

RATIONAL CHOICE OF MODELLING ASSUMPTIONS FOR SIMULATION OF BLOOD VESSEL END-TO-SIDE ANASTOMOSIS

IGOR I. TAGILTSEV^{1,2,*}, DANIIL V. PARSHIN^{1,2}
AND ALEXEY V. SHUTOV^{1,2}

Abstract. Blood vessels exhibit highly nonlinear, anisotropic behaviour with numerous mechanical interactions. Since exact modelling of all involved effects would yield a computationally prohibitive procedure, a practical clinical simulation tool needs to account for a minimum threshold of relevant factors. In this study, we analyse needed modelling assumptions for a reliable simulation of the end-to-side anastomosis. The artery wall is modelled in a geometrically exact setting as a pre-stressed fibre-reinforced composite. The study focuses on the sensitivity analysis of post-anastomosis stress fields concerning the modelling assumptions. Toward that end, a set of full-scale finite element simulations is carried out for three sensitivity cases: (i) The post-operational stresses are estimated with and without taking the residual stresses into account. (ii) Different geometries of the cut in the recipient vessel are examined. (iii) The influence of errors in material stiffness identification on the post-operational stress field is estimated. The studied cases (i)–(iii) have shown a substantial impact of the considered modelling assumptions on the predictive capabilities of the simulation. Approaches to more accurate predictions of post-operational stress distribution are outlined, and a quest for more accurate experimental procedures is made. As a by-product, the occurrence of the pseudo-aneurysm is explained.

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1. INTRODUCTION

Vascular bypasses are widely used in vascular surgery, frequently employed to correct blood flow. Imposition of bypasses is carried out during procedures like coronary artery bypass grafting [13], femoral artery bypass grafting in case of its occlusion [66], bypass grafting through the external carotid arteries in case of Moya-Moya disease [72] or during destructive operations in treatment of aneurysms [32]. The optimality of bypasses' functioning is under question, which requires computer modelling at the preoperative stage. For example, in [36] a rational approach to finding the optimal angle between the bypass and the recipient was studied. This paper focuses specifically on arteriotomy of recipient vessel and mechanics of blood vessels' walls during anastomosis. Modelling the arteriotomy stage is of paramount importance, because the surgical technique – a linear or the “fish mouth” type of vascular tissue incision – affects the distribution of stresses in the vessel wall. The choice of the technique affects the possible development of aneurysmal expansion in the area of the shunt junction or

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¹ Lavrentyev Institute of Hydrodynamics, Pr. Lavrentyeva 15, 630090, Novosibirsk, Russia.

² Novosibirsk State University, Ul. Pirogova 1, 630090 Novosibirsk, Russia.

* Corresponding author: i.i.tagiltsev@gmail.com

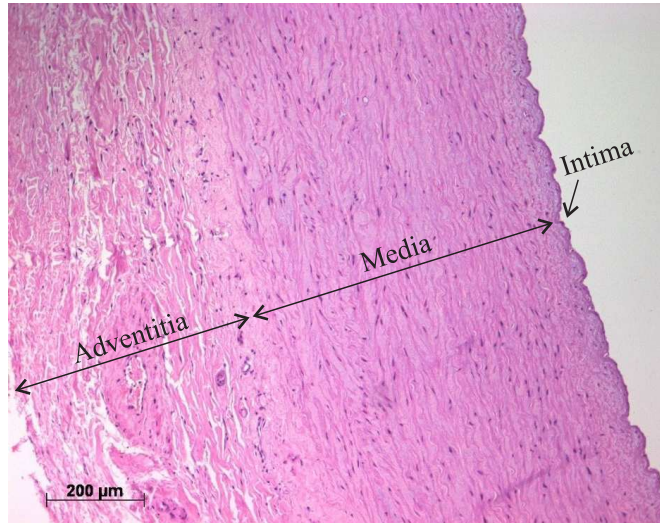


FIGURE 1. Radial cut of a healthy human internal carotid artery.

its possible thrombosis, causing a high risk of morbidity or mortality [11]. However, to this day not that many studies were made regarding this problem: in most of researches vessel's wall is simulated as a rigid surface [19, 36] or *via* implementing simple and inaccurate material models such as isotropic shells [23, 39, 45], neo-Hooke material [18] or Mooney-Rivlin material [50]. Only a few studies used state-of-the-art material models for the modelling of vessel wall, focusing on the several sensitivity studies: Incision length in recipient vessel and insertion angle between artery and graft were analysed in [7] and mismatch between the collagen fibre orientations in comparison with natural bifurcation was analysed in [46].

A patient-specific medical treatment requires numerical simulations of surgery, explicitly accounting for individual parameters of each patient. Such a simulation should be based on the geometry of the involved structures, applied loads, and mechanical properties of healthy and pathological tissues. However, development of material models and numerical algorithms inevitably leads to the following problem: it is unknown *a priori* which mechanical effects are important for a particular medical application. Blood vessels exhibit the typical multi-layer structure (Fig. 1). The presence of layers allows for redistribution of mechanical loads depending on properties of individual layers [24, 67]. Effectively, two of them carry the load in healthy arteries (the media and the adventitia), while the third inner layer (the intima) is usually taken into account only for ill arteries due to its weakness and thinness [47]. The current conventional representation of the tissue as a fibre-reinforced composite [24] allows reducing the problem to two simpler problems: modelling the isotropic matrix and transversally-anisotropic fibres. Viscoelastic [25, 37, 61, 70], damage-related [2, 21, 30, 74], as well as growth & remodelling [5, 12, 17, 33] models describe the stress-strain hysteresis, damage accumulation, and reorganisation/adaptation of soft tissue, respectively. Consideration of residual stresses [3, 24, 62] is crucial for analysing overall stress fields, kinematics of the structure, and its functional properties. Unfortunately, a simulation of several interacting non-linear phenomena can be computationally prohibitive for practical clinical use. Therefore, it is imperative to know which information regarding the considered system is necessary to obtain accurate predictions. Meanwhile, it benefits to understand the particular part of the model that is less relevant or which can be ignored or simulated with less accuracy.

The main challenges in computational modelling of blood vessels are insufficient amount of actual experimental data and wide range of experimental results. The insufficient experimental program naturally limits the complexity of implemented material models and thus the overall predictive capabilities of simulations. This study aims to highlight relevant mechanical effects which are still under-investigated from the experimental

point of view. One such effect is the individual layer contribution of the media and the adventitia to the overall mechanical response.

In the current work, parameters of a surgery simulation are examined in a number of new sensitivity studies, not considered before. The sensitivity of the simulation is tested with respect to applied modelling assumptions. Impacts of residual stresses, the geometry of the cut in recipient vessel and errors in parameter identification are investigated.

Following the iso-strain approach, the composite is represented as a soft isotropic matrix reinforced with two families of collagen fibres [24]. The so-called $\mathbf{F}_0$ -approach [62] captures residual stresses, which introduces an explicit relationship between load-free and stress-free configurations of the tissue's particle. For simplicity, inelastic effects like viscosity and plasticity are neglected. Neglecting these does not reduce the value of the study since under physiological loads after the shunt deposition, such effects can be ignored. Moreover, if needed, the inelastic effects can be combined with the $\mathbf{F}_0$ -approach (for details see [62] for multiplicative viscoelasticity or [71] for fractional viscoelasticity).

The paper is organised as follows. Section 2 recalls a geometrically exact model of a fibre-reinforced composite material. Section 3 briefly formulates the $\mathbf{F}_0$ -approach to residual stresses. Its specific setting to describe the self-opening effect of blood vessels is recapitulated. Section 4 presents the finite-element simulation of anastomosis and a set of sensitivity studies. Finally, we discuss the main results in Section 5.

2. CONSTITUTIVE BEHAVIOUR

Let $\mathbf{F}$ be the deformation gradient at a material point. It is a linear operator which transforms line elements from the reference configuration to the current configuration. We focus on the simulation of hyperelastic composite materials within the iso-strain approach. Hence, the local mechanical response of the material is supposed to be a function of the right Cauchy-Green tensor $\mathbf{C} = \mathbf{F}^T \mathbf{F}$. Given the near-incompressibility of soft living tissues, its unimodular part $\bar{\mathbf{C}} = (\det \mathbf{C})^{-1/3} \mathbf{C}$ is particularly relevant for the modelling. Application of the iso-strain approach implies the assumption of equal deformations for every constituent of composite, namely, its matrix and fibres. In terms of a rheological model, the iso-strain assumption corresponds to a parallel connection of constituents. The rheological interpretation yields the additive split of the free-energy function per unit mass into the matrix energy Ψ_{matrix} and the energy of the i th fibre family $\Psi_{\text{fibre},i}$:

$$\Psi = \Psi_{\text{matrix}} + \sum_{i=1}^N \Psi_{\text{fibre},i}. \quad (2.1)$$

Here, N is the total number of fibre families.

2.1. Matrix behaviour

To describe the isotropic part of a mechanical response corresponding to the matrix, we employ the two-term Mooney-Rivlin potential

$$\rho_R \Psi_{\text{matrix}}(\mathbf{C}) = \frac{c_1}{2} (\bar{I}_1 - 3) + \frac{c_2}{2} (\bar{I}_2 - 3), \quad (2.2)$$

where c_1 and c_2 are the shear moduli of the material; ρ_R is the mass density in the reference configuration; $\bar{I}_1 = \text{tr} \bar{\mathbf{C}}$ and $\bar{I}_2 = \text{tr} \bar{\mathbf{C}}^{-1}$. This model was initially introduced for rubber-like materials, but it is widely used to capture the mechanical response of cartilage tissue [34] and of cardiovascular components [43].¹ The second

¹In studies involving large strain of ruptured tissues, the 5-parametric Mooney-Rivlin potential is also used [44].

Piola-Kirchhoff stress on the reference configuration is obtained as

$$\tilde{\mathbf{T}}_{\text{matrix}} = 2\rho_{\text{R}} \frac{\partial \Psi_{\text{matrix}}(\mathbf{C})}{\partial \mathbf{C}} = \mathbf{C}^{-1}(c_1 \overline{\mathbf{C}} - c_2 \overline{\mathbf{C}^{-1}})^{\text{D}}. \quad (2.3)$$

Here, $\mathbf{A}^{\text{D}} = \mathbf{A} - \frac{1}{3}\text{tr}(\mathbf{A})\mathbf{1}$ stands for the deviatoric part of a tensor.

2.2. Fibre behaviour

To describe the anisotropic response of fibres, we follow the work of Holzapfel *et al.* [24]. Two families of fibres arranged in helical curves are considered. In the reference configuration, each family is characterised by its direction unit vector $\tilde{\mathbf{a}}_i$, giving rise to the corresponding structural tensor $\mathbf{M}_i = \tilde{\mathbf{a}}_i \otimes \tilde{\mathbf{a}}_i$, $i = 1, 2$. We assume that both unit vectors $\tilde{\mathbf{a}}_i$ are aligned symmetrically with respect to the hoop direction of blood vessel; the angle of slope β uniquely defines them. Now, for every fibre family we consider the well-known Holzapfel-Gasser-Ogden potential:

$$\rho_{\text{R}} \Psi_{\text{fibre}}(\lambda_i^2) = \frac{k_1}{2k_2} (\exp[k_2(\lambda_i^2 - 1)^2] - 1), \quad \lambda_i = \sqrt{\overline{\mathbf{C}} : \mathbf{M}_i}, \quad i = 1, 2, \quad (2.4)$$

where $k_1 > 0$ is a stress-like constant, $k_2 > 0$ is a non-dimensional parameter, and λ_i is the stretch of the i th fibre family. The corresponding second Piola-Kirchhoff stress on the reference configuration is then calculated with the chain rule

$$\tilde{\mathbf{T}}_{\text{fibre } i} = 2\rho_{\text{R}} \frac{\partial \Psi_{\text{fibre}}(\lambda_i^2)}{\partial \lambda_i^2} \frac{d(\overline{\mathbf{C}} : \mathbf{M}_i)}{d\mathbf{C}} = 2\rho_{\text{R}} f(\lambda_i^2) \mathbb{P}_{\overline{\mathbf{C}}} : \mathbf{M}_i, \quad (2.5)$$

where $f(\lambda_i^2) := \frac{\partial \Psi_{\text{fibre}}(\lambda_i^2)}{\partial (\lambda_i^2)} = k_1(\lambda_i^2 - 1) \exp[k_2(\lambda_i^2 - 1)^2]$ and $\mathbb{P}_{\overline{\mathbf{C}}} : \mathbf{X} = \mathbf{X} - \frac{1}{3}\text{tr}(\overline{\mathbf{C}}\mathbf{X})\overline{\mathbf{C}}^{-1}$.

Remark 2.1. In (2.4)₂ we use the unimodular part $\overline{\mathbf{C}}$ rather than the tensor $\mathbf{C}$ itself to define the fibre stretch. This assumption enforces a pure split of the stress response into the volumetric and deviatoric parts. However, such a pure split is not reasonable in compressible composites, leading to inconsistent results [22, 49]. In this study, we use Herrmann formulation to enforce the incompressibility of the material behaviour. In this case, the choice between $\mathbf{C}$ and $\overline{\mathbf{C}}$ becomes irrelevant.

We focus on the mechanical properties of two general families of fibres under tension in the current study; however, in a more complex setting, various generalisations of (2.4) are available, *e.g.* those accounting for fibre dispersion [15], slackness [40], and buckling under compression [61].

3. IMPLEMENTATION OF RESIDUAL STRESSES WITH $\mathbf{F}_0$ -APPROACH

3.1. General idea

Let $\tilde{K}_{\text{lf}}$ be a load-free configuration of the considered pre-stressed body. The deformation gradient $\mathbf{F}_{\text{lf}}$ transforms line elements from $\tilde{K}_{\text{lf}}$ to the current configuration K . In practical FEM-computations, the $\tilde{K}_{\text{lf}}$ is a natural choice for the reference configuration. Thus, the corresponding constitutive model of a pre-stressed material should be formulated on $\tilde{K}_{\text{lf}}$.

Starting from a load-free configuration, we consider the process of local unloading for an individual material particle, leading to the local stress-free configuration $\tilde{K}_{\text{sf}}$; the deformation gradient corresponding to this unloading process is denoted as $\mathbf{F}_0$. Therefore, the deformation gradient $\mathbf{F}_{\text{sf}}$ transforming $\tilde{K}_{\text{sf}}$ to K is given by the following expression [62]:

$$\mathbf{F}_{\text{sf}} = \mathbf{F}_{\text{lf}} \mathbf{F}_0^{-1}. \quad (3.1)$$

This equation allows for obtaining $\mathbf{F}_{\text{sf}}$ as a function of $\mathbf{F}_{\text{lf}}$. Substituting $\mathbf{F}_{\text{sf}}$ in place of the deformation gradient $\mathbf{F}$ into the material model from Section 2, we obtain the corresponding second Piola-Kirchhoff stress tensor. Since this stress tensor operates on the $\tilde{K}_{\text{sf}}$ configuration, we denote it as $\tilde{\mathbf{T}}^{\text{sf}}$. However, in order to carry out FEM-simulations, we need the stress tensor $\tilde{\mathbf{T}}^{\text{lf}}$, which operates on the $\tilde{K}_{\text{lf}}$ configuration. Knowing the $\mathbf{F}_0$ tensor, we calculate the required stress according to the push-forward transformation rule:

$$\tilde{\mathbf{T}}^{\text{lf}} = \mathbf{F}_0^{-1} \tilde{\mathbf{T}}^{\text{sf}} \mathbf{F}_0^{-\text{T}}. \quad (3.2)$$

Remark 3.1. Among the geometrically nonlinear inelastic constitutive equations we highlight the so-called w-invariant models [52]. They are characterised by the property that any isochoric change of the reference configuration can be counteracted by appropriate choice of initial conditions. This means that the reference configuration can be chosen at will and the particular choice of the reference configuration does not constitute a modelling assumption. The presented $\mathbf{F}_0$ -approach works with transformations of reference configurations. Hence, it is especially beneficial when working with material models which are w-invariant under reference change. An extensive class of w-invariant models is based on the multiplicative decomposition of the deformation gradient, allowing to consider various inelastic effects; in particular, simulation of viscoelasticity paired with $\mathbf{F}_0$ -approach is considered in [62], while the viscoplastic material behaviour is studied in [63].

Remark 3.2. The basic $\mathbf{F}_0$ -approach, implemented in the current paper, is limited to the case of $\det \mathbf{F}_0 = 1$. However, since the analysis of residual stresses is often coupled with growth and remodelling [6, 12, 17, 28, 29, 33], it is essential to account for volume change. Refined $\mathbf{F}_0$ -approach with $\det \mathbf{F}_0 \neq 1$ is discussed in [63, 64].

3.2. Setting of the $\mathbf{F}_0$ -field

As shown in [62], the analytical expression for the $\mathbf{F}_0$ -field in pre-stressed blood vessels can be derived if the geometry of a cylindric vessel is known both in $\tilde{K}_{\text{sf}}$ and $\tilde{K}_{\text{lf}}$ configurations; $\tilde{K}_{\text{sf}}$ configuration results upon cutting the pre-stressed vessel, followed by complete release of stresses. Specifically, let $\{\mathbf{e}_r, \mathbf{e}_\theta, \mathbf{e}_z\}$ be the orthonormal basis of cylindrical coordinates in $\tilde{K}_{\text{lf}}$; the blood vessel corresponds to the domain

$$r_i < r < r_o, \quad 0 < \theta < 2\pi, \quad 0 < z < l. \quad (3.3)$$

Here, r_i , r_o , and l are the inner and the outer radii and the length of the vessel. Analogously, let the cylindrical coordinates in $\tilde{K}_{\text{sf}}$ be governed by the orthonormal basis $\{\mathbf{e}_R, \mathbf{e}_\Theta, \mathbf{e}_Z\}$; the body of the unstressed vessel is then defined by

$$R_i < R < R_o, \quad 0 < \Theta < (2\pi - \alpha), \quad 0 < Z < L, \quad (3.4)$$

with R_i , R_o and L being the inner and outer radii and the length of unstressed vessel; α denotes the opening angle, measured from the centre of the inner circle.² Now, we can express the $\mathbf{F}_0$ -field in the matrix form [62]:

$$\mathbf{F}_0 = \begin{pmatrix} c\zeta & 0 & 0 \\ 0 & \frac{1}{\zeta} & 0 \\ 0 & 0 & \frac{1}{c} \end{pmatrix}. \quad (3.5)$$

²This definition of the opening angle is in agreement with [24].

Here, $c = l/L$ is the length ratio; the function ζ describes the distribution of strains upon relaxation of stresses. This kinematic function can be written both in $\tilde{K}_{\text{sf}}$ and $\tilde{K}_{\text{lf}}$ configurations:

$$\zeta_{\text{lf}}(r) = k \frac{r}{\sqrt{(r^2 - r_i^2)kc + R_i^2}}, \quad \zeta_{\text{sf}}(R) = k \frac{\sqrt{(R^2 - R_i^2)/(kc) + r_i^2}}{R}, \quad (3.6)$$

where $k = 2\pi/(2\pi - \alpha)$.

We assume that r_i , r_o , l , and α are known. The parameters R_i , R_o , and L are found by solving an inverse problem, *cf.* [62]. The idea behind the inverse problem is to identify a set of kinematic parameters that will render the values of required internal pressure and axial force precisely zero. In the current study, this problem is solved and stress-free kinematic parameters are found using a semi-analytical procedure described in [24, 61].

Remark 3.3. In the context of pre-stressed vascular mechanics the $\mathbf{F}_0$ -approach represents a generalisation of the opening-angle approach [24]. One of the advantages of the more general approach lies in the accelerated calculations: Whilst the opening-angle approach requires explicit modelling of the entire blood vessel in its global stress-free and load-free configurations [3, 7], the $\mathbf{F}_0$ -approach allows skipping this time-consuming simulation stage.

Remark 3.4. As common in incompressible materials, the field of residual stresses defined according to this procedure is unique up to unknown distribution of hydrostatic component. This distribution is defined in such a way as to enforce the equilibrium. Thus, the field of residual stresses is self equilibrated.

4. FINITE ELEMENT SIMULATIONS

Geometry of vessels. We consider end-to-side anastomosis of two blood vessels: a recipient and a relatively small donor. Both vessels are modelled as two-layer fibre-reinforced composites; the composite structure of the artery wall is due to the media and adventitia layers exhibiting essentially different mechanical properties. The following radii of the recipient vessel correspond to the load-free geometry of carotid artery from a rabbit [24]: $r_i^{\text{recipient}} = 0.71$ mm, $r_{\text{interface}}^{\text{recipient}} = 0.97$ mm and $r_o^{\text{recipient}} = 1.1$ mm; $r_{\text{interface}}^{\text{recipient}}$ corresponds to the interface between layers. The load-free radii of the donor vessel are taken as two times smaller values. Let γ be the angle between the bodies' axis. As is shown in [36], the optimal value of γ from the hemodynamics' point of view is $\pi/3$. The geometry of the problem is shown in Figure 2.

The material model from Section 2 is implemented into the commercial FEM code MSC.MARC. A three-dimensional mesh of both blood vessels is generated to simulate the process of end-to-side anastomosis (Fig. 3a). The mesh consists of hexahedral elements with the linear approximation of geometry and displacements. Hermann formulation is employed, including one extra degree of freedom for pressure, thus enabling consistent modelling of a near-incompressible behaviour.³ To avoid non-physical effects of element self-penetration, we use a relatively fine mesh. The recipient vessel is subdivided into $15 \times 16 \times 32$ elements in radial, circumferential, and axial directions, respectively (10 elements in radial direction represent the media of recipient and 5 elements correspond to the adventitia). In the same way, the donor vessel is subdivided into $8 \times 12 \times 16$ elements in radial, circumferential, and axial directions (5 elements in radial direction represent the media of the donor and 3 elements correspond to the adventitia). An additional mesh convergence analysis with the elements of the halved linear dimensions was carried out for the first sensitivity study, providing similar results and indicating sufficiency of the mesh for the study. To speed up the simulations, we introduce the symmetry plane $\{X = 0\}$, which allows considering only the half of the bodies (Fig. 3b); corresponding boundary condition is not applied to the nodes of the cut area in the recipient vessel, thus accounting for the arteriotomy window area.

Connecting threads are simulated with sufficiently stiff (Young's modulus $E = 3000$ MPa) two-node line elements of truss type. Attachment points are placed evenly along the lines of the cut in both vessels; we consider an edge-to-adventitia apposition of vessels, hence the points are placed on the internal radius of media

³For near-incompressible materials, an alternative physics-based approach is available [41].

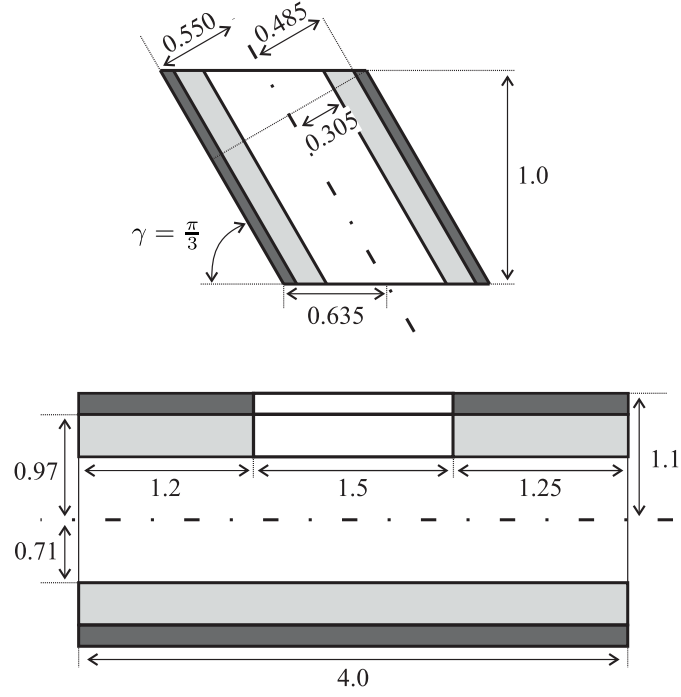


FIGURE 2. Schematic illustration of blood vessels and their geometric dimensions (in mm). Dark grey indicates the adventitia layer, light grey indicates the media layer, and the white area of 1.5 mm width corresponds to the cut.

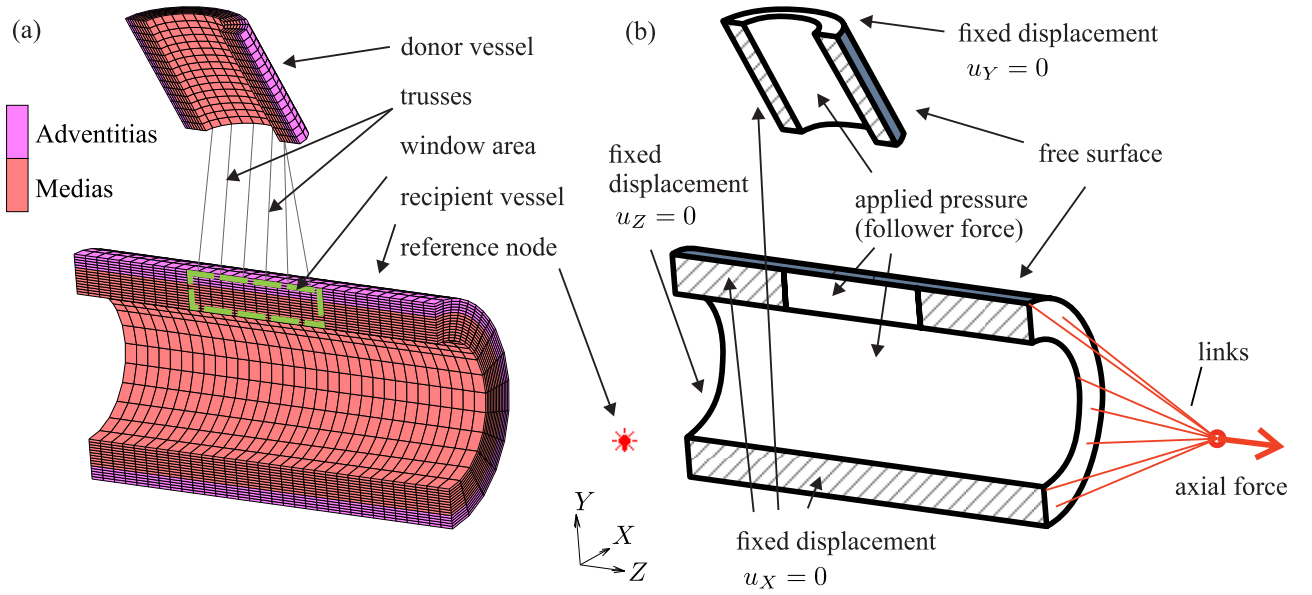


FIGURE 3. Simulation of anastomosis. (a) 3D FEM model. (b) Applied boundary conditions.

TABLE 1. Stress-free geometrical parameters of the vessels.

	Recipient	Donor
R_i , mm	1.3809	0.6904
R_o , mm	1.7824	0.8912
c	0.9997	0.9997
α , degrees	160	160

TABLE 2. Material parameters.

	Recipient		Donor	
	Media	Adventitia	Media	Adventitia
c_1 , KPa	3	0.3	3	0.3
c_2 , KPa	2	0.2	2	0.2
k_1 , KPa	2.3632	0.5620	2.3632	0.5620
k_2	0.8393	0.7112	0.8393	0.7112
β , degrees	29	62	29	62

for donor and on the external radius of adventitia for the recipient. The total number of trusses is six and their position is shown in Figure 3a.⁴ The trusses serve as actuators, with their length, chosen as a distance between attachment points, reducing linearly to 1% of their original length. This phase leads to opening of the window area in recipient vessel and connection of both vessels.

Accounting for the state of homeostasis. After the shortening of trusses, we apply the external loading, corresponding to the blood pressure in both vessels and axial stretch of the recipient artery. The blood pressure is simulated with the face load applied to all internal faces of tubes, including the surface of the cut (see Fig. 3b); the follower force option is activated for greater accuracy. Applied pressure rises as a linear function of time to 100 mmHg (13.33 KPa), reaching the approximate physiological value for that specific artery (*cf.* [10, 24]). Simultaneously, one of the recipient's edges is fixed in Z-direction, all the nodes on the other edge are linked in the axial direction to a reference node (Fig. 3b); additional axial force is applied to the recipient through the reference node. The point load rises linearly to 0.02 N. This specific value corresponds to the axial pre-stretch $\lambda_z = 1.7$ of the healthy artery in the homeostatic state [24].

4.1. Residual stresses' effect on stress distribution in the process of anastomosis

To assess the importance of residual stresses for the analysis of blood vessel anastomosis, we compare two FEM simulations: one with $\mathbf{F}_0 \equiv \mathbf{1}$ implying that configurations $\tilde{K}_{lf}$ and $\tilde{K}_{sf}$ coincide, *i.e.* no residual stresses are considered, and the other simulation with the $\mathbf{F}_0$ -field set as described in Section 3.2, incorporating circumferential residual stresses. Stress-free kinematics of both vessels are found in the aforementioned semi-analytical procedure; the parameters are specified in Table 1 for the simulation with residual stresses. Both simulations use material parameters listed in Table 2. In the subsequent sensitivity studies, this set of parameters will be considered as a “ground truth”, since these parameters roughly correspond to a real material, *cf.* [10, 24]. Note that the opening angles for both layers of vessels are equal leading to the same analytical expression for the $\mathbf{F}_0$ -field in the entire vessel; one should keep in mind that different layers may exhibit individual opening angles [58, 59], thus requiring more complex simulations [27, 62, 73].

Figure 4 shows the resulting distribution of stresses at the end of both simulations.⁵ It is worth emphasising that the final deformed configurations of vessels are almost identical for the considered cases, *i.e.* incorporation

⁴Every truss corresponds to the surgical thread used in operation. Thus, their number is governed by the operation procedure. Additional simulations were performed with four and eight trusses, indicating small difference of around 5% in stress field for the four-versus-six trusses comparison and nearly no difference for the six-versus-eight case.

⁵To improve the imagination of the process, we provide animated solution under <https://youtu.be/EDXHabehhGc>.

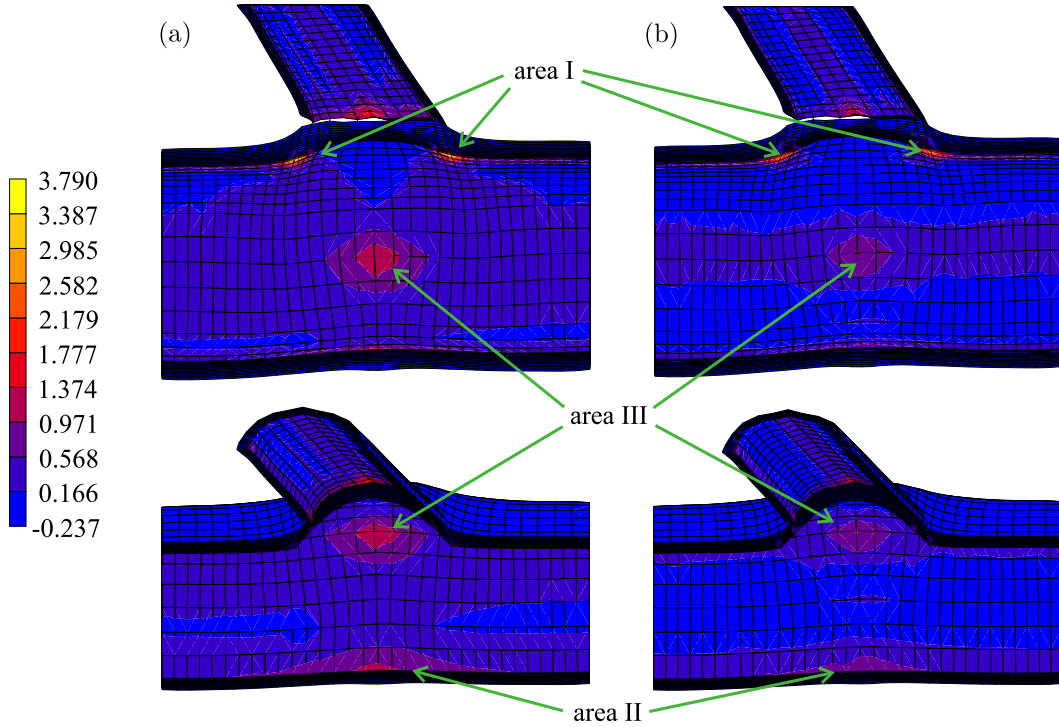


FIGURE 4. Distribution of major principal values of the Cauchy stress in arteries after anastomosis (stresses in MPa): (a) simulation without residual stresses, (b) simulation with residual stresses.

of residual stress did not affect the clearance width.⁶ The stresses in the recipient rise at the edges of the cut (area I) and in the area opposite to the cut (area II), potentially provoking subsequent rupture of the vessel or development of aneurysm in area I or area II, correspondingly. Unexpectedly, an additional spot of stress concentration (area III) is isolated from the cut; additional simulations show that area III corresponds to the intersection of force lines, arising due to the stress transfer along the fibres as shown in Figure 5. Thus, for a relatively big values of angle β the increased stresses in the area III can occur closer to the suture line and hereby contribute to the development of anastomotic aneurysm. Indeed, clinical studies report the occurrence of pseudo-aneurysm between areas I and III [65], see Figure 6. While the observed stress fields are similar from the qualitative point of view, they differ considerably in their values. In particular, major principal values of the Cauchy stress $\mathbf{T}_{\text{major}}^{\text{principal}}$ are confined in the interval $[-0.214 \text{ MPa}, 3.790 \text{ MPa}]$ for the simulation without pre-stresses. In the residual stress simulation, the major principal values lie within $[-0.237 \text{ MPa}, 3.013 \text{ MPa}]$. Thus, *neglecting the residual stresses leads to a substantial overestimation of stress peaks*. This modelling effect corresponds to the well-known fact that residual stresses reduce the stress peaks in arteries by redistributing the mechanical loads [14, 24].

Overestimation of stress peaks will affect stress-sensitive simulations, *e.g.* simulations accounting for tissue damage or growth and remodelling (G&R), especially at the sites of increased stresses. All the subsequent simulations in the paper are conducted with residual stresses incorporated by the $\mathbf{F}_0$ -approach.

⁶Thus, the clearance width seems to be essentially pre-determined by the geometrical parameters of the problem [7].

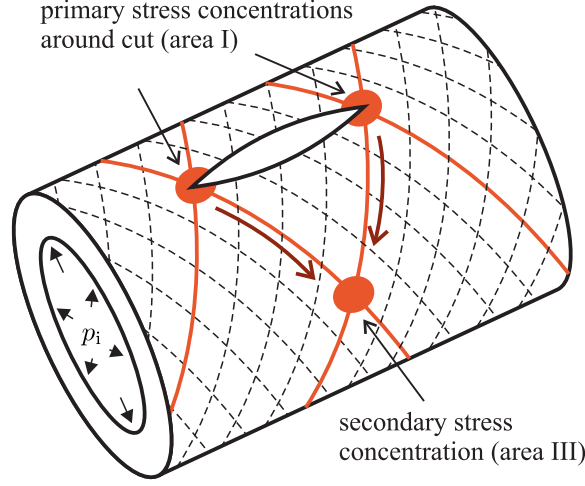


FIGURE 5. Schematic illustration of stress transfer mechanism along the force lines of fibres.



FIGURE 6. Sketch of a pseudo-aneurysm occurring at the site of anastomosis due to stress concentration. Figure adapted from [65].

4.2. Influence of the cut geometry

Next, we examine how the geometry of the cut affects the stress distribution in the same simulation. To do so, we repeat the simulation on the pre-deformed mesh, where the cut is now not a straight line but an ellipse. To account for the cut geometry, we modified the initial mesh whilst preserving the mesh topology. Nodes of the vessel top half are shifted away from the cut in the circumferential (hoop) direction. Maximum displacement appears at the center of the cut, and the maximum rotation angle $\phi_{\max}$ defines it.

To parametrise the cut geometry, we introduce the following function:

$$\chi(x, y, z) = \left(1 - \frac{\phi_{\max}}{90^\circ} \sqrt{1 - (z - z_c)^2/a^2}\right) \arccos \frac{x}{(x^2 + y^2)^{1/2}}. \quad (4.1)$$

Here, z_c is the z coordinate of the middle of the cut and a is the half of the cut's length, which defines the semi-major axis of the ellipse; $\langle x \rangle = \max(0, x)$ is the positive part of a real number. The resulting formulae for the smooth mesh transformation are then as follows:

$$\begin{cases} x_{\text{new}} = (x^2 + y^2)^{1/2} \cos(\chi(x, y, z)), \\ y_{\text{new}} = (x^2 + y^2)^{1/2} \sin(\chi(x, y, z)), \\ z_{\text{new}} = z. \end{cases} \quad (4.2)$$

The particular case of $\phi_{\text{max}} = 0^\circ$ corresponds to the absence of mesh transformation.

Three simulations were conducted for comparison: straight cut from the previous subsection ($\phi_{\text{max}} = 0^\circ$) and two simulations with new meshes defined by $\phi_{\text{max}} = 10^\circ$ and $\phi_{\text{max}} = 20^\circ$. The resulting distribution of the major principal value of the Cauchy stress for all three cases is shown in Figure 7. Again, the peak values are significantly different: The simulation with the straight cut predicts stresses in the interval of $[-0.237 \text{ MPa}, 3.013 \text{ MPa}]$, the simulation with $\phi_{\text{max}} = 10^\circ$ yields stresses in the interval of $[-0.212 \text{ MPa}, 1.592 \text{ MPa}]$, and the simulation with $\phi_{\text{max}} = 20^\circ$ results in stresses within the interval $[-0.210 \text{ MPa}, 3.943 \text{ MPa}]$. It is also an interesting point that the maximum stress values are obtained at the edges of the cut in the recipient for the first case. This effect fades away in the second case: a wider cut makes the stress distribution in the recipient more uniform while the stresses in the donor are rising. This trend goes on for the third case: the stress distribution in the recipient is even more uniform around the cut, but the stress peak in the donor becomes more distinct. This stress redistribution is apparently caused by a larger incision that leads to larger strains of the bonded donor. In addition to that, the stresses in area III increase with growing ϕ_{max} : the obtained values are 1.022 MPa, 1.165 MPa, and 1.459 MPa for $\phi_{\text{max}} = 0^\circ$, $\phi_{\text{max}} = 10^\circ$, and $\phi_{\text{max}} = 20^\circ$, respectively. Note that for large ϕ_{max} the spot of maximum stress concentration moves from area I to area III, which is potentially responsible for occurrence of pseudo-aneurysm [65].

We conclude that the widening of the recipient's cut decreases stresses near the cut (in area I) and decreases the probability of vessel's rupture. However, this may cause two other problems: First, the increase in donor's stresses can provoke rupture of the donor tissue. Second, the increase of stresses on the wall (in areas II and III) can accelerate the development of an aneurysm. Therefore, the optimal solution should be chosen based on the surgical intervention and mechano-biological criteria.

To clarify the non-monotonic behaviour of the maximum stress with respect to ϕ_{max} we plot the maximum major stresses in donor and recipient in Figure 8. For this figure two additional simulations with $\phi_{\text{max}} = 5^\circ$ and $\phi_{\text{max}} = 15^\circ$ were carried out. In the area of interest, donor's stresses are mainly increasing while recipient's stresses are decreasing. Based on these results we consider $\phi_{\text{max}} = 10^\circ$ to be the optimal cut parameter in the considered situation.

4.3. Impact of the stiffness ratios between media and adventitia

For the description of the mechanical behaviour of the vessel, one needs eight material constants, even if the directions of fibres and thickness of layers are known from the histology analysis. These constants are usually obtained from calibration against actual experimental data. Individual parameter identification for artery layers requires the separation of layers by mechanical incisions or chemical etching. However, since the vascular wall is an interconnected complex [60], such a separation inevitably changes the material properties of individual layers [26, 58, 67].⁷

To minimise undesired experimental artefacts, we limit considered tests to non-destructive loading of the artery after initial excision. Thus, we consider only tests in which the media and adventitia are *not separated*.

Since the layers of the recipient are not separated, the contribution of each individual layer to the overall response is not known. This lack of information leads to uncertainties in material parameters that fit the experimental results. Therefore, we perform a sensitivity study, investigating how the change of stiffness ratio

⁷Still, a number of techniques is available for an approximate study of individual mechanical properties of these layers [9, 38, 42]. Moreover, for a patient-specific modelling, the angioarchitectonics of the patient's Wilisian circle can be taken into account [31].

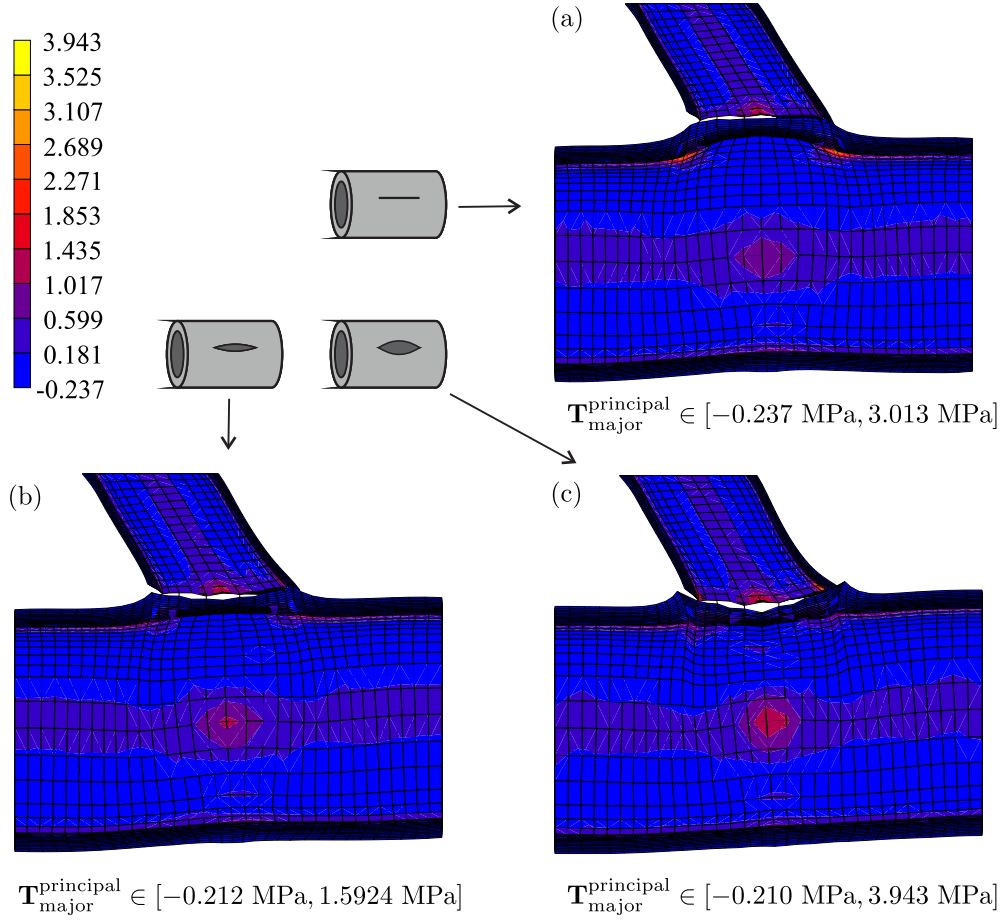


FIGURE 7. Distribution of the major principal values of the Cauchy stress (in MPa) in the arteries after anastomosis for different cut geometries: (a) straight cut with $\phi_{\max} = 0^\circ$, (b) mouth cut with $\phi_{\max} = 10^\circ$, (c) mouth cut with $\phi_{\max} = 20^\circ$.

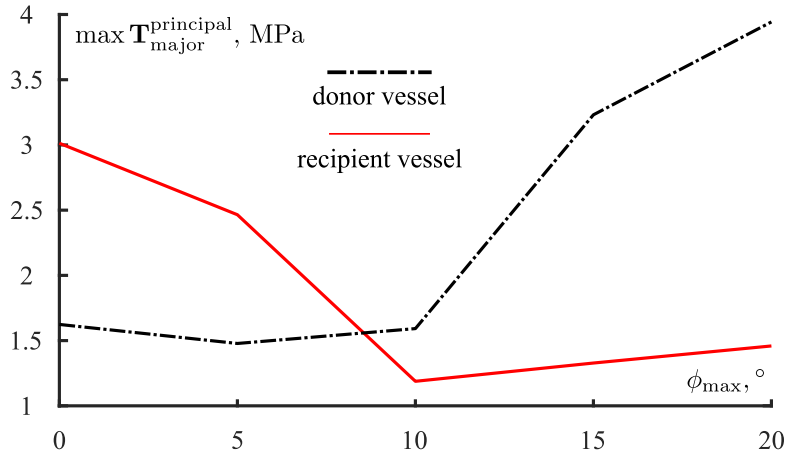


FIGURE 8. Maximum major stresses in donor and recipient versus the cut angle $\phi_{\max}$.

between recipient's media and adventitia affects the post-anastomotic stress distribution. For a deeper insight, different types of experimental tests are used to assess the reliability of the inverse problem.

For every type of test, we conduct the following procedure. Let vector P encapsulate unknown parameters of the vessel. These are the parameters c_1 , c_2 , k_1 and k_2 for both layers. First, the set of material parameters P^{origin} , listed in Table 2, is used to obtain original test-specific synthetic data $\text{Data}_i^{\text{original}}$. Here, $i = 1, 2, \dots, N$ and N is the number of experimental measuring (tracking) points. Next, we perturb material constants c_1 , c_2 , and k_1 in the media layer of the recipient, increasing/decreasing them by 10 % of their original values; the parameter k_2 of the media layer is fixed since it is associated with the nonlinearity of fibre behaviour, not with its stiffness. The dimensions of the artery in the load-free configuration and the parameters α and β are considered to be known and constant. For the new set of parameters P^* , we obtain numerical predictions $\text{Data}_i^*(P^*)$, $i = \overline{1, N}$. Using them, we build the error functional:

$$\Phi(P^*) = \sum_{i=1}^N \omega_i (\text{Data}_i^*(P^*) - \text{Data}_i^{\text{original}})^2, \quad (4.3)$$

where ω_i are weighting coefficients, introduced to adjust the dimensions of Data_i and increase the robustness of optimisation [4, 53].

The procedure-specific reidentified set P^{proc} minimises the error functional (4.3):

$$\{c_1, c_2, k_1, k_2\}_{\text{adventitia}}^{\text{proc}} = \arg \min \Phi, \quad \{c_1, c_2, k_1, k_2\}_{\text{media}}^{\text{proc}} \text{ fixed}. \quad (4.4)$$

The minimisation is carried out numerically using a trust-region reflective algorithm and implying lower bounds to ensure that the obtained parameters remain non-negative. Finally, we use the identified set P^{proc} in a full-scale FEM simulation with incorporated residual stresses and ellipse-type cut of $\phi_{\text{max}} = 10^\circ$.

Calibration against tensile test. The tensile test is conventional, providing the axial force as a function of the specimen's actual length (or, equivalently, axial strain). However, the incorporation of residual stresses can lead to discrepancies of axial strains for different sets of material parameters due to differences in stress-free lengths.

All computations are performed with the semi-analytical procedure reported in [24, 61]. This procedure allows us to obtain the internal pressure p_{int} and the reduced axial force $F = N - \pi r_i^2 p_{\text{int}}$ as a function of vessel geometry in the current configuration (N is the total axial force). In a synthetic test, we use 101 measurement points, uniformly changing the current length of the vessel from 100% to 170% of the original load-free length. At every measurement point, the internal pressure is zero.

Reidentified sets of parameters $P_{\text{tension test}}^{\text{weak media}}$ and $P_{\text{tension test}}^{\text{strong media}}$ correspond to reduced and increased stiffness parameters of the media, respectively (Tab. 3); geometrical parameters of stress-free configurations are specified in Table 4. Force-length curves for the original and both reidentified sets of parameters are shown in Figure 9a. The relations are almost identical, providing the same force-length curves for all parameter sets. Next, we carry out a full-scale FEM simulation of anastomosis with the new sets of parameters. The results are shown in Figure 9b,d and the FEM simulation based on the original parameters is shown in Figure 9c, which is considered to be "ground truth". The stress values for these three simulations are essentially different, although parameter sets are identical regarding the sample behaviour within the uniaxial tensile test. Particularly, while the major principal values of the Cauchy stress are in the interval $[-0.212 \text{ MPa}, 1.592 \text{ MPa}]$ for P^{origin} , the simulations with $P_{\text{tension test}}^{\text{weak media}}$ and $P_{\text{tension test}}^{\text{strong media}}$ are in the intervals of $[-0.242 \text{ MPa}, 1.540 \text{ MPa}]$ and $[-0.231 \text{ MPa}, 1.449 \text{ MPa}]$, respectively. In addition, the stresses at area III are higher for simulation with $P_{\text{tension test}}^{\text{weak media}}$ (1.3069 MPa) and lower for simulation with $P_{\text{tension test}}^{\text{strong media}}$ (1.0909 MPa).

Calibration against inflation test. Another experiment is monotonic loading of the blood vessel by internal pressure, cf. [20, 48]. Two variables are measured in this case: the length change respective to the load-free configuration and the inner radius of the vessel. Analogously to the previous section, the internal pressurisation problem is solved with the same semi-analytical procedure. We use 101 measurement points,

TABLE 3. Parameter sets for weak and strong media layer, identical with respect to the tensile test.

	$P^{\text{weak media}}_{\text{tension test}}$		$P^{\text{strong media}}_{\text{tension test}}$	
	Media	Adventitia	Media	Adventitia
c_1 , KPa	2.7	0.7036	3.3	0.0000
c_2 , KPa	1.8	0.6373	2.2	0.0000
k_1 , KPa	2.1269	0.5733	2.5995	0.4877
k_2	0.8393	0.7100	0.8393	0.7679

TABLE 4. Geometric parameters of recipient stress-free configuration for material properties from Table 3.

	$P^{\text{weak media}}_{\text{tension test}}$	$P^{\text{strong media}}_{\text{tension test}}$
R_i , mm	1.3872	1.3776
R_o , mm	1.7871	1.7801
c	0.9991	1.0004

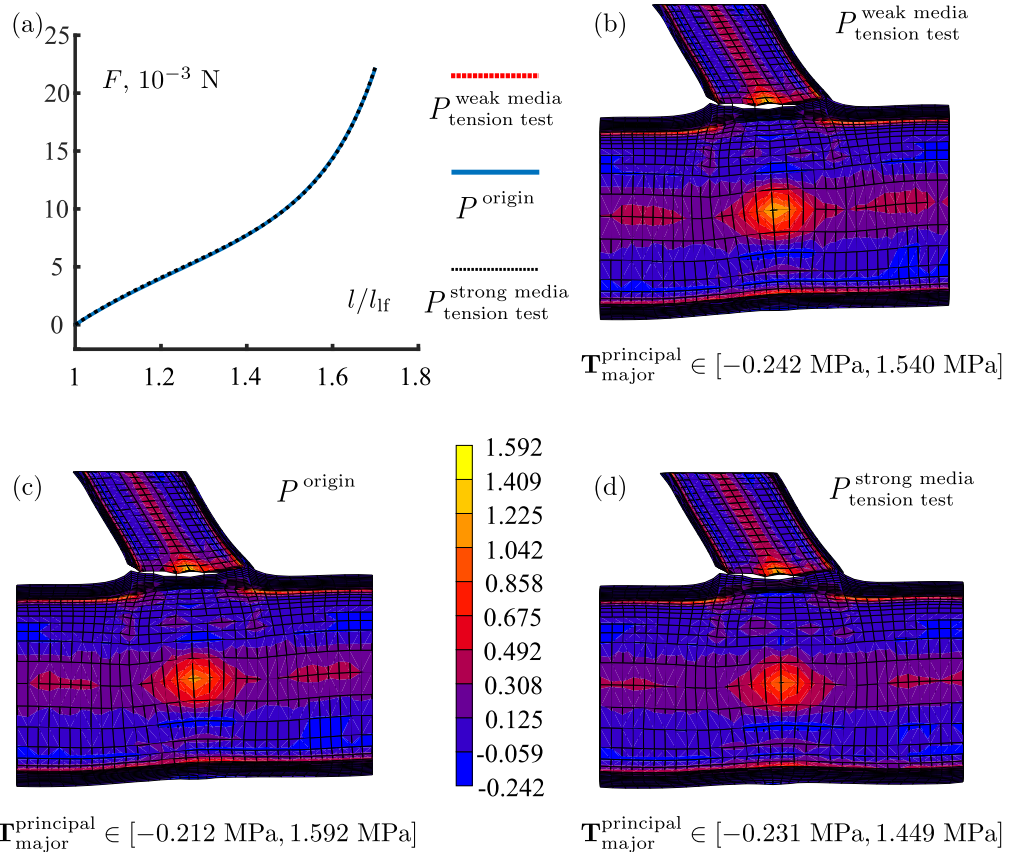
FIGURE 9. (a) Calibration based on the tensile test. (b), (c), (d) Distribution of major principal values of Cauchy stress (in MPa) in arteries after anastomosis for the calibration against tensile test; (b) simulation based on $P^{\text{weak media}}_{\text{tension test}}$, (c) simulation based on P^{origin} , (d) simulation based on $P^{\text{strong media}}_{\text{tension test}}$.

TABLE 5. Parameter sets for weak and strong media layer, identical with respect to the pressurisation test.

	$P^{\text{weak media}}$ inflation test		$P^{\text{strong media}}$ inflation test	
	Media	Adventitia	Media	Adventitia
c_1 , KPa	2.7	0.0000	3.3	1.2674
c_2 , KPa	1.8	0.0000	2.2	0.0000
k_1 , KPa	2.1269	1.2119	2.5995	0.1554
k_2	0.8393	0.4188	0.8393	1.2659

TABLE 6. Geometric parameters of recipient stress-free configuration for material properties from Table 5.

	$P^{\text{weak media}}$ inflation test	$P^{\text{strong media}}$ inflation test
R_i , mm	1.3764	1.3860
R_o , mm	1.7780	1.7870
c	0.99703	1.00147

changing internal pressure from 0 KPa to 15 KPa with a constant step of 0.15 KPa. The reduced axial force is now kept zero at every point.

The reidentified material parameters are listed in Table 5; Table 6 represents corresponding stress-free kinematics. Simulated data for original and reidentified sets are shown in Figure 10a. We see that the results of the inflation test for the reidentified parameters are close to the original synthetic data. Note that calibration against the inflation test includes fitting both for axial and circumferential strains, thus revealing their stiffness in two different directions, while the tensile test reveals only the axial stiffness of the specimen.

Next, full-scale FEM simulations of the anastomosis are carried out. The resulting stress distributions are shown in Figure 10b–d. Intervals of major stress values slightly differ: $[-0.234 \text{ MPa}, 1.527 \text{ MPa}]$ for $P^{\text{weak media}}$ inflation test and $[-0.241 \text{ MPa}, 1.547 \text{ MPa}]$ for $P^{\text{strong media}}$ inflation test. However, one should keep in mind these are intervals of stresses in both vessels, where stresses in the donor overlap ones in the recipient. Limiting ourselves to stresses in *recipient* vessel, we see a much more considerable difference: Major principal values of Cauchy stress are in $[-0.198 \text{ MPa}, 1.321 \text{ MPa}]$ for $P^{\text{weak media}}$ inflation test, $[-0.194 \text{ MPa}, 1.188 \text{ MPa}]$ for P^{origin} and $[-0.187 \text{ MPa}, 1.111 \text{ MPa}]$ for $P^{\text{strong media}}$ inflation test. Area III stresses are again lower with strengthening of media layer (1.0651 MPa) and higher with its weakening (1.3210 MPa).

Calibration against both tests. As a next step, we identify the material parameters of adventitia using the data of both considered tests. The resulting parameters and stress-free kinematics are listed in Tables 7 and 8, respectively; the best possible fits are shown in Figure 11. As we see, incorporation of additional experimental data to the calibration procedure does not prevent it from obtaining a good fit of simulation to (synthetic) experiment. The post-anastomotic stress distribution in full-scale FEM simulations basically replicates the results of the calibration based on the tensile test. Intervals for the major principal values of the Cauchy stress are $[-0.242 \text{ MPa}, 1.540 \text{ MPa}]$ for $P^{\text{weak media}}$ combined test and $[-0.231 \text{ MPa}, 1.455 \text{ MPa}]$ for $P^{\text{strong media}}$ combined test.

We conclude that it is not possible to reliably identify the relation between the layer stiffnesses, even with the extended experimental data set from both considered tests. Thus, new identification protocols based on the introduction of additional data are urgently needed. For example, possible experimental set-ups are (i) inflation of pressurised artery with fixed length or (ii) upsetting of an artery with fixed internal volume (which corresponds to hermetically sealed ends of the fluid-filled artery during the compression test). Moreover, a large class of tests includes experiments strongly heterogeneous along the axis of the sample (*e.g.* bending [68, 69], compression [8], biaxial tension of a patch [16, 38]).

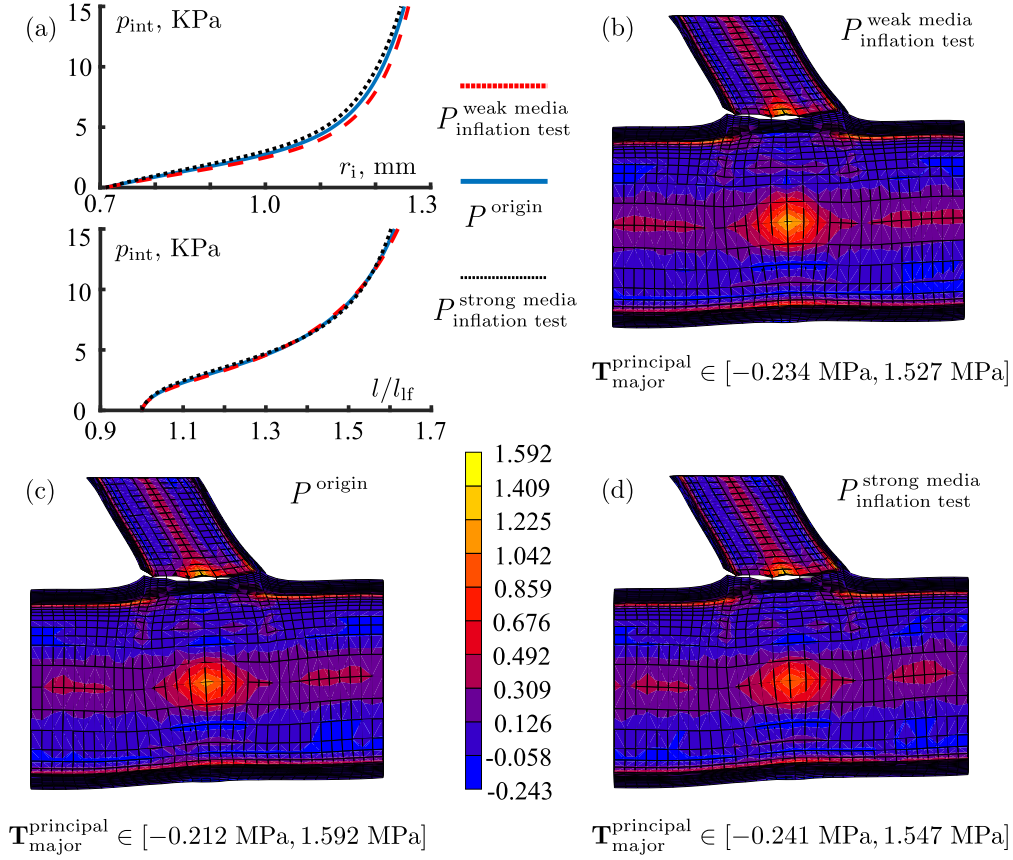


FIGURE 10. (a) Calibration against the inflation test. (b), (c), (d) Distribution of major principal values of Cauchy stress (in MPa) in arteries after anastomosis for the pressurisation calibration; (b) simulation based on $P^{\text{weak media inflation test}}$, (c) simulation based on P^{origin} , (d) simulation based on $P^{\text{strong media inflation test}}$.

TABLE 7. Parameter sets for weak and strong media layer, identical with respect to both tensile and inflation tests.

	$P^{\text{weak media combined test}}$		$P^{\text{strong media combined test}}$	
	Media	Adventitia	Media	Adventitia
c_1 , KPa	2.7	0.3973	3.3	0.0000
c_2 , KPa	1.8	0.9608	2.2	0.0000
k_1 , KPa	2.1269	0.5953	2.5995	0.4877
k_2	0.8393	0.6985	0.8393	0.7680

5. CONCLUSION AND DISCUSSION

A full-scale numerical simulation of blood vessel end-to-side anastomosis is carried out within a geometrically exact setting. Both the recipient and donor arteries are modelled as double-layer fibre-reinforced composite tubes; the iso-strain assumption is implemented to describe the deformation of the matrix and two families of fibres. Since the paper mainly deals with the passive static response of blood vessels, only the hyperelastic response of material is considered. However, all the simulations carried out in the study can be reproduced with

TABLE 8. Geometric parameters of recipient stress-free configuration for material properties from Table 7.

	$P^{\text{weak media}}$ combined test	$P^{\text{strong media}}$ combined test
R_i , mm	1.3871	1.3776
R_o , mm	1.7869	1.7802
c	0.9987	1.00036

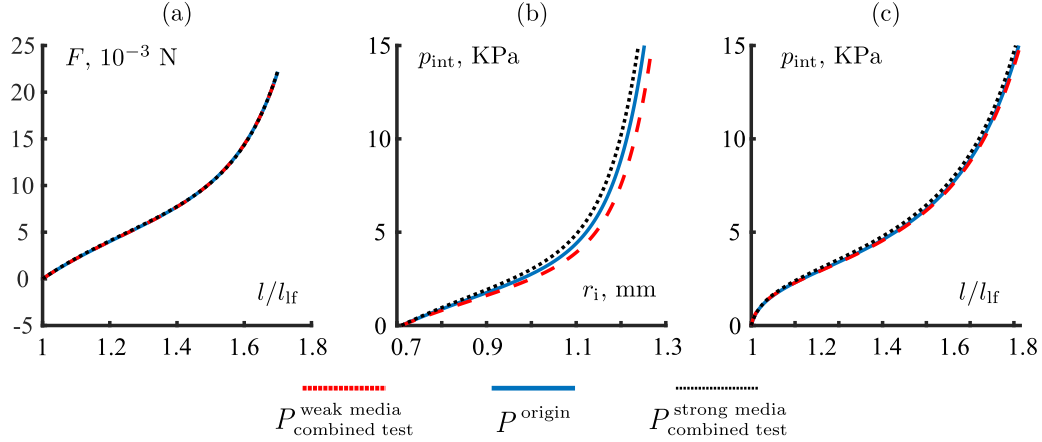


FIGURE 11. Results of calibration against combination of both tests. (a) tensile test; (b), (c) pressurisation test.

the inelastic properties taken into account by a multiplicative decomposition of deformation gradient [61]. In this case the introduction of residual stresses by the $\mathbf{F}_0$ -approach does not increase the complexity of numerical algorithms [62].

A new domain of secondary stress concentration (area III) is discovered. It occurs due to interacting force lines emanating from primary stress-concentration areas (Fig. 5). Thus, an essential contribution of the study is that the pseudo-aneurysm [65] is explained in terms of the anisotropic mechanical model.

Several sensitivity studies are carried out for the anastomosis problem. Residual stresses are incorporated with the general $\mathbf{F}_0$ -approach [62]. Variation of the cut geometry is examined by the parametrisation of the cut as an ellipse. Inaccuracies of parameter identification are analysed with artificial alterations in stiffness of one of the layers, whilst the parameters of the other are fitted against experimental curves.

The main conclusions of the paper are as follows:

- Taking residual stresses into account is necessary for accurate predictions of stress redistribution during and after surgical intervention. However, the residual stresses do not affect the clearance width, which is an unexpected result.
- The sensitivity study shows that the cut width has a considerable impact on the post-operational stress field. The most significant differences are invoked near the cut (area I) and at the intersection of force lines emanating from area I (area III).
- The reliable identification of mechanical properties of media and adventitia is an open question. It is shown that standard tests like uni-axial tension and internal pressurisation as well as their combination do not allow for the identification of the stiffness relation between the media and adventitia. Thus, in practice, this relation often remains unknown. The problem is aggravated by the substantial impact of the unknown stiffness relation on the post-operational stress field.

The present study motivates experimental research aimed at a reliable identification of media and adventitia properties without separation since the separation changes the mechanical properties of layers. This experimental issue is also related to the problem of mutual influence of layers, including their locking, *cf.* [62].

In the highly stressed areas of the vessel wall, prolonged bleeding may occur [1], which is an undesirable surgical complication. In present clinical practice, this effect is understood only qualitatively. Further development of the computer simulation techniques is highly promising to determine the conditions that separate the normal postoperative process from surgical complications.

Author contributions

I.I.T., D.V.P. and A.V.S. designed the problem statement; I.I.T. implemented numerical procedures and carried out the computational experiments; I.I.T., D.V.P. and A.V.S. analysed and interpreted the simulation results; I.I.T., D.V.P. and A.V.S. wrote the paper. All authors have read and agreed to the published version of the manuscript.

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