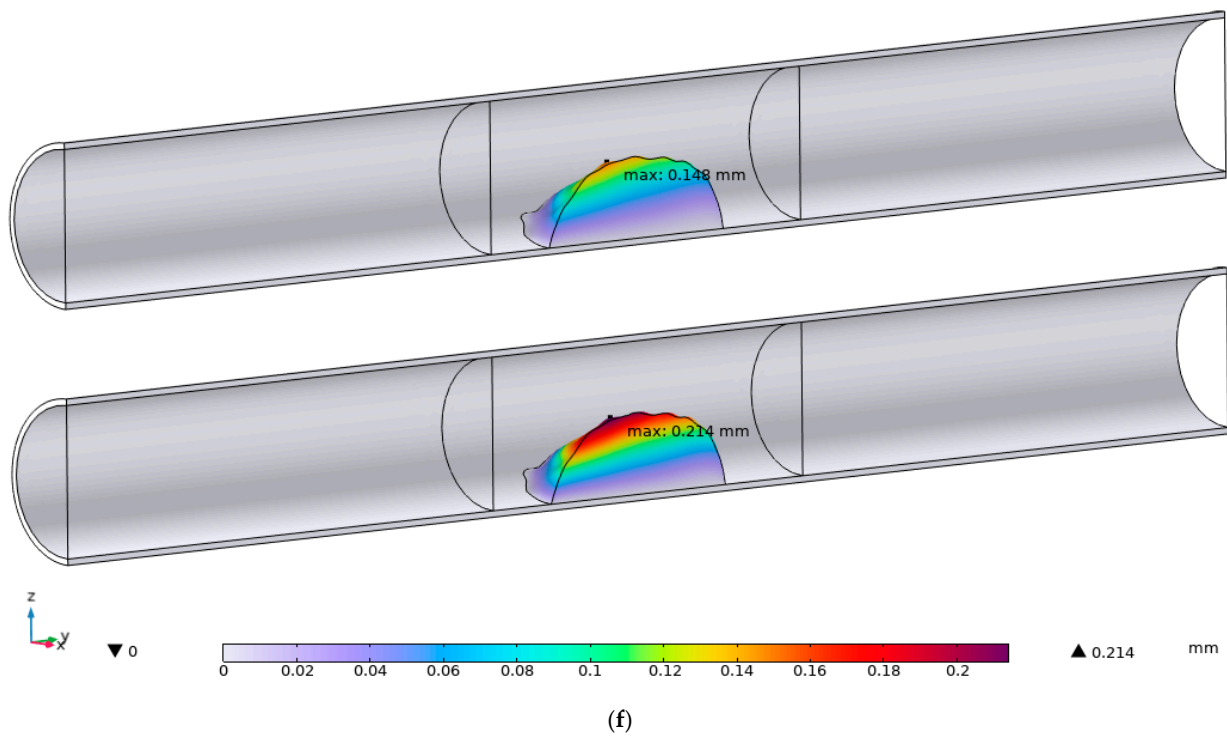
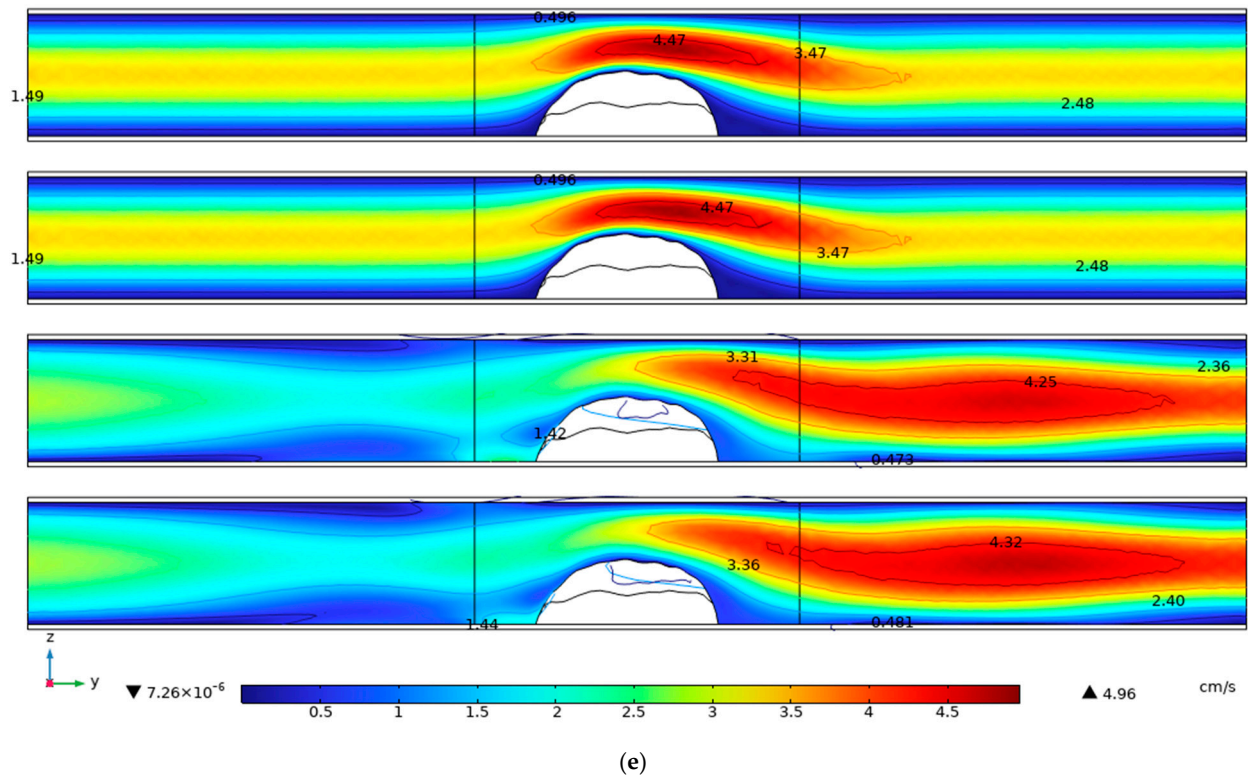


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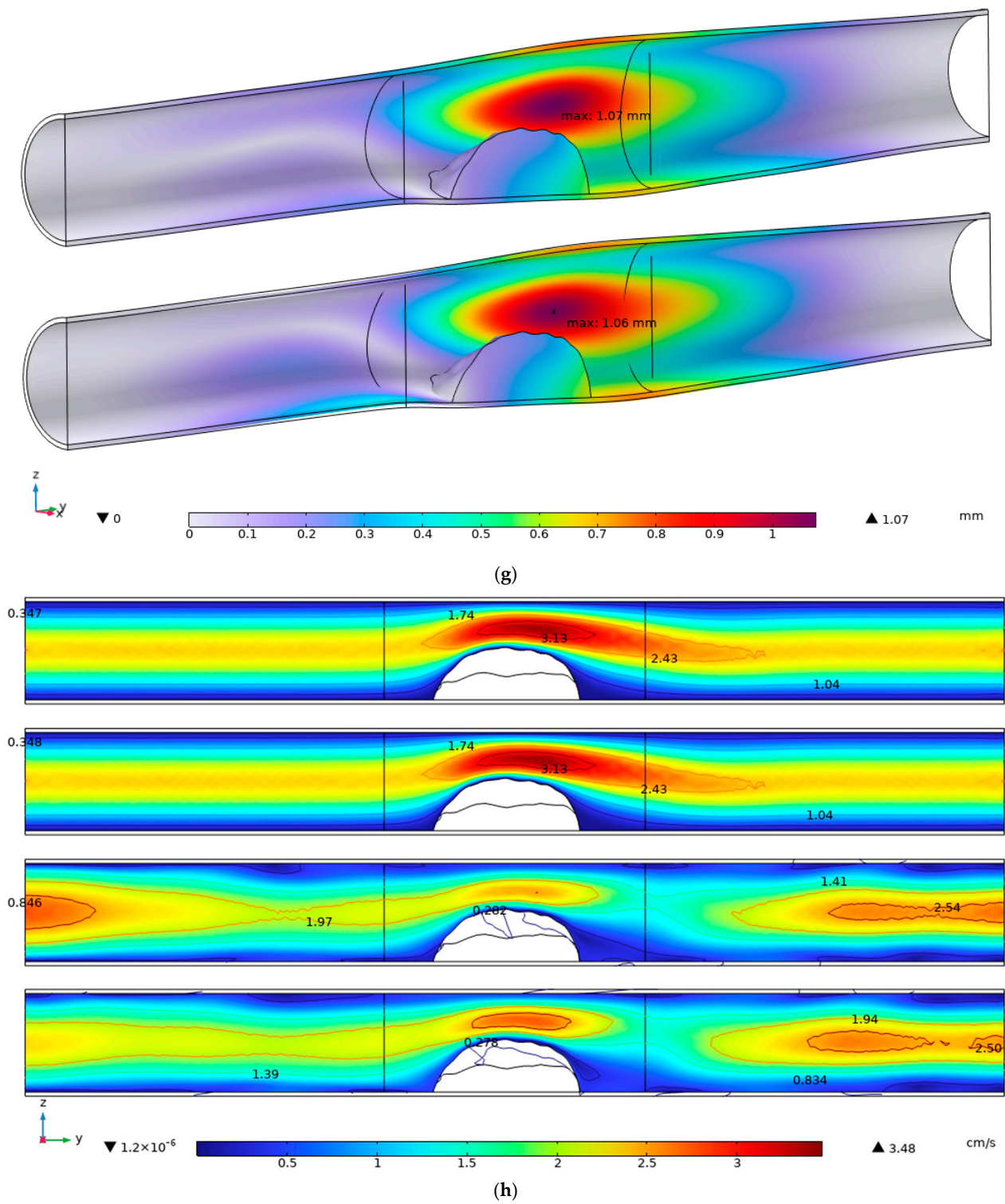


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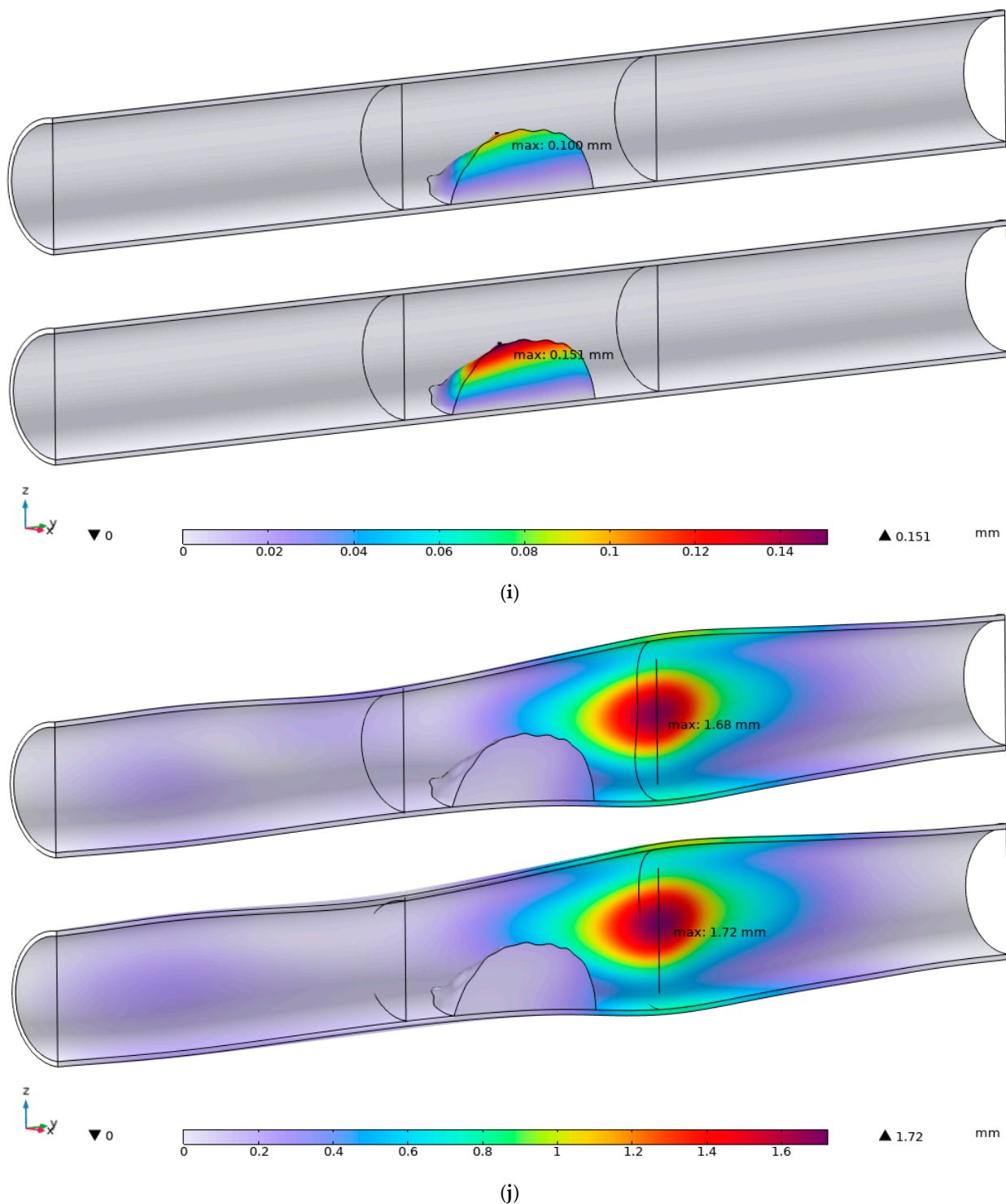


Figure 4. Simulation results. (a) Velocity distribution at the cross-section plane at the time step of 1.03 s; (b) deformation distribution of both the blood clot and the vein, at the time step of 1.03 s; (c) velocity distribution at the cross-section plane at the time step of 1.16 s; (d) deformation distribution of both the blood clot and the vein, at the time step of 1.16 s; (e) velocity distribution at the cross-section plane at the time step of 1.31 s; (f) deformation distribution of the blood clot at the time step of 1.31 s; (g) deformation distribution of both the blood clot and the vein, at the time step of 1.31 s; (h) velocity distribution at the cross-section plane at the time step of 1.45 s; (i) deformation distribution of the blood clot at the time step of 1.45 s; (j) deformation distribution of both the blood clot and the vein, at the time step of 1.45 s.

In Figure 4a,b, at the time step of 1.03 s, velocities in veins begin to increase and velocity differences between fixed and flexible vein walls can be seen. In fixed vein wall simulations, the velocity is very evenly distributed with an increase in the clot location, while in flexible vein wall simulations, the velocity increases in the first part of vein, while the velocity after the clot is very low. However, the difference caused by different viscoelasticity parameters seems to be close to zero. The vein wall in flexible variants is still only slightly deformed; therefore, deformations of the clot are quite similar in all variants, yet with the second set of viscoelasticity parameters, the clot is noticeably more deformed.

In Figure 4c,d, at the time step of 1.16 s, the velocities reach maximum values in all variants at the clot location. Through the color-coding, it can be seen that the velocities in flexible vein wall variants are a somewhat higher compared to those of the fixed vein wall variants. Again, the viscoelasticity parameters seem to have a minimal influence on velocity. Considering the velocity only gradually increased and reached the clot location with main flow, the vein wall in the flexible variants had not yet been significantly deformed, so the deformations were quite similar in both flexible and fixed vein walls using the same viscoelasticity parameters. The deformation differences for the second set of viscoelasticity parameters are significantly larger.

In Figure 4e, at the time step of 1.31 s, the velocity gradually decreases and starts to leave the length of the vessel. As can be seen using the color legend, the velocities in the fixed vein wall variant remain longer at the clot location, while in the flexible vein wall, they move further. This is influenced by the deformations of the vein wall seen in Figure 4g. The vein wall deforms just behind the clot, which was previously the location of the highest velocity and, therefore, the highest stress in the wall. The blood clot starts to retract to its original shape, and lower deformations are seen in Figure 4f. However, the deformations in the variant with the second set of viscoelasticity parameters are still considerably larger.

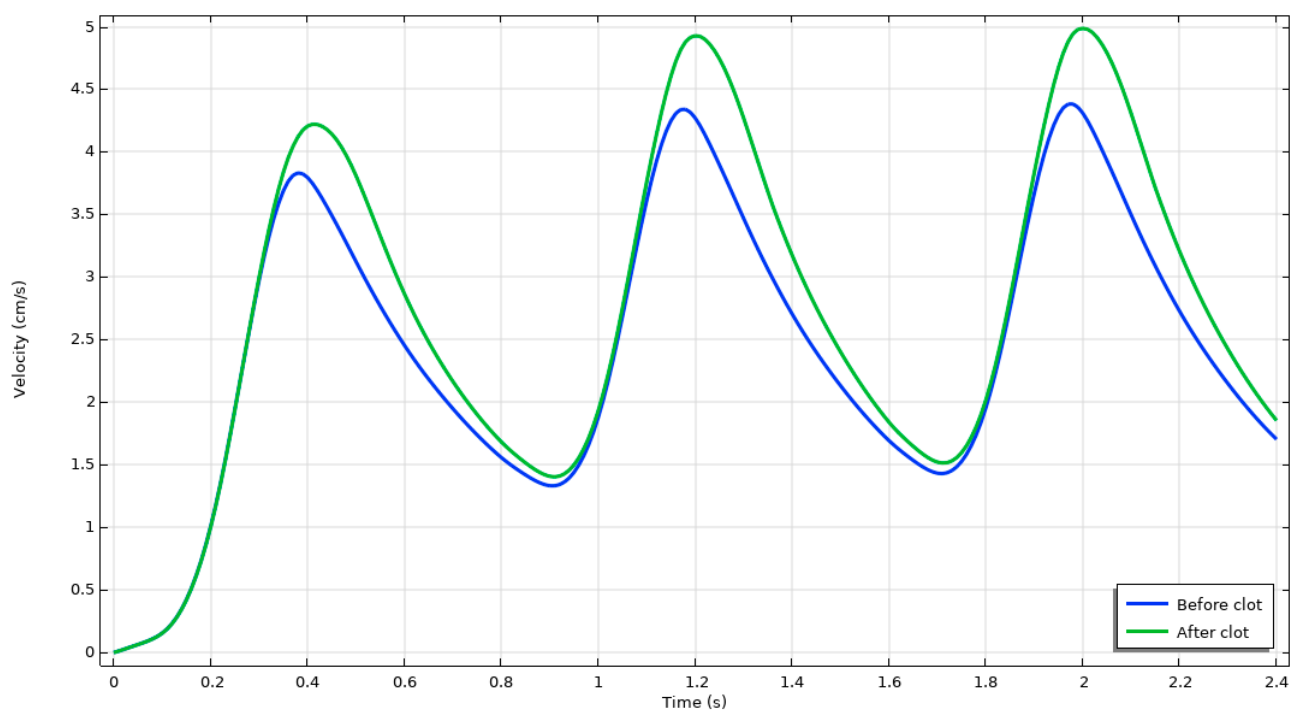
In Figure 4h, at the time step of 1.45 s, the velocity in the fixed vein wall variants retains a very similar flow pattern as in previous time step, just with a slightly lower value; however, in flexible wall variants, the velocity is drastically reduced, especially in the location immediately behind the clot. This is influenced by the large vein wall deformations seen in Figure 4j, where the vein wall can be seen to have both expanded and shrunk. The deformations of the clots in all variants decreased even more. In Figure 4i, the clot has almost retracted to its original shape, but the deformations seen with the second set of viscoelasticity parameters are still noticeably higher.

The exact differences between these four variants are illustrated using graphs.

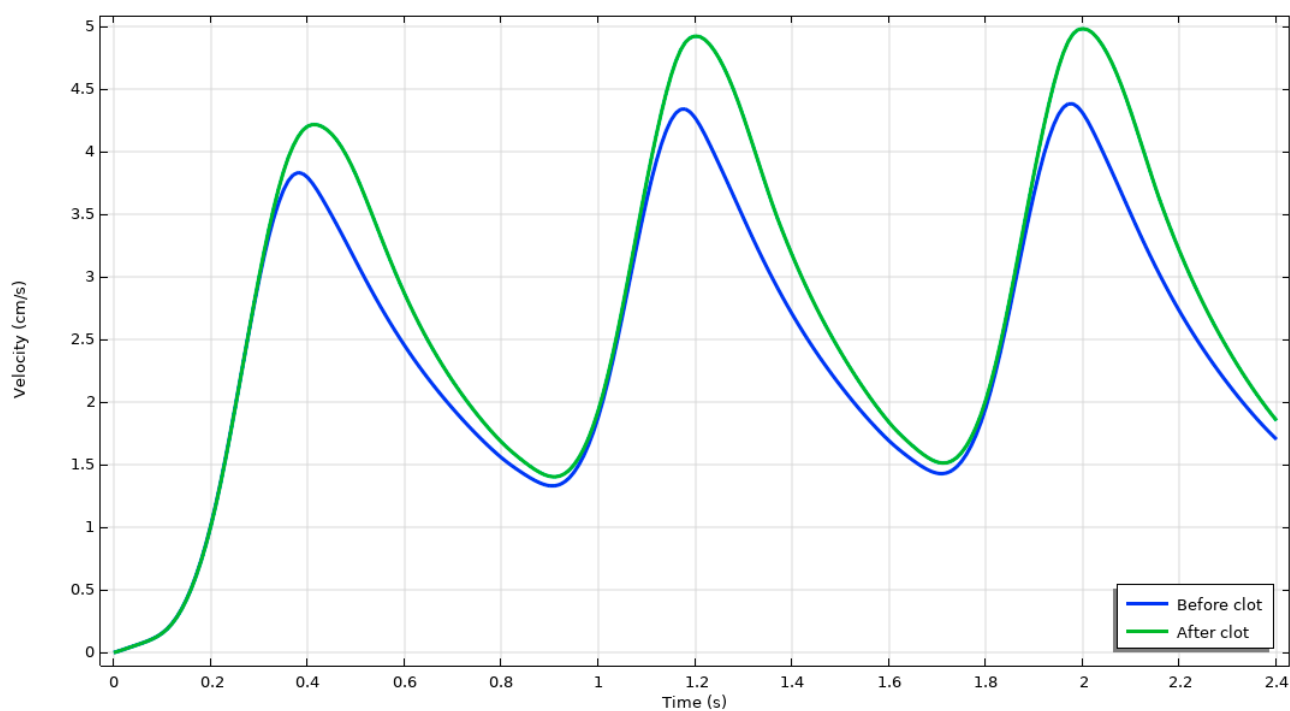
Before analyzing the results, it is important to mention that in Figure 5a–d, the terms “before clot” and “after clot” mean the planes before and after the clot seen in Figure 4. The “before” plane is 3 mm distance to the first point of clot geometry; the “after” plane is 4 mm distance after the last point of clot geometry.

Blood flow velocities in Figure 5a,b look almost exactly the same, which means that the influence of the viscoelasticity parameter set on the velocity is negligible. The velocities seen in Figure 5c,d are very similar, but some differences can be observed, especially in terms of the 2.2 s mark in both of them. Yet this velocity difference comes from the deformation of the blood clot (location and shape), which consequently influences the velocity. In the graphs of the fixed vein wall, the second and third heartbeats are almost identical, while the velocity in the first heartbeat is significantly lower. The maximum value of the second heartbeat before the blood clot was $u_1 = 4.34$ cm/s, while after the blood clot, it was $u_2 = 4.93$ cm/s, which indicates an increase of around 13.6%. In the graphs of the flexible vein wall, the second and third heartbeats are similar in value, but the patterns are slightly different. Also, as with fixed vein wall, the differences between first and the second/third heartbeats are very significant. The maximum value for the second heartbeat

before the blood clot was $u_3 = 4.36$ cm/s, and after a blood clot, it was $u_4 = 6.20$ cm/s, which is an increase of around 42.2%.

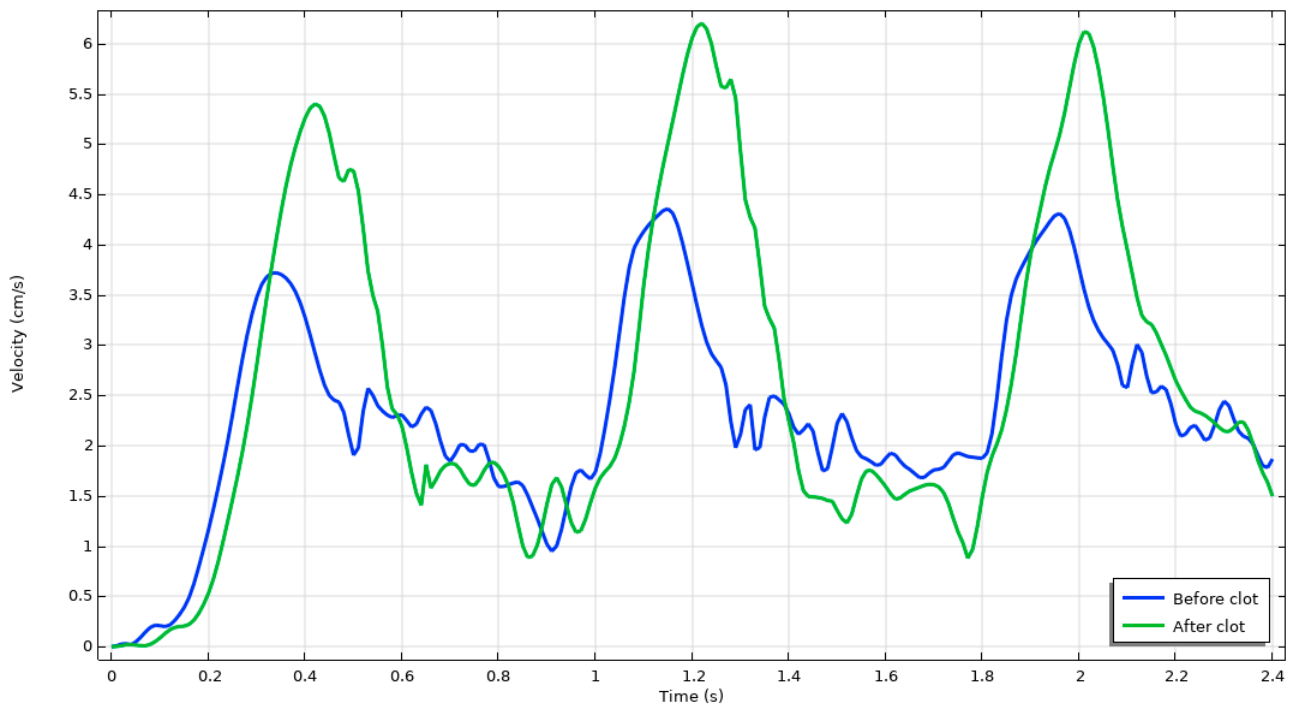


(a)

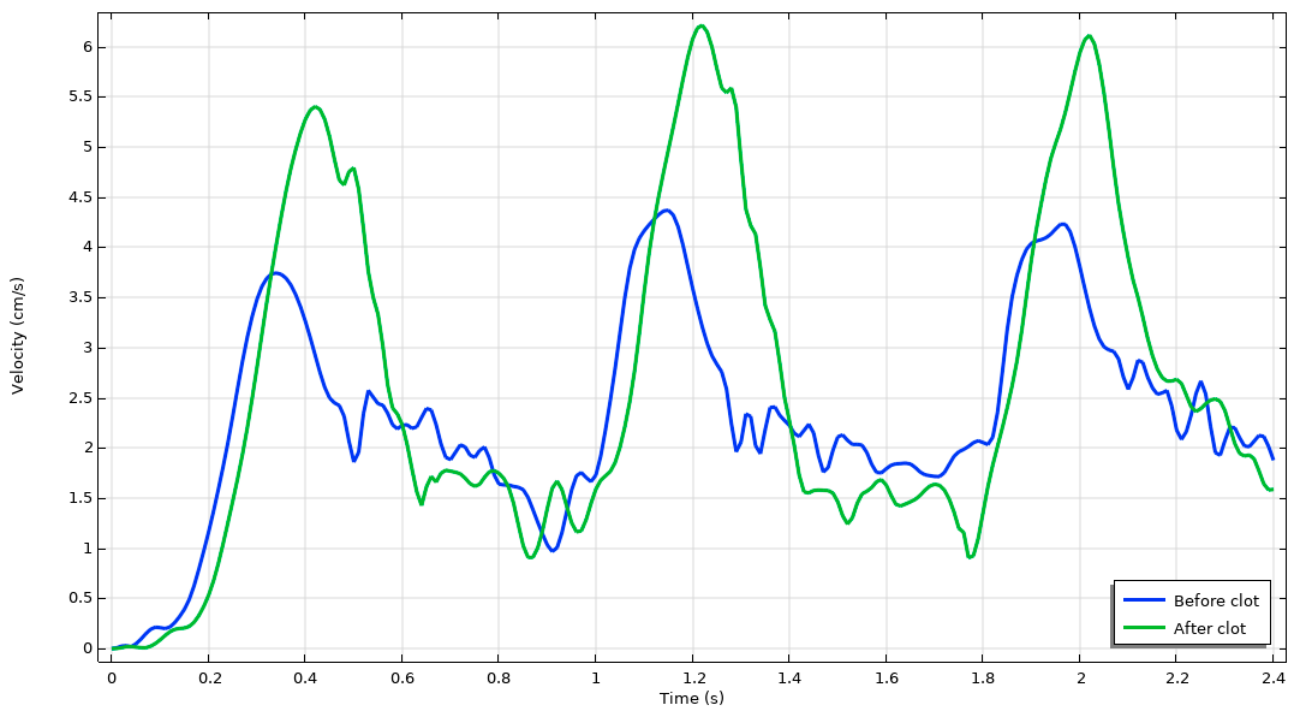


(b)

Figure 5. Cont.



(c)

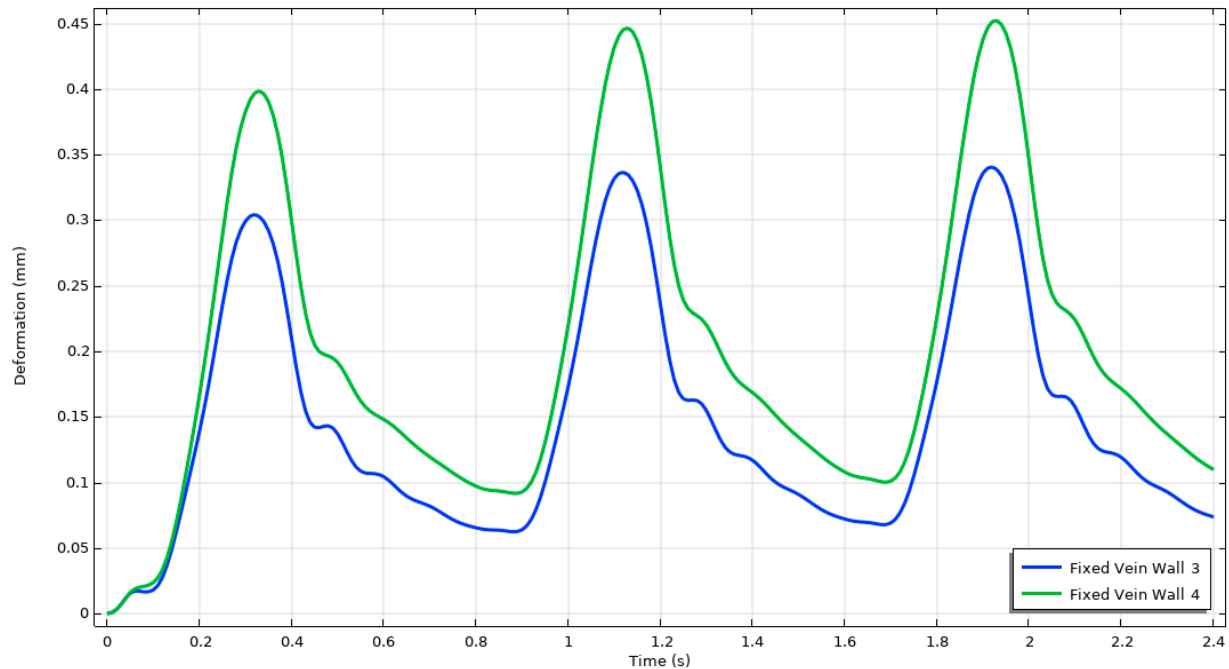


(d)

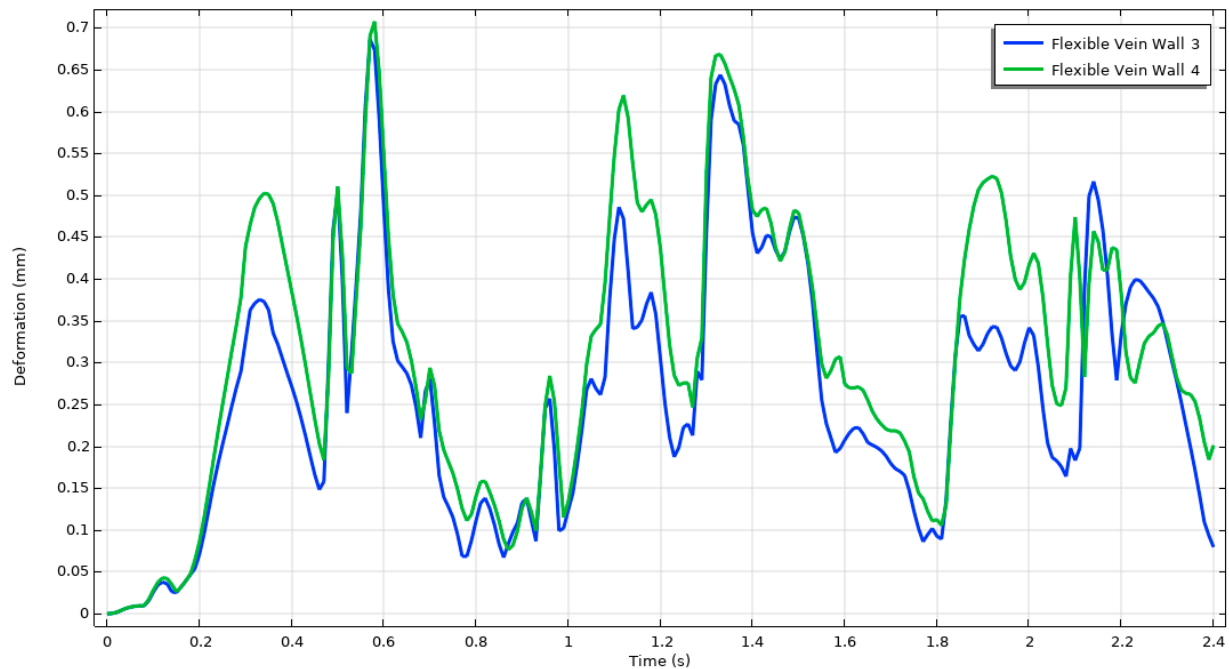
Figure 5. Simulation results as graphs. Fixed vein wall (FixVW); flexible vein wall (FlexVW). (a) Maximum blood flow velocity graph at planes before and after clot in FixVW3 simulation; (b) maximum blood flow velocity graph at planes before and after clot in FixVW4 simulation; (c) maximum blood flow velocity graph at planes before and after clot in FlexVW3 simulation; (d) maximum blood flow velocity graph at planes before and after clot in FlexVW4 simulation.

In Figure 6a,b, the maximum blood clot deformations are compared between two different viscoelasticity parameter sets using both a fixed and flexible vein wall. The deformations in the fixed vein wall variants seem to follow almost identical trajectories, but with different values. The maximum deformation during the second beat of the heart

in FixVW3 was $\Delta x_1 = 0.335$ mm, while using another set of viscoelasticity parameters (FixVW4), the deformation was $\Delta x_2 = 0.445$ mm, which means an increase of around 32.8% in the deformation. Deformations in the FlexVW3 and FlexVW4 variants at the same times were $\Delta x_3 = 0.486$ mm and $\Delta x_4 = 0.619$ mm, respectively. This indicates an increase of around 27.4% in deformation.

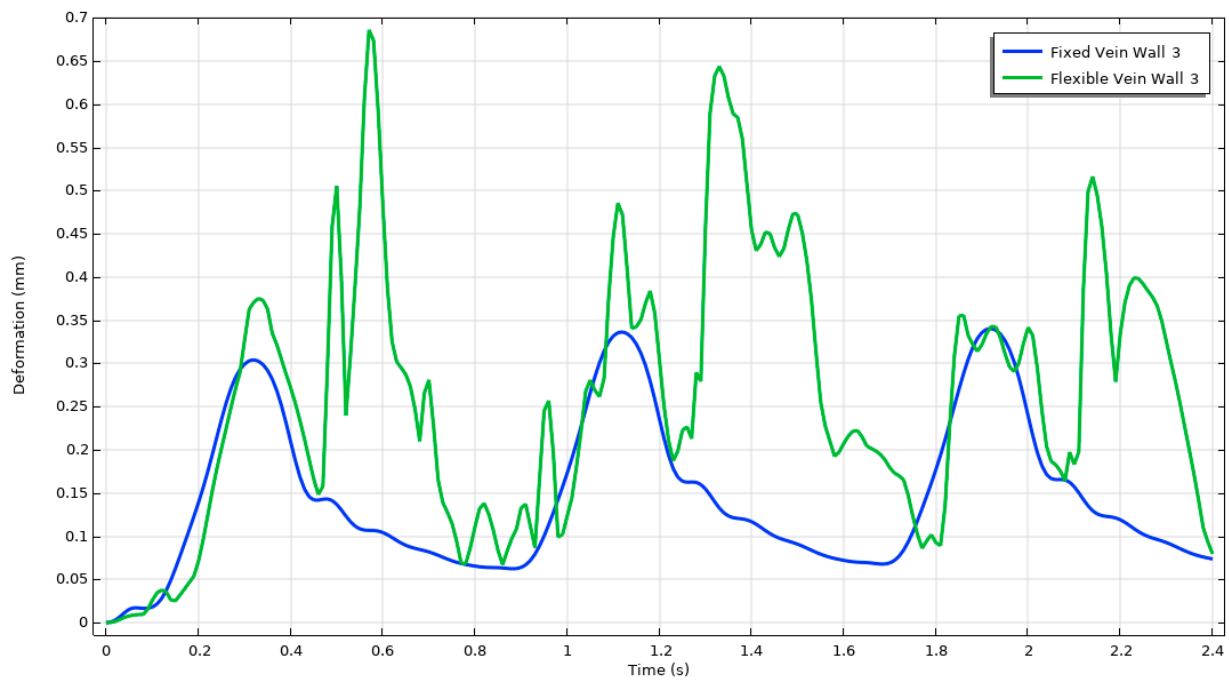


(a)

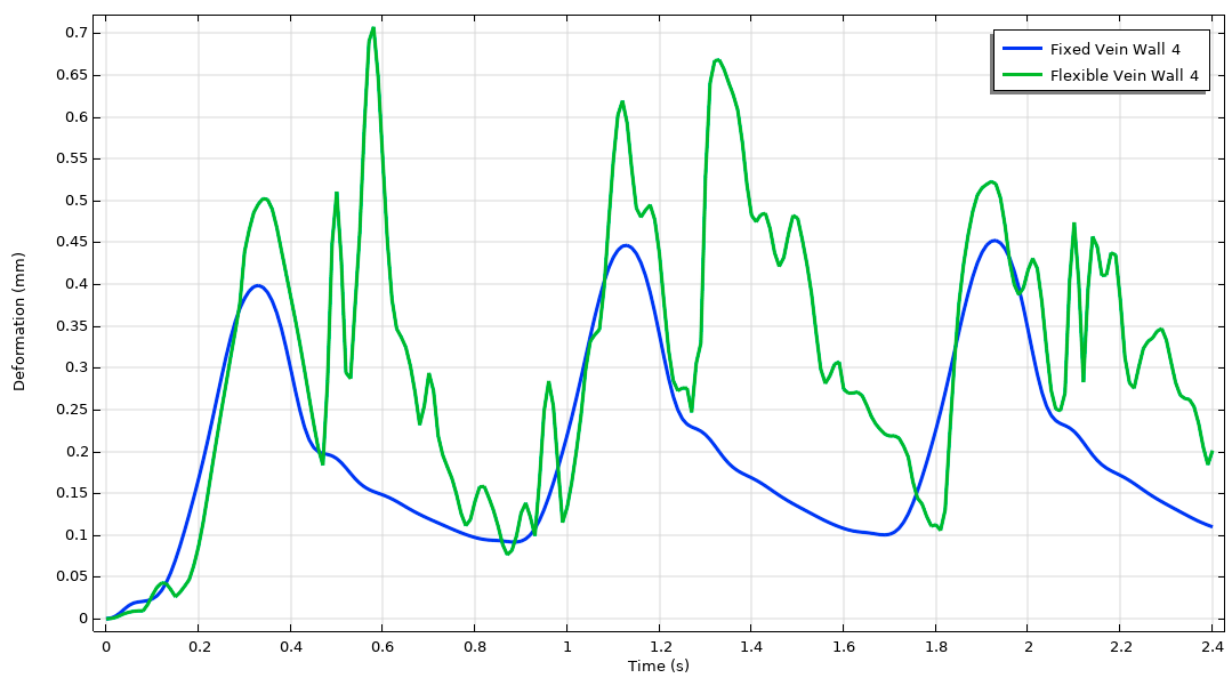


(b)

Figure 6. Cont.



(c)



(d)

Figure 6. Simulation results in graphs. Fixed vein wall (FixVW); flexible vein wall (FlexVW). (a) Maximum blood clot deformation graph in FixVW3 and FixVW4 simulations; (b) maximum blood clot deformation graph in FlexVW3 and FlexVW4 simulations; (c) maximum blood clot deformation graph in FixVW3 and FlexVW3 simulation; (d) maximum blood clot deformation graph in FixVW4 and FlexVW4 simulation.

In Figure 6c,d, the fixed and flexible vein wall variants are compared with each other using the same viscoelasticity parameter sets. It should be said here that the blood clot is fixed to the vein wall, and when the vein wall is deformed, the clot follows the deformation. The data in the graph show the comparisons of the initial clot position and the current at particular time steps. Therefore, deformations observed at the time steps of around 0.6 s; 1.4 s; and 2.2 s are mostly influenced by the deformations of the vein wall and not

by the clot itself; therefore, it cannot be evaluated (Figure 4g,j illustrates the difference). When comparing the deformations of the second heartbeat in fixed and flexible vein wall variants, the difference in the flexible vein wall compared with the fixed vein wall is around 45.1% when using the first set of viscoelasticity parameters and is around 39.1% when using the second set of viscoelasticity parameters. The crucial factor for analysis here is the maximum blood clot deformation values of all three heartbeats. In fixed vein wall variants, as expected from Figure 5 results, there is an increase between the second and first heartbeats, while the third is very similar to the second. Contrary to fixed vein wall variants, in flexible vein wall simulations, the deformation values in the second and the third heartbeats are different not only in terms of values but also in terms of the path of the curve, especially in the FlexVW3 variant.

The absolute blood clot reaction force graph, shown in Figure 7a, shows the sum of the absolute reaction forces of the blood clot in all directions (x , y , z). Both the fixed vein wall simulations yielded nearly identical curves. Even though the absolute reaction force in flexible vein wall simulations is similar for the first two heartbeats, for the third heartbeat we can see differences in the path of the curve. In addition, it is very interesting to note that in the fixed vein wall variants, the maximum absolute reaction force value remained consistent across the three heartbeats, while in the flexible vein wall variants, the maximum value increased for the second heartbeat and then significantly decreased for the third, reaching lower values than for the first heartbeat. Figure 7b,c shows the behavior of the vein wall: the viscoelasticity of the blood clot only minimally influences the deformation and stress values of the wall. It is interesting that the deformations of the wall seem to be very different in terms of both values and curves across the three heartbeats. Deformations that occur during the second heartbeat are significantly larger compared to the deformations that occur during the first heartbeat, though the maximum values of deformations that occur during the third heartbeat are more similar to the maximum values of deformations that occur during the first heartbeat, and only the curvature differs.

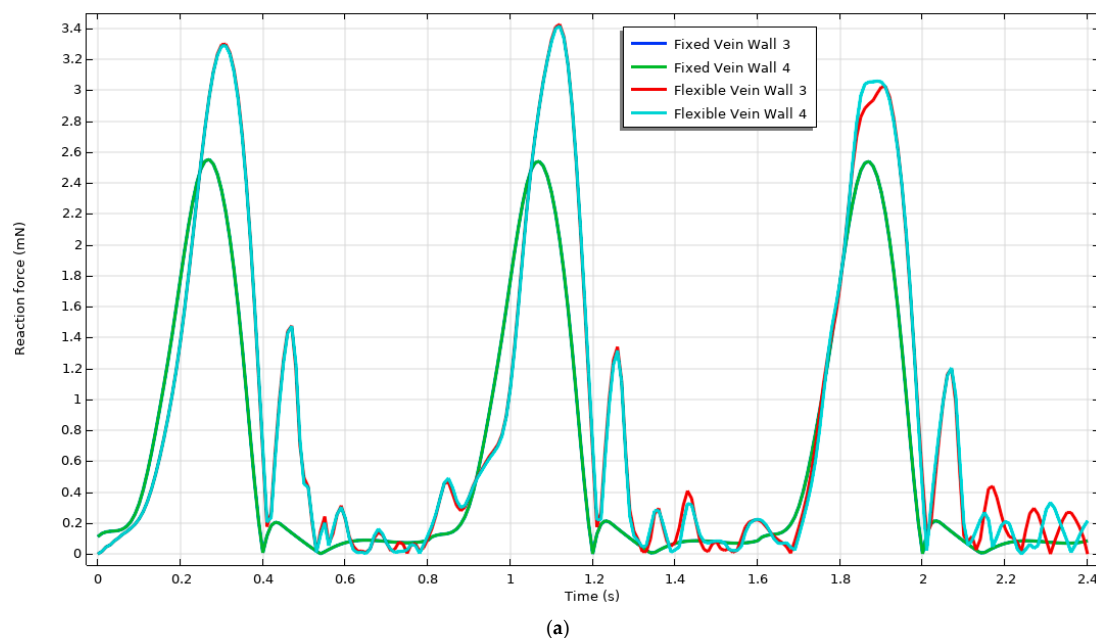


Figure 7. Cont.

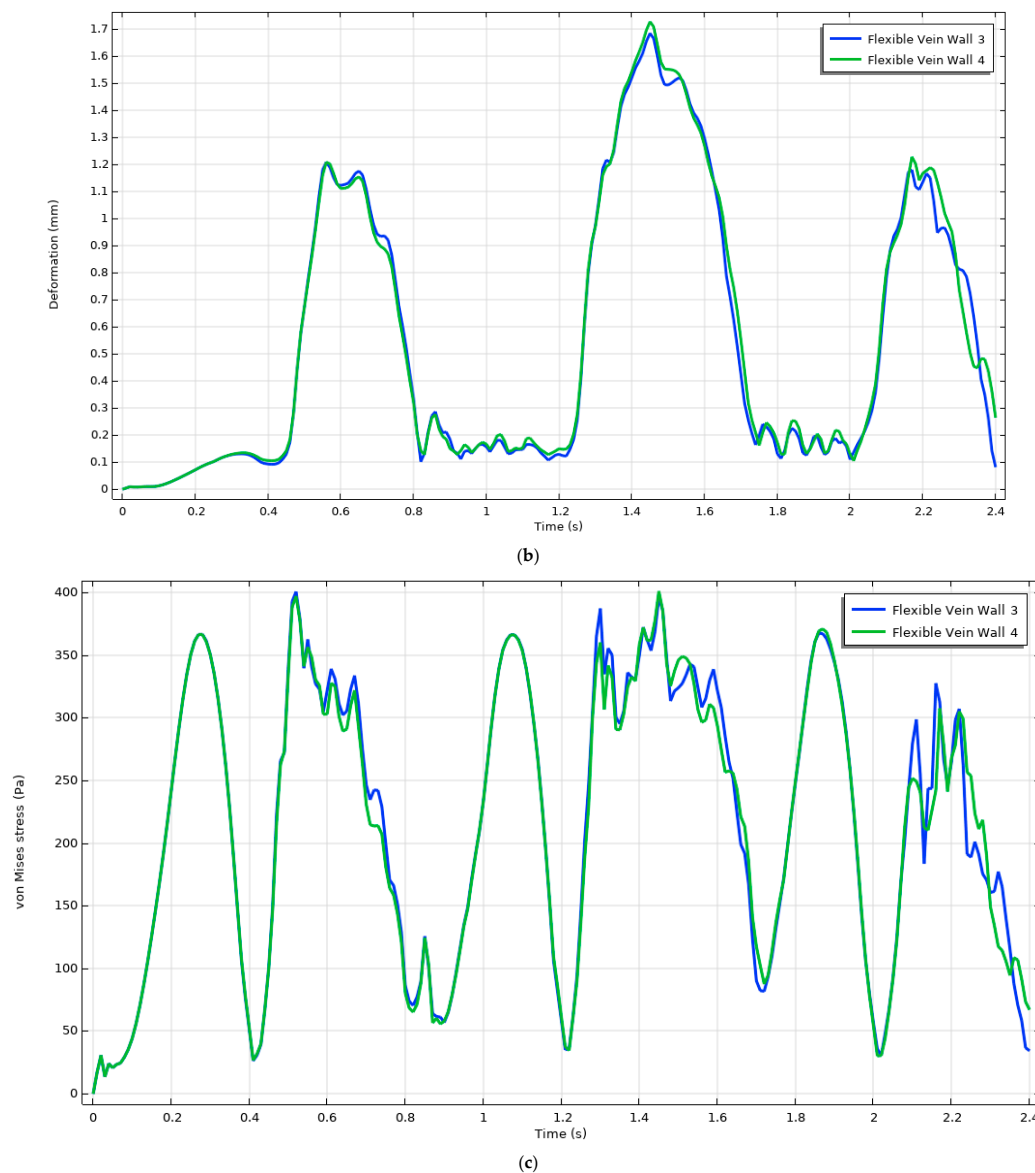


Figure 7. Simulation results in graphs. Fixed vein wall (FixVW); flexible vein wall (FlexVW). (a) Absolute reaction forces to the blood clot graph; (b) maximum vein wall deformation graph; (c) vein wall stress graph.

5. Discussion

From the results shown in Figure 5a–d, it can be observed that such blood clot simulations must contain at least two heartbeats in order to account the effect of continuous blood flow, as the results during the first heartbeat showed increased values compared to the subsequent heartbeats. Another interesting aspect is that the velocity increase before and after a clot in simulations with a flexible vein wall was significantly higher (42.2%) compared to that of the fixed vein wall (13.6%), which means that the flexible vein wall had a significant influence on the blood flow velocity and must be taken into account.

From the results of Figure 6a–d, it can be observed that in fixed vein wall variants, the viscoelasticity parameters influence only the values but do not change the curve path. In contrast, when analyzing variants with a flexible vein wall, differences start to appear not only for values but also for the curve path. It is important to note here that in both articles from which viscoelasticity parameters were taken [19,20], the viscoelasticity values were found using a blood clot made in vitro. Furthermore, every blood clot is unique not only in shape but also according to its composition/parameters; there-

fore, parameter fluctuations are expected. Nevertheless, studies of *in vivo* or *ex vivo* blood clot viscoelasticity parameters would be useful to more accurately determine the parameter range.

From the results of Figure 7a–c, it can be observed that the analysis of the blood clot using a flexible vein wall is a very complex task, since the process does not seem to be stable within the three heartbeats. Moreover, blood clot deformations, absolute blood clot reaction forces, and vein wall deformation/stress values do not correlate with the blood flow velocity graphs (Figure 5c,d). While the blood flow velocity in the second and third heartbeats are quite similar, blood clot deformations, absolute blood clot reaction forces, and vein wall deformation/stress values become chaotic and do not follow any particular pattern. In future studies, we plan to analyze blood clots with a flexible vein wall using a higher number of heartbeats (longer time span) to find out when/if the process stabilizes.

In contrast to a previous article by Brusokas and Jasevičius [34], there were no signs of vortexes in the blood flow after a blood clot in a fixed vein wall simulation. For this simulation, we used a relatively slow blood flow (around 3–4 cm/s before the clot); however, the velocity was able to increase up to 28 cm/s [35], depending on the human activity, the position of the leg, etc.) compared to the previous study. It could be that the velocity was too low to achieve a turbulent flow after a clot, and thus, there were no signs of vortexes. It could also be due to the fact that this study was carried out using a 3D clot model, unlike the 2D model of the previous study. For future experiments, it would be beneficial to analyze the causes and conditions needed for the formation of vortexes after a blood clot.

Moreover, the model used in this article works both for flexible and fixed vein walls, as well as for different viscoelasticity models. In future research, it would be interesting to utilize this model but to change the size and shape of the blood clot as well as blood flow velocity in order to see whether there are differences or similarities when compared to this work.

We observed that vein deformations play a crucial role in the behavior of a blood clot. We analyzed vein deformations in conjunction with certain elasticity parameters: Young's modulus 5000 Pa and Poisson's ratio 0.47. We think that in order to obtain a full picture of the blood vein behavior analysis, it is necessary to analyze the situation with possible variations (in the stiffness) of the mechanical parameters.

6. Conclusions

In this article, the behavior of a blood clot was analyzed numerically. The experiment was performed using a 3D numerical simulation of a blood clot in a vein. The influence of the mechanical effect caused by the blood flow was observed both for the thrombus and the blood vessel. In order to study the mechanical effect of blood flow on the thrombus and blood vessel, the experiment was performed under different conditions, and different parameters of the blood vessel wall were evaluated. In one case, the blood vessel geometry was fixed and non-deformable. In the second case, the blood vessel was flexible, meaning its geometry changed over time depending on the blood flow. This was done in order to identify the behavior of the blood vessel itself and its influence.

In order to understand the effect of wall deformation on blood flow and consequently on the blood clot, vein models with blood clots inside a fixed and flexible vessel wall were compared using two different sets of viscoelasticity parameters found in the literature, specifically in *in vitro* studies. It was observed that when the blood vessel wall was fixed, the simulation with a duration of two heartbeats was sufficient to reach a stable process (blood flow velocity, blood clot deformations), while when the vein wall is flexible, a time frame of three heartbeats, as was used in this study, is not enough.

It was observed that in the numerical experiment, the viscoelasticity parameters of a blood clot of this shape/size had no significant influence on either the blood flow velocity or the reaction force of the blood clot when the wall was fixed. When the wall was flexible—due to deformations of both the vein wall and the clot, which occurred separately but simultaneously—the difference was visible. It was observed that with the same inlet parameters and the same blood clot geometry, when the wall is flexible and can be deformed, the maximum blood flow velocities and blood clot deformations found during the numerical experiments changed (increased) compared to the results using a fixed vein wall. It was also observed that the variations in the blood velocity distribution graph according to the heart rate were not directly related/proportional to the deformations of the blood clot, the deformations of vein walls, the stresses of the vein wall, and the absolute reaction force of the blood clot.

Our future research will focus on examining the process by increasing the duration of the simulation by adding more heartbeats when the vein wall is flexible. It would also be interesting to study such a vein model using different blood clot sizes and shapes, as well as different blood flow parameters.

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Nomenclature

FlexVW3	Flexible Vein Wall 3
FlexVW4	Flexible Vein Wall 4
FixVW3	Fixed Vein Wall 3
FixVW4	Fixed Vein Wall 4
MR	magnetic resonance
CT	computed tomography
CVD	cardiovascular diseases
EVT	Endovascular thrombectomy
<i>Roman</i>	
u	blood velocity (cm/s)
p	pressure of the fluid (Pa)
J_{el}	elastic volumetric deformation
P	first Piola–Kirchhoff stress tensor
S	second Piola–Kirchhoff stress tensor
E	Young’s modulus (Pa)
C	Cauchy–Green deformation tensor
t	time (s)
W_s	total strain energy density
W_{iso}	isochoric strain energy density
W_{vol}	volumetric strain energy density
C_{10}	Mooney–Rivlin hyperelasticity parameter
C_{01}	Mooney–Rivlin hyperelasticity parameter
<i>Greek</i>	
ρ	density of the fluid (blood) (kg/m ³);
μ	dynamic viscosity of the fluid (cP);
κ	bulk modulus (Pa).

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