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Arterial Clamping: Finite Element Simulation and In Vivo Validation

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Abstract

Commonly used techniques in cardiovascular interventions such as arterial clamping always entail a certain degree of unavoidable iatrogenic tissue damage. Therefore, studies have been directed towards the decrease of undesired intraoperative trauma, for example, through the design of less traumatic surgical instruments. Obviously, the effectiveness of new clamp designs and techniques depends on how well damage mechanisms are understood and how accurate thresholds for safe tissue loading can be set. This information can in part be derived from reliable finite element simulations. This study is the first to describe a finite element simulation of the clamping of a rat abdominal aorta with occlusion and *in vivo* validation. Material nonlinearity, large deformations, contact interactions and residual strains are hereby taken into account. The mechanical parameters of the model are derived from inflation experiments. The effect of the residual strains, different clamp geometries as well as the effect of variations in material properties are studied. In all simulations, stress concentrations in different regions of the tissue are noticed, especially for a corrugated clamp design. This shows the importance of finite element modeling in understanding the relation between mechanical loading and damage mechanisms. The inclusion of residual strains has its effect not only in the physiological loading regime, but also during clamping. Just as in the physiologic regime, it lowers the stress gradients through the wall thickness. Varying the material properties with the measured standard deviation between specimens leads

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to an average change of $\pm 17\%$ in the maximum and minimum principal stresses. Finally, the model is validated with an *in vivo* clamping experiment of a Wistar rat in which the clamping force was measured, showing good correspondence with the modeled clamping force.

Keywords: aorta, finite element model, clamping, mechanical properties

1. Introduction

Surgical interventions always entail a certain degree of unavoidable iatrogenic tissue damage. Therefore, studies have been directed towards decreasing this undesired intra-operative trauma, for example, through the design of less traumatic surgical instruments (Ozalp et al., 2009). A step further in this direction is the development of ‘smart’ instruments, that can assess the applied load and guide the surgeon to minimize tissue damage (see, for example, De et al., 2007; Kobayashi et al., 2007; Famaey and Vander Sloten, 2008). The effectiveness of these new designs and techniques clearly depends on how well damage mechanisms are understood and how accurate thresholds for safe tissue loading can be set.

The case study examined here is that of arterial clamping, which is commonly used to guarantee a blood-free zone for manipulation, for example, for an anastomosis in bypass surgery. However, the mechanical load due to this clamping is known to cause injury to the arterial wall, leading to intra- and postoperative complications (Aukland and Hurlow, 1981; Remes et al., 1990; Manchio et al., 2005). In Famaey et al. (2010) it was shown that, for the case of the clamping of a rat abdominal aorta, loading thresholds can be set such that the smooth muscle cells of the medial layer remain intact. However, this study only measured the macroscopic force exerted by the clamping device, whereas the resulting damage was clearly location-specific due to the heterogeneous nature of the tissue and the deformation pattern.

Generalized thresholds for safe tissue loading should therefore be set on a microscopic level, i.e. by studying the local tissue deformation/stress and the corresponding damage. This requires reliable finite element modeling, as it can reveal how the macroscopic clamping force relates to local tissue deformation and stress. For example, De et al. (2007) have described this concept to find damage thresholds for porcine liver tissue, utilizing simple, isotropic material models. Here, finite element modeling will be applied to the case study of arterial clamping. Gasser et al. (2002), for example, simulated the process of arterial clamping with finite elements up to the point before self-contact of the artery.

31 In the present work the clamping process is simulated up to clamping forces
32 beyond artery closure and with different clamp designs. In particular, the present
33 article describes an integrated approach leading to a reliable three-dimensional
34 (3D) finite element model simulating the clamping of a rat abdominal aorta. Com-
35 putational complexities such as material nonlinearity and heterogeneity, large de-
36 formations, contact interactions and residual strains are taken into account. The
37 material parameters are defined experimentally through extension-inflation tests
38 of aortic segments, and the effect of residual strains and the variations in the ma-
39 terial properties are evaluated. Finally, the finite element results are validated with
40 an *in vivo* clamping experiment.

41 2. Materials and Methods

42 2.1. Material model

43 As a first approach the rat abdominal aorta was used as a model for human
44 arteries. The experiments described in this article were performed on 12 male
45 JCR rats at 10 weeks of age¹. All experiments were performed conforming to the
46 Guide for the Care and Use of Laboratory Animals of the US National Institute of
47 Health.

48 Anatomically, the abdominal aorta is located in the abdomen adjacent to the
49 vena cava, running parallel to the spinal chord. The segment is proximally bounded
50 by the diaphragm, and distally by the bifurcation leading to the legs. Any artery
51 consists of three distinct layers. In healthy arterial tissue, the inner layer, or in-
52 tima, consists of a subendothelial layer. The middle layer is the media, which is
53 the most important load-bearing layer of the artery within the physiological load-
54 ing domain. It consists of collagen, elastin and of smooth muscle cells separated
55 by fenestrated elastic laminae. The outer layer, the adventitia, is surrounded by
56 loose connective tissue and it consists mainly of thick bundles of collagen fibres
57 in a helical structure (Schriebl et al., 2011). For a more detailed description of ar-
58 terial wall morphology, the reader is referred to, for example, Rhodin (1979) and
59 Holzapfel et al. (2000).

60 The aorta was approximated by the material model, as proposed in Holzapfel
61 et al. (2000); Gasser et al. (2006). In particular, a fiber-reinforced tube was used,

¹JCR rats are a strain incorporating the autosomal recessive corpulent gene (Russell et al., 1998). In this study, however, only the homozygous normal (+/+) or heterozygous (+/cp) were used, which are both lean and normotensive.

62 and dispersion of the collagen fibers was considered. In healthy rat abdominal aor-
 63 tas the two load bearing layers are the media and, within the physiological loading
 64 domain, to a lesser extent the adventitia. In contrast to human arteries, however,
 65 the layers cannot easily be separated from each other without compromising the
 66 integrity, making it impossible to define the mechanical properties of each layer
 67 separately. Therefore, in this study, the media and the adventitia were studied as
 68 a (combined) single layer.

69 The biomechanical response of the aortic wall can be described through a
 70 strain-energy function with respect to reference volume, say Ψ . This may be writ-
 71 ten as the sum of an isotropic contribution (Holzapfel and Weizsäcker, 1998), i.e.
 72 the matrix material, and an anisotropic contribution, i.e. two collagen fiber fami-
 73 lies embedded in the matrix material. Thus,

$$\Psi(I_1, I_4^*, I_6^*) = \frac{c}{2}(I_1 - 3) + \frac{k_1}{2k_2} \sum_{i=4,6} \exp[k_2(I_i^* - 1)^2] - 1, \quad (1)$$

74 where $c > 0$ and $k_1 > 0$ are stress-like parameters, $k_2 > 0$ is a dimensionless
 75 parameter, and I_1 is the first invariant of the right Cauchy-Green tensor, which
 76 can be written as a function of the three stretches λ_i , $i = r, \theta, z$, in the radial,
 77 circumferential, and axial directions, respectively. Thus,

$$I_1 = \lambda_r^2 + \lambda_\theta^2 + \lambda_z^2. \quad (2)$$

78 By taking into account the assumption of incompressibility ($\lambda_r \lambda_\theta \lambda_z = 1$), eq. (2)
 79 may be written as

$$I_1 = \lambda_r^2 + \lambda_\theta^2 + (\lambda_r \lambda_\theta)^{-2}. \quad (3)$$

80 The second term in (1) describes the anisotropic contribution, where I_i^* is the
 81 invariant related to the fiber direction of a fiber family, and can be written as
 82 (Gasser et al., 2006)

$$I_i^* = \kappa I_1 + (1 - 3\kappa)I_i, \quad I_i = \lambda_\theta^2 \cos^2 \alpha + \lambda_z^2 \sin^2 \alpha, \quad i = 4, 6, \quad (4)$$

83 where I_i , $i = 4, 6$, are two invariants (Holzapfel, 2000), α is the angle between
 84 the (mean) fiber direction and the circumferential direction of the cylindrical tube,
 85 and $\kappa \in [0, 1/3]$ is a parameter related to the dispersion of the fibers. In our case
 86 it is assumed that two fiber families are included in the model, which are oriented
 87 symmetrically with respect to the tube axis, which is in accordance with the results
 88 of the recent experimental study by Schriefl et al. (2011). The two fiber families
 89 have the same mechanical properties and are located within the tangential plane

of the cylinder so that $I_4 = I_6$ (hence the collagenous fiber orientations have no components in the radial direction).

The described material model contains three material parameters (c, k_1, k_2) and two structural parameters (α, κ) which need to be defined, in our case for rat abdominal aortas. The average angle α of the collagen fibers was set to $\pm 5^\circ$ (approximately the circumferential direction), which is according to results described by O’Connell et al. (2008). The four remaining parameters c, k_1, k_2 and κ , were obtained by fitting the model to the experimental data of the inflation tests.

2.2. Extension-inflation test

Each animal was anesthetized with isoflurane and subsequently euthanized by perfusion with Krebs buffer. The abdominal aortas were excised and stored for a maximum of 10 hours at 4°C in Krebs buffer (with final concentration in mmol/liter: NaCl 118.3; KCl 4.7; MgSO_4 1.2; KH_2PO_4 1.2; CaCl_2 2.5; NaHCO_3 25.0; glucose 11.1, and $\text{Na}_2\text{Ca-EDTA}$ 0.026).

Extension-inflation tests were performed on a screw-driven high-precision tensile testing machine (Messphysik). The samples were immersed in a Perspex container filled with Krebs buffer maintained at $37 \pm 0.1^\circ\text{C}$ by a heater-circulation unit (Ecoline E 200, Lauda). The aorta segments were mounted on 22G blunt needles with luer fitting which were in turn connected to a load cell on one end and to a pressure pump on the other end of the tensile machine. A 10 N load cell (AEP transducers) measured the axial force F^{exp} (‘exp’ stands for experimental) and a pressure pump (model $\mu 333$, Neuhold) controlled the internal pressure p^{exp} with an accuracy of 20 Pa. The outer radius r_o was measured optically with a video-extensometer (model ME 46-350, Messphysik). An accuracy of approximately 0.1 mm could be obtained for the edge detection. For a more detailed description of the test setup, see, for example, Schulze-Bauer et al. (2002).

After mounting, samples were first stretched to an axial pre-stretch of 50%, thus $\lambda_z = 1.5$. Next the samples were subjected to a saw-tooth profile of three loading and unloading cycles for the internal pressure going from 0 to 20 kPa at 20 Pa/s, during which F^{exp} and r_o were continuously recorded.

2.3. Parameter fitting

The four parameters (c, k_1, k_2, κ) are obtained by means of a nonlinear optimization with Matlab.R2010a. Thereby, the ‘lsqnonlin’ routine and the ‘trust-region-reflective’ optimization algorithm was used. We minimize the objective

124 function

$$E^2 = \sum_{j=1}^n \left\{ [w_p (p_j^{\text{mod}} - p_j^{\text{exp}})]^2 + [w_F (F_j^{\text{mod}} - F_j^{\text{exp}})]^2 \right\}, \quad (5)$$

125 where n is the number of data points considered, and w_p and w_F are weighting
 126 factors for the internal pressure p and the axial force F , respectively. The internal
 127 pressure and the axial force predicted by the function Ψ for the j -th data record
 128 are denoted by p_j^{mod} and F_j^{mod} ('mod' stands for model), and p_j^{exp} and F_j^{exp} are the
 129 related experimentally measured values. The weighting factors w_p and w_F were
 130 identified to equate contributions of the internal pressure and the axial force in the
 131 objective function E^2 .

132 Starting from the equilibrium equation, i.e.

$$\frac{d\sigma_{rr}}{dr} + \frac{1}{r}(\sigma_{rr} - \sigma_{\theta\theta}) = 0, \quad (6)$$

133 where r is the radius and σ_{rr} and $\sigma_{\theta\theta}$ are the stresses in the radial and circum-
 134 ferential direction, respectively, in Ogden (2009) it is shown how the following
 135 function between the internal pressure p^{mod} and the stretches λ and λ_z can be
 136 derived. Thus,

$$p^{\text{mod}} = \int_{\lambda_o}^{\lambda_i} (\lambda^2 \lambda_z - 1)^{-1} \frac{\partial \Psi}{\partial \lambda} d\lambda, \quad (7)$$

137 where, subsequently, λ denotes the stretch in the circumferential direction so that
 138 λ_i and λ_o are the circumferential stretches at the inner and outer wall, respectively.
 139 These stretches can be described as a function of the radius and the axial length as

$$\lambda = \frac{r}{R}, \quad \lambda_i = \frac{r_i}{R_i}, \quad \lambda_o = \frac{r_o}{R_o}, \quad \lambda_z = \frac{l}{L}, \quad (8)$$

140 where r and R denote the deformed and initial radii at a certain position, respec-
 141 tively, r_i and r_o denote the deformed radii at the inner and outer wall, respectively,
 142 and l and L the deformed and initial axial length of the sample, respectively. The
 143 initial inner radius R_i was derived by subtracting the measured initial wall thick-
 144 ness from the initial outer radius. Subsequent values for r_i were derived for each
 145 measurement point by assuming incompressibility, i.e.

$$\lambda_z = \frac{R_o^2 - R_i^2}{r_o^2 - r_i^2}. \quad (9)$$

Figure 1: Load-free and stress-free configuration of a ring segment of a rat abdominal aorta.

146 The axial force F^{mod} can then be found as the integral of the axial stress over
 147 the wall thickness subtracted with the pressure exerted on the inner surface, also
 148 called ‘reduced axial force’ (Holzapfel et al., 2000; Ogden, 2009):

$$F^{\text{mod}} = \pi R_o^2 (\lambda_i^2 \lambda_z - 1) \int_{\lambda_o}^{\lambda_i} (\lambda^2 \lambda_z - 1)^{-2} \left(2\lambda_z \frac{\partial \Psi}{\partial \lambda_z} - \lambda \frac{\partial \Psi}{\partial \lambda} \right) \lambda d\lambda. \quad (10)$$

149 2.4. Stress-free geometry

150 An accurate finite element model starts from an initial geometry that is stress
 151 free. The aorta can be approximated by a cylinder of which the average circum-
 152 ference S and wall thickness T in the unloaded state are measured. However, due
 153 to residual strains, the *in situ* unloaded state does not coincide with the stress-
 154 free state in arterial tissues (Vaishnav and Vossoughi, 1987; Rachev and Green-
 155 wald, 2003; Holzapfel and Ogden, 2010). The main components of these residual
 156 strains, which depend on the species and the location, can be found along the cir-
 157 cumferential and the axial directions, and they were experimentally determined
 158 for the 12 arterial samples used for the inflation tests.

159 The axial residual strains were derived by comparing the *in vivo* length of the
 160 arterial sample to its length after excision. The circumferential residual strains
 161 were measured by cutting open a ring-shaped segment of the artery and determin-
 162 ing the steady-state opening angle θ , as shown in Fig. 1.

163 2.5. Finite element model

164 The 3D finite element model was built in Abaqus/Explicit version 6.9-2. The
 165 initial geometry for the model was a cylindrical segment cut open with an opening

Input parameters	
Geometry	Wall thickness $T = 0.14$ mm Section circumference $S = 2.75$ mm Length $L = 0.2$ mm Opening angle $\theta = 61^\circ$
Mechanics/Structure	Compressibility $D = 0.2$ Fiber angle $\alpha = \pm 5^\circ$ $c = 23.63 \pm 4.13$ kPa $k_1 = 32.51 \pm 6.13$ kPa $k_2 = 3.05 \pm 1.32$ (-) $\kappa = 0.16 \pm 0.01$ (-)

Table 1: Parameters used in the finite element model.

166 angle of $\theta = 61^\circ$, a section circumference $S = 2.75$ mm, a wall thickness $T =$
 167 0.14 mm and an initial length $L = 0.2$ mm. This particular geometry was used
 168 as a basis for our subsequent finite element simulations, hence these geometrical
 169 data were considered to be representative. Symmetry allowed for only half of the
 170 segment to be modeled as a self-contact problem.

171 The element size was set to ensure at least six elements through the thick-
 172 ness for accurate modeling of bending. Hexahedral, linear, reduced integration
 173 elements (C3D8R) were assigned to the mesh, and the model by Holzapfel et al.
 174 (2000); Gasser et al. (2006), in Abaqus referred to as the Holzapfel-Gasser-Ogden
 175 material, was used with the parameters, as explained in the previous paragraph.

176 Due to the explicit nature of the solver, a certain amount of compressibility
 177 was needed. This means that an extra dilatational function Ψ_{dil} was added to the
 178 strain-energy function (1), and that was of the form

$$\Psi_{\text{dil}}(J) = \frac{1}{D} \left(\frac{J^2 - 1}{2} - \ln J \right), \quad (11)$$

179 where J denotes the determinant of the deformation gradient $\mathbf{F}$. After a sensitivity
 180 analysis the parameter D was set to 0.2, proving the value to be low enough to
 181 ensure that the material is nearly incompressible, but high enough to enable a
 182 smooth calculation. Table 1 provides an overview of all the parameters used in
 183 the finite element model.

184 Four different loading steps were applied, as schematically shown in Fig. 2.
 185 In the first loading step the cylindrical segment was closed to form a half cylin-
 186 der. This was performed by constraining the surface A in the x -direction and by

Figure 2: Schematic overview of the applied four loading steps.

187 imposing a displacement x_1 and x_2 to the edges b and c , without constraining the
 188 vertical degree of freedom (see Fig. 3). Next, the cylinder was axially stretched
 189 by a factor of $\lambda_z = 1.5$. The axial direction remained fixed for all nodes at the
 190 edges for the remainder of the simulation. In the third step, the segment was pres-
 191 surized with an internal pressure of 16 kPa while in the fourth step the internal
 192 pressure pulsed between the physiological levels of 10 and 16 kPa (diastole and
 193 systole) at a rate of 1 Hz and the clamps were moved towards each other over a
 194 time span of 10 seconds. Fixed mass scaling was applied to enable time incre-
 195 ments of $5 \cdot 10^{-6}$ s, for steps 1 to 3. During clamping, i.e. step 4, the time step
 196 was reduced to $1 \cdot 10^{-6}$ s. Note that we are here dealing with a quasi-static anal-
 197 ysis so that we are computing sufficiently slow processes whereby enough time
 198 remains for the system to adjust itself internally. Hence, time does not influence
 199 our computational results. However, we want to keep the notation of ‘time’ for
 200 comparative purposes to become clear in the experimental part of the study. To
 201 ensure that the analyses were in fact quasi-static, the total kinetic energy was com-

Figure 3: Circumferential residual strains are added by constraining the surface A in the x -direction and by moving the edges b and c over a distance x_1 and x_2 , without constraining the degree of freedom along the y -direction.

202 pared to the total strain energy of the model. The kinetic energy was found to be
 203 negligible throughout the entire analysis, by a factor of 10^{-5} .

204 To simulate the pressure drop during the closing of the vessel, the pulsating
 205 pressure was modulated with an exponential decay function. The vessel was
 206 closed until the clamping force reached at least 1.0 mN, i.e. the clamping force
 207 for one half of the aortic ring. Contact, enforced with the penalty method, was
 208 defined between all contact surfaces, nonlinearity due to large displacements was
 209 taken into account and the analysis was run in double precision.

210 Two different clamp designs were used; both modeled as rigid bodies. In the
 211 first model, subsequently referred to as the SRA model (for explanation of the
 212 acronym see Table 2), the clamp arms were flat surfaces. In the second model, ab-
 213 breviated as MRA, a corrugated surface was modeled, similar to a typical surgical
 214 mosquito clamp. To test the sensitivity, calculations were performed with average
 215 values for the material parameters and plus and minus the (sample) standard devi-
 216 ation (SD), abbreviated as SRA+ and SRA-, respectively. To evaluate the effects
 217 in the lateral edges of the clamp, a longer segment was also modeled (abbrevi-
 218 ated as LRA), with a smooth clamp design, slightly curved at the lateral edges.
 219 The stress-free segment length was 4 mm, the length of the clamp was 0.8 mm.
 220 To evaluate the effect of the residual strains on the biomechanical response, the
 221 calculations were repeated for the same geometry, but with the strain energy reset
 222 to zero after step 2, i.e. after applying the residual strains, subsequently abbrevi-
 223 ated as SA. Table 2 gives an overview of the different model variations that were
 224 studied.

Model variations				
Model	Clamp design	Residual strain	Material parameter	Segment length
SRA	Smooth	Yes	Average	0.2 mm
SRA+	Smooth	Yes	Average + SD	0.2 mm
SRA-	Smooth	Yes	Average – SD	0.2 mm
SA	Smooth	No	Average	0.2 mm
MRA	Mosquito	Yes	Average	0.2 mm
LRA	Smooth	Yes	Average	4 mm

Table 2: Overview of the model variations (SD = standard deviation).

2.6. *In vivo clamping experiment*

The finite element simulation was then compared with the actual *in vivo* clamping of a 10 week old male Wistar rat. The animal was anesthetized with an isoflurane-oxygen mixture through a semi-closed circuit inhalation system. The animal was placed on a heating pad to control body temperature. An incision in the abdominal cavity was made, upon which the surrounding organs and fatty tissues were retracted to free a length of approximately 1.5 cm of the abdominal aorta and the vena cava. One segment was clamped with a custom made clamping device described in Famaey et al. (2010), with an integrated clamping force measurement system. The abdominal aorta and the vena cava were clamped together. Namely, a separation of the two vessels would induce an uncontrollable amount of damage which would counterfeit the results. During clamping, the force between the clamp arms was continuously recorded.

3. Results

3.1. *Mechanical properties*

Figure 4 shows the experimentally obtained relation between the internal pressure p^{exp} versus the circumferential stretch λ and the axial force F^{exp} versus λ obtained from 9 specimens of rat abdominal aortas. In the three remaining specimens, slippage occurred during testing so that the axial force and stretch were unusable. The thin curves in Fig. 4 represent the biomechanical behaviors which were obtained by filtering the experimental data with a 5 Hz second-order low-pass filter. In Table 1 the values for c , k_1 , k_2 and κ (average and standard deviation – SD) are summarized resulting from a parameter optimization procedure for these

Figure 4: Internal pressure versus circumferential stretch (left plots), axial force versus circumferential stretch (right plots). Thin curves characterize the experimental results obtained from 9 specimens of rat abdominal aortas (p^{exp} and F^{exp}), while thick curves indicate the calculated internal pressure and axial force versus the circumferential stretch (p^{mod} and F^{mod}) for the average parameters c , k_1 , k_2 and κ according to Table 1. Thick dashed curves indicate the internal pressure p^{num} and the axial force F^{num} versus the circumferential stretch generated by a finite element simulation using the model SRA.

248 data sets. The sample standard deviation of the four fitted material parameters c ,
 249 k_1 , k_2 , and κ are ± 17.5 , 18.9 , 43.3 and 6.2% , respectively. The thick solid curves
 250 in Fig. 4 indicate the calculated internal pressure p^{mod} and axial force F^{mod} versus
 251 λ for the average parameters according to Table 1.

252 The thick dashed curves in Fig. 4 indicate the internal pressure p^{num} and axial
 253 force F^{num} versus λ , generated by a finite element simulation using model the
 254 SRA, slightly modified to allow an inflation up to 20 kPa, as in the experiments.
 255 Note that in p^{num} and F^{num} , residual strains are taken into account in contrast to
 256 p^{mod} and F^{mod} .

257 3.2. Clamping simulation

258 The following section describes the finite element results, highlighting the
 259 effect of model variations (see Table 2) on different stress components. All results
 260 are compared at the point at which the clamps exert a force of 1.0 mN. This value
 261 was chosen as it ensures vessel occlusion for all models without causing excessive
 262 distortion to the finite element mesh.

263 Table 3 lists all maximum and minimum Cauchy stress values that occur in
 264 the artery at this clamping force for the different model variations, and it also lists
 265 stress values encountered at an internal pressure of 16 kPa (i.e. systole), expressed

Model	σ_{11}		σ_{22}		σ_{33}		σ_{12}		von Mises	
10^{-2} MPa	min	max	min	max	min	max	min	max	min	max
SRA	-9.44	-0.31	-10.87	7.76	-6.58	5.93	-3.48	3.51	3.75	7.66
SRA+	-11.28	-0.31	-12.66	9.50	-7.80	7.61	-3.80	3.85	4.43	9.49
SRA-	-7.91	-0.28	-9.01	6.31	-5.48	4.68	-2.96	2.98	3.10	6.26
SA	-14.75	-0.42	-17.82	11.44	-16.87	0.59	-4.87	4.92	0.12	11.73
MRA	-11.62	-0.06	-11.22	10.13	-7.07	6.56	-3.35	4.91	3.74	12.95
systole	0	-1.16	6.98	9.60	6.04	6.10	0	0	6.67	9.49
% of SRA	min	max	min	max	min	max	min	max	min	max
SRA+	119	100	116	122	119	128	109	110	118	124
SRA-	84	89	82	81	83	79	85	85	83	82
SA	156	134	164	147	256	10	140	140	3	153
MRA	123	-20	103	130	107	111	96	140	100	169
% of systole	min	max	min	max	min	max	min	max	min	max
SRA	$-\infty$	27	-156	81	-109	97	$-\infty$	∞	56	81
MRA	$-\infty$	-6	-161	105	-117	107	$-\infty$	∞	56	136

Table 3: Overview of the minimum and maximum values of the Cauchy stress components in the radial σ_{11} , circumferential σ_{22} and axial σ_{33} directions, the Cauchy shear stress component σ_{12} and the von Mises stress for the different model variations according to Table 2 at 1.0 mN contact force, expressed in 10^{-2} MPa. The sixth row describes the stress values encountered at an internal pressure of 16 kPa (i.e. systole). These values are compared with the corresponding value of the SRA model, expressed in %. The values for the models SRA and MRA are also expressed with respect to the corresponding values at a systolic pressure of 16 kPa.

in 10^{-2} MPa. The table also compares these values with the corresponding value of the SRA model in % (i.e. the model with smooth clamp design, incorporation of residual strains and average material parameters). For the models SRA and MRA, the values are also expressed relative to the corresponding values encountered in the physiological state in % (i.e. systolic state at an internal pressure of 16 kPa). The Cauchy stresses are described in a cylindrical coordinate system, with the radial, circumferential and axial directions denoted as σ_{11} , σ_{22} and σ_{33} , respectively. Also the Cauchy shear stress component σ_{12} and the von Mises stress are shown in Table 3. Note that the maximum and minimum values for each of the stresses do not necessarily occur in the same finite element so that the maximum and minimum von Mises stress can not directly be derived from these values.

3.2.1. Material parameter variation

Figure 5 shows deformed arterial sections with related distributions of the von Mises stresses for the different models SRA+, SRA, and SRA- (see Table 2), i.e.

Figure 5: Deformed arterial sections subjected to a clamping force of 1.0 mN for the three models SRA+, SRA and SRA- (compare with Table 2). Color shows the distribution of the von Mises stresses.

the model with the smooth clamp design, considering residual strain in the artery, and with varying material parameters $\pm$ SD. The von Mises stresses are plotted at a clamping force of 1.0 mN. The effect of this inter-specimen variation on the calculated stresses can also be seen from Table 3, and was on average $\pm$ 17%.

3.2.2. Residual strain

Figure 6 shows deformed arterial sections with related distributions of the Cauchy stress components in the radial σ_{11} , circumferential σ_{22} and axial σ_{33} direction, in addition to the shear stress component σ_{12} , for the same clamping force and for the models SRA and SA. Recall that the SRA model has a smooth clamp design, considers average material parameters and residual strains in the aorta (circumferential and axial), while the model SA does not consider residual strains.

The two curves in Fig. 7 show the distribution of the circumferential Cauchy stress σ_{22} through the wall thickness for the two models SRA and SA in the diastolic state, i.e. at an internal pressure of 10 kPa. From this figure it is clear that residual strains tend to homogenize the stresses through the wall thickness. The results in Table 3 show, for example, a 53% increase in the maximum von Mises stress in the model without residual strain, and a 97% decrease in the minimum von Mises stress.

Figure 6: Deformed arterial sections subjected to a clamping force of 1.0 mN for the two models SRA and SA (compare with Table 2). Color shows the related distributions of the Cauchy stress components in the radial σ_{11} , circumferential σ_{22} and axial σ_{33} direction, in addition to the shear stress component σ_{12} .

Figure 7: Distribution of the circumferential Cauchy stress σ_{22} through the wall thickness for the models SRA and SA in the diastolic state, i.e. at an internal pressure of 10 kPa.

3.2.3. Inhomogeneous stress distribution

To evaluate the inhomogeneity of the stress distribution in the artery wall, the stresses were monitored during the simulation of the SRA model at four different locations. Figure 8 shows the evolution of the circumferential stress σ_{22} (in MPa) as a function of time (in s) for four nodes, each with a specific location in the mesh.

Figure 8: Evolution of the circumferential stress σ_{22} in the artery wall at four different locations for the clamping process of the SRA model.

Figure 9: Deformed arterial sections subjected to a clamping force of 1.0 mN for the MRA model (compare with Table 2). Color shows the related distributions of the Cauchy stress components in the radial σ_{11} , circumferential σ_{22} and axial σ_{33} direction, in addition to the shear stress component σ_{12} .

3.2.4. Clamp design

Figure 9 shows deformed arterial sections at the same clamping force for model MRA, i.e. the model with average material parameters, including residual strains in the artery wall, and with a corrugated clamp design. The deformed sections also represent the distribution of the Cauchy stress components in the radial σ_{11} , circumferential σ_{22} and axial σ_{33} direction, in addition to the shear stress component σ_{12} .

Table 3 shows a 69% increase in the maximum von Mises stress in the MRA model with respect to the SRA model, whereas the minimum von Mises stress is basically equal for both models.

3.2.5. Segment length

Figure 10 shows deformed arterial sections at an equivalent clamping force for model SRA and model LRA, i.e. the longer segment with a smooth clamp with slightly curved lateral edges. Slight differences are recognized, for example, higher maximal radial and circumferential stresses, and lower maximal axial stresses for the shorter segment. Analyzing the stresses in the longer segment along the axial direction (shown in Fig. 11) shows some slight stress concentrations at the lateral edges where the clamp comes into contact with the artery.

3.3. In vivo clamping experiment

Figure 12 shows the clamping force per clamped surface as a function of the displacement for the *in vivo* clamping experiment and for the numerical simulation of the SRA model. The pulsating pressure is visible until occlusion of the artery. The clamping force that corresponds to this point is called the minimum occlusion force.

4. Discussion

A finite element model was built to study the stress distributions in arterial tissue due to clamping. Extension-inflation tests of the rat abdominal aortas were performed to define the material parameters, and the experimental data were fitted to the material model by Holzapfel et al. (2000). The results of this fit are acceptable considering the fact that certain features such as hysteresis and damage are not captured by the used material model.

Note also that in the finite element model, the artery was modeled as a single homogeneous layer, even though the wall consists of two solid mechanically

Figure 10: Principal stresses in the central cross section of the arterial segment, at a clamping force of 1 mN for the SRA model, and at the equivalent clamping force of 5.33 mN for the LRA model. Each of the top images represents the SRA model, while the bottom image is the LRA model. Slight differences are recognized, for example, higher maximal radial and circumferential stresses, and lower maximal axial stresses for the SRA model compared with the LRA model.

Figure 12: Measured clamping force per clamped surface (in N/mm^2) as a function of displacement (in mm) during the *in vivo* clamping of the abdominal aorta of a Wistar rat with a smooth clamp design (dashed curve). The solid curve shows the finite element result of the SRA model.

338 relevant layers, i.e. the media and the adventitia. However, in the case of a rat ab-
 339 dominal artery, the complete wall thickness is only approximately 0.14 mm thick,
 340 and in contrast to human tissue, it is impossible to separate these two layers from
 341 each other. Therefore, the most accurate approach was to test the wall in its total-
 342 ity, and model it as a single layer. The values found for the different parameters are
 343 of the same order of magnitude as the ones derived, for example, by Gasser et al.
 344 (2006), where the mechanical properties of human iliac arteries were described.

345 The effect of the tissue variation on the material parameters was evaluated by
 346 also calculating model variations such as SRA+ and SRA-. Overall, by varying
 347 the material parameters with plus and minus the standard deviation we obtained a
 348 shift in the peak stresses by $\pm 17\%$. The values described here should, however,
 349 be evaluated with caution, as all four material parameters c , k_1 , k_2 , κ were simul-
 350 taneously reduced or increased, which might not reflect a specific tissue sample.
 351 A full parametric study is required to get a better understanding of the effect of
 352 the variability of the different parameters.

353 It is clear how residual strains/stresses influence the physiological wall stresses
 354 in the aortic wall. As has already been described in numerous studies (see, e.g.,
 355 Vaishnav and Vossoughi, 1987; Rachev and Greenwald, 2003; Holzapfel and Og-
 356 den, 2010), the effect of incorporating circumferential residual strains is that they
 357 tend to homogenize the circumferential stresses through the arterial wall thickness
 358 in the physiological state, which was confirmed by our results as shown in Fig. 7.
 359 The effect of the axial residual strains (or pre-stretch λ_z) is that during physiolog-
 360 ical loading and unloading, the axial force remains almost constant, as described
 361 in, for example, Weizsäcker et al. (1983) and Schulze-Bauer et al. (2003). In
 362 our study the axial force remains constant for the lower range of circumferential
 363 strains and thus internal pressure, but tends to decrease in the higher range of cir-
 364 cumferential strains (see the right graph in Fig. 4 obtained for $\lambda_z = 1.5$). This
 365 indicates a slight underestimation of the actual *in vivo* pre-stretch in our experi-
 366 ments.

367 From the results described in Table 3 and Fig. 6 it can be seen that the effect of
 368 the residual strains propagates into the supra-physiological domain: also during
 369 clamping residual strains/stresses ‘protect’ the tissue by leveling out the maximum

370 stresses. Clearly, residual stresses cannot be ignored, even when modeling supra-
371 physiological phenomena.

372 In general, all results indicate that the stress distribution due to the macro-
373 scopic clamping force is highly inhomogeneous. This can also be seen in Fig. 8,
374 where, depending on the location in the mesh, the circumferential Cauchy stress
375 differs already in the physiological state, and this difference grows exponentially
376 during the clamping process. The effect of the inhomogeneous stress distribution
377 is even stronger in the MRA model, i.e. the model with the corrugated clamp
378 design, which gives rise to pronounced stress concentrations in different regions
379 of the model, reaching levels up to 69% higher than with a smooth clamp de-
380 sign. These results substantiate the fact that improved clamp designs can lower
381 tissue trauma, and that finite element modeling is an indispensable tool during this
382 design process.

383 Figure 12 shows a fairly good correlation between the model and the validation
384 experiment. Again, caution is required when comparing the results as one should
385 take into account the fact that a different type of rat was used for the validation
386 experiment and that the parameters used for the mechanical model are average
387 values derived from a group of animals. In addition, in the *in vivo* experiment
388 the vena cava was clamped along with the aorta which slightly alters the geo-
389 metrical situation. The comparison was shown to indicate that, when used more
390 methodically, this type of *in vivo* clamping experiment can be a reliable validation
391 method.

392 All these results indicate the potential of finite element modeling to under-
393 stand the loading conditions and subsequent damage mechanisms in vascular tis-
394 sue. However, the model described here is still situated on a supra-cellular level,
395 whereas the actual damage processes obviously initiate on a cellular or subcellular
396 level. The rupture of collagen fibers and the death of smooth muscle cells cannot
397 be captured by the material model of Holzapfel et al. (2000), which is why the
398 simulation could only reliably be performed up to a relatively low clamping force.
399 Adaptation of this model to incorporate damage mechanisms will lead to more
400 accurate results in the higher loading regimes. Also, more refined modeling of the
401 fluid-structure interaction would allow a better definition of the pressure load on
402 the inner wall of the vessel, as well as the wall shear stresses.

403 The ultimate aim of this research direction is to derive reliable damage thresh-
404 olds for biological soft tissues such as artery walls to optimize clamp designs and
405 to increase the safety required during tissue manipulations.

406 In current surgical practice, the amount of load that can safely be applied on a
407 certain tissue is highly subjective, i.e. depending on the surgeon's experience and

judgement. Different steps are needed to improve and objectify this judgement. In a previous work by, for example, Famaey et al. (2010), clamping experiments, in which the clamping force was measured, were performed on rat abdominal arteries. Subsequently, the damage to the artery was assessed through quantification of the functionality of the endothelial and smooth muscle cells, and through the evaluation of histological images. Currently, these experiments are being extended to an increased sample size, to additional load levels, and damage is being assessed after different periods of ‘repair time’. This will provide the surgeon with quantitative information by facilitating a more objective approach.

However, in the experimental setup, the quantitative damage results are only linked to the macroscopic clamping force of the clamp used in the experiment and are, therefore, not yet generalizable to other loading situations. As was shown in this article, macroscopic force levels give rise to inhomogeneous stress distributions, which is why these thresholds should be defined on a local tissue level.

Therefore, the finite element model described in the present work acts as a bridge between the experimental results described in Famaey et al. (2010) and the local tissue damage. In the present work, the focus was put on tissue stress. However, more research is required to define which quantitative measure should be used for the thresholds, i.e. stress, stretch, strain rate, energy, or a weighted combination.

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