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EFFECTS OF LONGITUDINAL PRE-STRETCH ON THE MECHANICS OF HUMAN AORTA BEFORE AND AFTER THORACIC ENDOVASCULAR AORTIC REPAIR (TEVAR) IN TRAUMA PATIENTS

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Abstract

Thoracic endovascular aortic repair (TEVAR) has evolved as a first line therapy for trauma patients. Most trauma patients are young, and their aortas are compliant and longitudinally pre-stretched. We have developed a method to include longitudinal pre-stretch in computational models of human thoracic aortas of different ages before and after TEVAR. Finite Element Models were built using Computerized Tomography Angiography data from human subjects in 6 age groups 10–69 years old. Aortic properties were determined with planar biaxial testing, and pre-stretch was simulated using a series of springs. GORE C-Tag stent-graft was computationally deployed in aortas with and without pre-stretch, and the stress-strain fields were compared. Pre-stretch had significant qualitative and quantitative effects on the aortic stress-strain state before and after TEVAR. Before TEVAR, mean intramural aortic stresses with and without pre-stretch decreased with age from 108 kPa and 83 kPa in the youngest age group, to 60 kPa in the oldest age group. TEVAR increased intramural stresses by an average of 73 ± 15 kPa and 48 ± 10 kPa for aortas with and without pre-stretch, and produced high stress concentrations near the aortic isthmus. Inclusion of pre-stretch in young aortas increased intramural stresses by 30%, while in >50-year-old subjects it did not change the results. Computational modeling of aorta-stent-graft interaction that includes pre-stretch can be instrumental for device design and assessment of its long-term performance, and in the future may help more accurately determine the stress-strain characteristics associated with TEVAR complications.

Keywords

pre-stretch; aorta; computational modeling; thoracic endovascular aortic repair; stent-graft

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Conflict of interest

Authors declare that they have no conflict of interest.

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1. INTRODUCTION

Injuries in the United States account for 51 % of all deaths among people younger than 44 years(Sauaia et al. 1995; Web-based Injury Statistics 2009; Evans et al. 2010), more than all non-communicable and infectious diseases combined. Blunt thoracic aortic injuries caused by high-speed motor vehicle accidents, falls from heights, and crushes or explosions are the leading causes of mortality in trauma patients(Miller 2012). Rapid deceleration or sudden chest compression can produce high shear, torsion and compression forces in and around the aortic arch. Most cases lead to disruption at the aortic isthmus, just distal to the origin of the left subclavian artery on the inner curve of the proximal thoracic descending aorta near the ligamentum arteriosum(Schumacher et al. 2006). Approximately 80–90% of thoracic aortic injury victims die at the scene from massive hemorrhage(Parmley et al. 1958; Hartford et al. 1986). Of the patients who arrive at the hospital alive, the mortality rate is 65% unless aortic repair is performed(Arthurs et al. 2009).

Traditional open surgical intervention for thoracic aortic injury requires large chest incisions, clamping of the aorta, and often other adjunctive maneuvers in patients that are frequently unstable and have other serious injuries. As a result, short-term morbidity, mortality and blood transfusion requirements are high(Atkins et al. 2009; Miller 2012). In comparison, thoracic endovascular aortic repair (TEVAR) using stent-grafts does not require aortic clamping and is performed via percutaneous techniques or small incisions that access peripheral arteries remotely from the actual area of injury. Stent-grafts, also known as covered stents, are similar to traditional tubular textile surgical bypass grafts, but the textile component (usually polytetrafluoroethylene (PTFE) or polyethylene terephthalate (PET)) is attached to a metallic Nitinol skeleton, the stent. This allows compression of the stent-graft device into a small delivery system that can then be guided through the vasculature from a remote access artery to the site of injury using fluoroscopy, where it can then be deployed, springing open within the flowing blood to permanently reline and reconstruct the torn aorta.

Because endovascular surgery produces significantly improved short-term outcomes compared to open surgery(Xenos et al. 2008; Cheng et al. 2010), it is currently recommended as the first-line therapy for thoracic aortic injury(Reuben et al. 2007). But despite these short-term advantages, sustained benefits, particularly in young trauma patients, are much less understood(Miller 2012). The mean age of patients with thoracic aortic injury is only 31 years(Schumacher et al. 2006), and their life expectancy is almost 10-fold longer than that of patients with degenerative aortic diseases(Gongalves et al. 2016) for which TEVAR stent-grafts were originally developed. This raises important concerns regarding long-term device durability in young TEVAR patients, and calls for experimental and computational assessments of long-term stent-graft function. Computational modeling can be particularly instrumental in studying device performance under various loading conditions, and can be used to improve stent-graft design, but these models heavily rely on input parameters to assure realistic predictions. Importantly, young aortas are compliant(Learoyd and Taylor 1966; Haskett et al. 2010; Herrera et al. 2010; Kamenskiy et al. 2014b) and have substantial longitudinal pre-stretch(Horny et al. 2011; Horny et al. 2013; Horny et al. 2016) that is often overlooked in computational models of device-aorta interactions. The fundamental role of pre-stretch has been demonstrated by multiple studies

in different arterial beds (Van Loon et al. 1977; Humphrey et al. 2009; Kamenskiy et al. 2016), but its Finite Element (FE) implementation in complex aortic geometries remains insufficiently explored.

The goal of our study was to develop a framework that allows accounting for the longitudinal pre-stretch of the thoracic aorta and its main branches. This framework was used in combination with age group-specific aortic mechanical properties and geometries to quantify the effects of pre-stretch on stress-strain states of the aorta before and after TEVAR with a commercial trauma stent-graft (GORE C-TAG). Proposed methodology can help more accurately describe the stress-strain state of the aortic wall in different age groups, and in the future can be used to help determine optimal stent-graft characteristics that balance the properties of the implant with the morphometry and mechanics of young host aortas. These models can also assist with the development of new standards for safer, more effective, and longer-lasting endovascular aortic repairs for patients with traumatic aortic injuries.

2. METHODS

2.1. Parametric model of the thoracic aortic geometry during aging

A segment of the thoracic aorta from the aortic valve to the aorta at the level of the xiphoid process was parameterized using age-dependent aortic arch radius R_{arch} , length of the descending thoracic aorta L , positions of the arch branches (i.e. the brachiocephalic artery (BA), the left common carotid artery (LCCA), and the left subclavian artery (LSA)), the diameters D_{dLSA} and $D_{at\ xiphoid}$ of the aorta immediately distal to the LSA and at the level of the xiphoid process, and the longitudinal pre-stretches λ_z^{aorta} and λ_z^{br} of the aorta and the arch branches (Figure 1). Geometric parameters and positions of the aortic arch branches were adopted from our previous study (Kamenskiy et al. 2015), and longitudinal pre-stretch values were determined previously by Horny et al (Horny et al. 2013; Horny et al. 2016):

$$\begin{aligned}\lambda_z^{br} &= 1.461 - 0.00538 \cdot age \\ \lambda_z^{aorta} &= 2.3969 \cdot age^{-0.1952}\end{aligned}\tag{1}$$

Though pre-stretch determined by eq (1) was originally measured for the abdominal aorta and the LCCA, we have used the same equations for the thoracic aorta and all aortic arch branches due to lack of available human data. Age-group specific values were determined evaluating pre-stretches at the middle age of each age group (Table 1). Thickness of the aortic wall for each age group was adopted from Goyal (V.K. Goyal 1982). All geometric parameters used to generate age group-specific aortic models are presented in Table 1 for subjects 10 to 69 years old.

2.2. Mechanical characterization and constitutive modeling of human thoracic aortas

Fresh human descending thoracic aortas (n=6), one specimen per decadal age group, were obtained from Live On Nebraska, and mechanically tested within 24h of death after receiving consent from next of kin. Subjects (Table 2) were 16–69 years old, predominantly

male (83.3%), and most had prior history of tobacco use (83.3%). One subject (16.7%) had hypertension and diabetes mellitus, none were diagnosed with dyslipidemia or coronary artery disease.

Rings of the proximal descending thoracic aorta were photographed to measure thickness, and mechanical characterization was performed on 13×13 mm radially-cut specimens that were free from gross pathology using planar biaxial extension on a CellScale Biotester. Longitudinal and circumferential directions of the artery were aligned with the test directions, and the rake system was used to mount and stretch the aortic specimens since in our previous tests of thoracic aortas we have not observed significant shear (Kamenskiy et al. 2014b). Tests were done with 0.01 s⁻¹ strain rate in 37°C 0.9% Phosphate-Buffered Saline, and the specimens were sprinkled with graphite markers to allow measurement of the deformation gradient in the center of the sample as described previously (Kamenskiy et al. 2014a). The Biotester device was equipped with 5N load cells that had 0.2% max load accuracy. All tissues were preloaded with a 0.1N tare load and preconditioned using 20 equibiaxial cycles to achieve repeatable force-stretch curves. After that, a total of 21 stretch-controlled multi-ratio protocols were used to obtain sufficient data density for constitutive modeling. These protocols covered circumferential to longitudinal stretch ratios of 1:0.1 to 1:0.9 and 0.9:1 to 0.1:1 with 0.1 step, intermixed with three 1:1 equibiaxial protocols in the beginning, middle, and the end of the test sequence to ensure absence of tissue damage. Maximum stretch levels were selected for each specimen to ensure non-linearity in force-stretch curves while avoiding excessive stretch that can cause tissue damage. Cauchy stresses averaged through the specimen thickness were calculated as a function of the applied stretches and forces in both the longitudinal and the circumferential directions as:

$$\sigma_{zz}^{exp} = \lambda_z \frac{P_z}{HL_\theta}; \quad \sigma_{\theta\theta}^{exp} = \lambda_\theta \frac{P_\theta}{HL_z}, \quad (2)$$

Where λ_θ , λ_z are in-plane stretches, P_i are applied forces, H is the undeformed specimen thickness, and L_i are undeformed lengths over which applied loads act.

Experimental data were used to determine constitutive parameters of the classic two-fiber family Holzapfel-Gasser-Ogden (HGO) model (Holzapfel et al. 2000) with strain energy density U expressed as (Eq. 3):

$$U = \frac{c_0}{2}(I_1 - 3) + \frac{c_1^{col}}{2c_2^{col}} \sum_{i=1,2} \left[\exp\left(c_2^{col}(I_4^i - 1)^2\right) - 1 \right]. \quad (3)$$

Here c_0 is the initial shear modulus of the isotropic ground substance, $c_1^{col} > 0$ is a stress-like material parameter, c_2^{col} is a dimensionless material parameter, and I_1 and I_4^i are the first and fourth invariants of the right Cauchy-Green tensor $\mathbf{C}$. The fourth invariant is equal to the square of the stretch in the i^{th} fiber direction $I_4^i = \mathbf{M}^i \cdot (\mathbf{C}\mathbf{M}^i) = \lambda_i^2$, where $\mathbf{M}^i$ is a unit vector of the i^{th} fiber direction in the reference configuration, making an angle γ^i with the longitudinal axis. Fibers phenomenologically represented collagen families that were

symmetric about the longitudinal axis of the aorta with angles $\gamma^1 = -\gamma^2 = \gamma$, and assumed to contribute to the strain energy function only when stretched. The latter was achieved by using Macaulay brackets $\langle (\cdot) \rangle = \frac{1}{2}[(\cdot) + |(\cdot)|]$ in Eq. 3 to filter out negative values. In the case of biaxial testing, and assuming tissue incompressibility, Cauchy stresses can be derived from Eq. 3 as:

$$\begin{aligned}\sigma_{\theta\theta} &= c_0\lambda_\theta^2 + 4c_1^{col}\langle I_4^{col} - 1 \rangle e^{\frac{c_2^{col}(I_4^{col}-1)^2}{2}} \lambda_\theta^2 \sin^2\gamma, \\ \sigma_{zz} &= c_0\lambda_z^2 + 4c_1^{col}\langle I_4^{col} - 1 \rangle e^{\frac{c_2^{col}(I_4^{col}-1)^2}{2}} \lambda_z^2 \cos^2\gamma,\end{aligned}\quad (4)$$

Constitutive parameters in Eq. 4 were determined from the experimental data using Levenberg-Marquardt minimization algorithm in OriginPro 2017 (OriginLab, Northampton, Massachusetts, USA) in multi-data global fit mode while constraining parameters to be non-negative (Kamenskiy et al. 2014b; Kamenskiy et al. 2014a). Several different initial guesses were used to ensure parameter uniqueness. Coefficient of determination R^2 was used as a measure of goodness of fit.

2.3. The Finite Element model

The Finite Element analysis (FEA) was used to model the thoracic aorta before and after TEVAR. Abaqus/Explicit 2017 was used for all simulations.

2.3.1. Model of the aorta—Parameterized aortic geometry is demonstrated in Figure 1. Models of the aorta with and without longitudinal pre-stretch were constructed for each of the six age groups using age group-specific geometries (Table 1). Aortic geometry without internal pressure or longitudinal pre-stretch was constructed first using an annular cross-section lofted along the aortic centerline. Thickness varied linearly along the length of the aorta from 110% (proximal) to 90% (distal) of the average value presented in Table 1. All distances along the centerline were scaled with the inverse of the aortic pre-stretch λ_z^{aorta} for the models that included longitudinal pre-stretch. Inner aortic diameters at the proximal and distal ends of the thoracic aortic segment were iteratively changed to match the diameters measured using CTAs at end diastole of 80 mmHg (Table 1). A Python script was written to automate the process and on average 3–4 iterations were required to match diastolic aortic diameters D_{LSA} and $D_{at\ xiphoid}$ within less than 0.1 mm tolerance (maximum error of 0.6%). Please note that this approach does not account for the circumferential residual stresses present in the unloaded state. These stresses homogenize transmural stress distribution (Holzapfel and Gasser 2007; Bellini et al. 2014) in the loaded configuration, but since our analysis was based on mean aortic wall stresses, they were not included.

Hyperelastic anisotropic two-fiber HGO constitutive formulation was used to model the aorta using constitutive parameters determined from the experimental data. Aortic density was set at $\rho = 1 \text{ g/cm}^3$. Since Abaqus/Explicit cannot enforce complete incompressibility due to convergence issues, small material compressibility was introduced by modifying Eq. 3 as:

$$U = \frac{C_0}{2}(I_1 - 3) + \frac{c_1^{col}}{2c_2^{col}} \sum_{i=1,2} \left[\exp\left(c_2^{col} \langle I_4^i - 1 \rangle^2\right) - 1 \right] + \frac{1}{D} \left(\frac{J^2 - 1}{2} - \ln J \right), \quad (5)$$

where parameter $D = 2/K_0$, K_0 is initial bulk modulus, and J is the third invariant of the right Cauchy-Green tensor. Compressibility was introduced by setting the ratio of initial bulk modulus to shear modulus as K_0/C_0 1 000 (which corresponds to Poisson's ratio of 0.4995) because higher K_0/C_0 ratios had <1% effect on stress values. Linear hexahedral reduced integration elements (C3D8R) were used for meshing, and all models had 4 elements through the aortic wall thickness. Sensitivity analysis was conducted, and the aortic wall mesh density was chosen to achieve <3% error in von Mises stresses when modeling stent-graft deployment. The resulting mesh had 63k-75k elements, with larger element numbers in older, larger aortas.

Longitudinal pre-stretch was simulated by applying displacements to the proximal and distal aortic cross-sections, while the top of the aortic arch was supported by springs representing aortic arch branches. Springs that simulated BA, LCCA, and LSA were vertical, and springs that represented intercostal branches were directed radially (Figure 1). Lengths of all springs were set at 20 mm in the pre-stretched state, and in the load-free configuration were scaled down by an inverse of λ_z^{br} (eq. (1)). Displacements were then applied to each spring in the load-free configuration, stretching them to 20 mm. The aorta was loaded with pre-stretch and internal pressure at the same time that the pre-stretch was applied to the springs that represented arch branches. This changed spatial location of aortic arch branch origins, and required adjustment in the calculations of aortic arch spring displacements. Spring stiffness of the BA, LCCA, and LSA was iteratively changed to match 20 mm length at diastolic aortic pressure and pre-stretch. Stiffness of the intercostal springs was set to one-half of that of the BA, LCCA, and LSA due to their significantly smaller caliber. Diastolic pressure and pre-stretch were applied over a 0.15s interval in an explicit dynamics step using variable mass scaling. Kinetic and internal energies were monitored to ensure that kinetic energy stayed within 5% of the internal energy so that the loading remained quasi-static.

2.3.2. Model of the stent-graft—A model of a GORE C-TAG stent-graft was built in two nominal sizes: 21mm and 26mm diameter. Lengths of both devices were 10cm. The stent-grafts consisted of two parts: the superelastic Nitinol stent and the ePTFE graft. For each geometry, stent-grafts were sized based on the aortic diameter immediately distal to the LSA (Table 1, D_{dLSA}) as recommended by the manufacturer's sizing guide. A 21mm device was used for the 10–19 and 20–29 year-old aortas, and the 26mm stent-graft was used for the 30–39 and 40–49 year-old subjects.

Stent skeleton was built in Abaqus/CAE using Python scripting. Geometry of the main stent body was modeled by the following equations obtained by parameterization of the actual device:

$$z(t) = A \cdot \exp(-\lambda) \cdot \sin\left(2\pi Nt - \frac{\pi}{2}\right) + A \cdot [1 - \exp(-\lambda)] \cdot Nt$$

$$x(t) = R \cdot (2\pi t).$$
(6)

Here, A is an amplitude of the sine wave, $\lambda = 2\ln(I_1/I_2)$ where I_1 and I_2 are the longer and shorter links of the sine wave, $N = 9 - 1/50$ is the number of periods per 2π revolution angle, and R is the nominal diameter of the stent-graft. Table 3 contains geometric parameters for both devices. Circular cross-section with $r = 0.17$ mm was swept along the centerline in 2D, meshed with reduced integration 8-node elements C3D8R, and then wrapped into a 3D cylindrical pattern using *wrapMesh* plug-in of Abaqus. Two sinusoidal Z -rings were added to the ends of the main stent body producing the geometry depicted in Figure 2. Stent skeleton was modeled using a superelastic material model with parameters adopted from Kleinstreuer et al. (Kleinstreuer et al. 2008). For convenience, these properties are summarized in Table 4. Mesh sensitivity analysis was performed on an end section of the stent applying crimping loads, and mesh density was chosen to keep average maximum principal strain at <2.5% error. The resulting mesh had 142.5k – 150.6k elements depending on the stent size.

Stent-graft fabric was modeled as a 0.1mm thickness tube with an elastic modulus of $E = 5.2$ M Pa (Demanget et al. 2013), Poisson's ratio of $\nu = 0.46$, and density of $\rho = 1$ g/cm³. The graft was meshed with membrane elements M3D4R of 0.45mm mean edge length. The resulting mesh had 25k – 32.5k elements depending on the size of the device.

GORE C-TAG's stent skeleton is attached to the graft by a thin film that secures half of the stent's wave to the graft in the middle of the device, and fully encapsulates the Nitinol wire at the stent-graft ends except for a part of the proximal ring (Figure 2A). This attachment prevents the stent from sliding along the graft, while also allowing conformation of the device to tortuous aortic arch geometries. To model these features, spiral strip regions were defined on the graft surface, and a tie constraint was used between the strip and the stent as demonstrated in Figure 2B.

2.3.3. TEVAR simulation—TEVAR simulation started with the longitudinal pre-stretch and pressurization of the aorta with a diastolic pressure of 80mmHg. The stent-graft was simultaneously crimped and bent by a displacement-driven catheter to a position along the arterial centerline. During this step, the only active contact was between the stent and the catheter. The catheter was modeled using surface elements SFM3D4R with density of 7 g/cm³. The catheter was then dilated, opening the stent-graft from the center to its ends as observed with the actual GORE C-TAG device. At this point the contact between the inner aortic wall and the stent was activated. Following deployment, a mechanical equilibrium step was implemented. The entire simulation sequence is presented in Figure 3.

Variable mass scaling was used to speed up the simulation procedure, and small viscous pressure of 3 Pa was applied to the aorta during device deployment to damp the dynamic vibrations coming from the initial stent-aorta contact. All contacts used 0.2 friction coefficient, but we have also performed simulations using 1.0 friction coefficient and have

found no difference in the results. Kinetic and internal energies were monitored to ensure that kinetic energy stayed within 5–10% of the internal energy and the loading remained quasi-static.

2.3.4. Endpoints—For consistency with other studies investigating aorta-stent-graft interactions (Li et al. 2005; Ma et al. 2018), aortic models were compared in terms of intramural von Mises stresses. While von Mises stress is usually used to evaluate yielding of ductile materials, here it was used in a different context – as a mere combination of Cauchy stresses that characterizes the overall “gross stress response” of the tissue. Mean stresses were computed for the entire aorta with the exclusion of the deformable elements closest to the spring attachments. In aortas after TEVAR, mean stresses were evaluated in the aortic wall behind the stent-graft, while stress distributions were obtained for the entire model. Pearson correlation coefficient r was used to assess the strength of linear relation between continuous variables, with values closer to ± 1 demonstrating stronger relations. Statistical significance of the observed correlations was assessed by testing the hypothesis of no correlation against the alternative hypothesis of nonzero correlation using the *corr* function of MATLAB. A value of $p < 0.05$ was considered statistically significant.

3. RESULTS

3.1. Constitutive parameters for the aortic wall

Equibiaxial experimental curves and HGO model fits for human descending thoracic aortas of different ages are presented in Figure 4. Aortas stiffened with age both longitudinally and circumferentially, but longitudinal stiffening occurred faster than circumferential.

Anisotropy of the specimens increased with age, and older thoracic aortas tended to be more compliant circumferentially than longitudinally under equibiaxial loading. HGO constitutive parameters for the 6 tested aortas along with the R^2 values for the fits are summarized in table 5.

3.2. Effect of age and longitudinal pre-stretch on intramural stress distribution

Distribution of von Mises stresses at end diastole (80 mmHg) in aortas of different ages is demonstrated in Figure 5. The top row represents models without longitudinal pre-stretch, while pre-stretched aortas are presented in the bottom row. Figure 6 illustrates mean intramural stresses in the aorta and error bars represent one standard deviation. In aortas without pre-stretch, intramural stresses did not change significantly with age ($p=0.09$) ranging 83–60 kPa and fluctuating around 67 kPa. In aortas with pre-stretch, mean intramural stresses were higher in younger subjects but gradually decreased with age ($r=-0.85$, $p=0.03$). In the youngest age group, incorporation of longitudinal pre-stretch increased mean stresses by 30%. The difference between pre-stretched and non-pre-stretched aortas decreased with age, and was less than 2% for subjects older than 40 years. In young aortas, high stresses localized primarily around the arch branch origins, but in older subjects stress distribution became significantly more uniform.

3.3. Effect of age and longitudinal pre-stretch on TEVAR

Due to significantly reduced pre-stretch in >50 year-old subjects, differences in intramural stresses between longitudinally pre-stretched and non-pre-stretched aortas were negligible (Figure 5 and Figure 6), and therefore TEVAR simulations were performed only for the 4 youngest age groups. Figure 7 illustrates von Mises stress distributions after TEVAR for aortas without (top) and with (bottom) longitudinal pre-stretch, and Figure 9 illustrates von Mises stresses in the stent skeleton and graft fabric. Figure 8 shows the change of mean intramural stresses in the stent-grafted aorta with age. Longitudinal pre-stretch had both qualitative and quantitative effects on intramural aortic stresses after TEVAR. Locally high stresses moved proximally after inclusion of longitudinal pre-stretch and became 49% higher compared with the non-pre-stretched case. Differences between the pre-stretched and the non-pre-stretched aortas decreased with age as longitudinal pre-stretch reduced. For the 40–50 year-old group, pre-stretch increased mean intramural stresses only by 7%. Stresses in the stent-graft (Figure 9) were also 40% and 12.5% higher in the stent and in the fabric, respectively, when the aortic pre-stretch was taken into account. Stresses in the stent and fabric ranged 68–112 MPa and 1.2–1.3MPa when the aorta was pre-stretched, and 47–93 MPa and 1.1–1.2MPa when it was not ($p<0.01$), with higher values observed in older aortic models. High stresses were concentrated in stent apexes and proximal and distal ends of the fabric, particularly at the outer part of the aortic arch curvature.

Compared with the aortas without TEVAR, implantation of a GORE C-TAG stent-graft increased mean intramural stresses in the repaired segment by 73 ± 15 kPa, which was consistent for all 4 age groups. In aortas without pre-stretch, mean stress increase associated with TEVAR was 48 ± 10 kPa.

4. DISCUSSION

Computational simulations of aorta-device interaction can help evaluate existing stent-grafts and inform the development of new endovascular devices. The *in silico* approach is particularly useful for parametric and long-term device assessments that are difficult and expensive to perform in humans or large animals. In addition, computational modeling allows to determine mechanical stresses that result from the interaction of the device with the aortic wall. These stresses cannot be directly measured, but are thought to play paramount roles in clinical complications after endovascular aortic repair which include endoleaks(Figueroa et al. 2009; Prasad et al. 2011), device migration(Li et al. 2005; Fung et al. 2008; Figueroa et al. 2009), stent-graft-induced new entry tears(Burdess et al. 2018; Ma et al. 2018; Canaud et al. 2019; Hughes 2019), device collapse and bird-beak configuration(Pasta et al. 2013; Rinaudo et al. 2015; Pasta et al. 2016), and mechanical device failure(Bussmann et al. 2017).

Computational modeling of endovascular aortic repair has advanced significantly, and now includes patient-specific aortic geometries(Perrin et al. 2015a; Cuomo et al. 2017; Ma et al. 2018; Romarowski et al. 2018), *in vivo*-determined boundary conditions(Cuomo et al. 2017; Romarowski et al. 2018), and detailed stent-graft models(Demanget et al. 2012; Demanget et al. 2013; Perrin et al. 2015a; Perrin et al. 2015b). However, most simulations focus on endovascular repair of aortic aneurysms or dissections in older subjects with stiff aortas and

rarely investigate trauma TEVAR in younger patients. Young aortas are significantly more compliant, and have substantial longitudinal pre-stretch (Horny et al. 2013; Horny et al. 2016), that to the best of our knowledge, has not yet been incorporated into the 3D computational models of the aortic arch repaired with TEVAR. Our data demonstrate that inclusion of longitudinal pre-stretch has significant quantitative and qualitative effects on aortic stress-strain state before and after TEVAR, and needs to be taken into account when modeling aortas younger than 50 years old. In addition, the pulling effect of longitudinal pre-stretch may affect stresses and strains in the stent-graft, and contribute to tighter aortic arch angulations that are more typically seen in younger patients (Kamenskiy et al. 2015). In combination with smaller aortic diameters and higher pulsatility, this may predispose younger aortas to higher degree of stent-graft malapposition along the lesser arch curvature also known as the “bird-beak” protrusion (Muhs et al. 2007; Jonker et al. 2010; Rinaudo et al. 2015; Pasta et al. 2016). Stent-graft “bird-beaking” is considered to be one of the factors contributing to an increased probability of device collapse, and incorporation of longitudinal pre-stretch into computational models investigating this phenomena (Pasta et al. 2013) may help improve their fidelity.

Longitudinal pre-stretch plays a fundamental role in vascular pathophysiology (Humphrey et al. 2009). It is thought to be determined by the pre-stretched elastic fibers and lamellae sheets in the aortic wall that are produced and organized primarily during the perinatal period, mature early in life, and stretch substantially as aorta grows in size and length (Mithieux and Weiss 2005; Cocciolone et al. 2018). Since elastic lamellae in human aortas are organized in sheets that run both circumferentially and longitudinally (Kamenskiy et al. 2014b), young aortas have smaller diameters (Kamenskiy et al. 2015) and circumferential opening angles (Saini et al. 1995), but significantly larger longitudinal pre-stretch (Horny et al. 2013) than those of older subjects. As elastic fibers and sheets degrade and fragment with age, aortic diameters widen (Kamenskiy et al. 2015), and longitudinal pre-stretch reduces (Horny et al. 2013). By the age of 45 years, diameter of the thoracic descending aorta immediately distal to the left subclavian artery increases by 18% compared with the 15-year-old aorta (Kamenskiy et al. 2015), and the longitudinal pre-stretch drops 3-fold to 1.14 (Horny et al. 2013). By the age of 65 years, diameter increases by 40% compared with the 15-year-old aorta, and the longitudinal pre-stretch drops 7-fold to 1.06.

In addition to widening and elongation due to reduction in *in situ* longitudinal pre-stretch, aortas also thicken (V.K. Goyal 1982) and stiffen (Learoyd and Taylor 1966; Haskett et al. 2010; Herrera et al. 2010; Kamenskiy et al. 2014b) with age, producing a complex stress-strain state. Our results demonstrate that when longitudinal pre-stretch is not taken into account, changes in aortic morphology balance increase in stiffness and result in a relatively constant average intramural diastolic stress of 67 kPa, although a slight decrease of 3.6 kPa per decade of life was still observed. When aortas were longitudinally pre-stretched, intramural stresses decreased 8.3 kPa per decade of life and ranged 108 kPa to 60 kPa. This finding corroborates previous results reporting 63–75 kPa average intramural stress in thoracic ascending and descending aortas modeled as a straight cylinder (Rocccbianca et al. 2014), although these previous studies used a much lower longitudinal pre-stretch values for younger subjects (1.2 vs 1.42 considered here) and higher mean pressures for older anatomies. Our results demonstrating reduction in intramural stresses with age also

corroborate previous finding in human muscular arteries(Kamenskiy et al. 2017; Jadidi et al. 2019), and suggest that the aortic wall also remodels to reduce intramural stresses, perhaps in an attempt to minimize the possibility of mechanical injury that can initiate an aortic dissection. Indeed, older aortas are known to delaminate more easily, perhaps due to accumulated proteoglycans and glycosaminoglycans which increase the swelling pressure(Humphrey 2012).

Our data demonstrate that the inclusion of longitudinal pre-stretch qualitatively changed the distribution of intramural stresses in the aortic wall. In aortas before TEVAR, stress concentrations localized to the outer curve of the aortic arch, primarily due to the influence of the originating aortic arch branches that are also pre-stretched. In the aorta after TEVAR, high stress concentrations were observed at both the inner and the outer curves of the aortic arch, and the former resulted from the outward force produced by the proximal end of the stent-graft. This high stress concentration area wrapped around the aortic isthmus in combination with the anatomic tethering at the ligamentum arteriosum(Schumacher et al. 2006), may contribute to the disruption of the aortic wall and initiation of the aortic dissection after TEVAR. Similar results describing high stress concentrations at the proximal end of the stent-graft in older aortas after TEVAR were recently reported by Ma et al(Ma et al. 2018), who attributed the initiation of retrograde type A aortic dissection to these high mechanical stresses.

Quantitatively, inclusion of the longitudinal pre-stretch resulted in the increase in aortic intramural stresses. In young aortas before and after TEVAR, this increase was 30% and 50%, while in 45-year-old aortas before TEVAR the increase was ~2%, and after TEVAR, ~7%. In older subjects, inclusion of longitudinal pre-stretch did not appear to have a significant effect on intramural stresses, producing an increase of <1%.

While presented methodology proposed a way to include longitudinal pre-stretch in computational models of the aorta before and after TEVAR, and results demonstrated the importance of accounting for the longitudinal pre-stretch in young and middle-aged aortas, they need to be considered in the context of study limitations. First, the aortic arch branches were approximated by springs. While computationally efficient, this approach may produce more localized stress concentrations at branch origins. To help address this issue, we have excluded the inner most layer of the aortic wall elements connected to spring attachments from the stress analysis, but a higher fidelity model with explicit tubular branch geometry may offer smoother stress fields.

The second limitation is related to the lack of hemodynamic analysis, as we have exclusively focused on the effect of pre-stretch on aortic mechanics in this study. Hemodynamic variables, particularly the wall shear stress and the stent-graft displacement forces produced by flow(Figueroa et al. 2009) may have profound effects on device mechanical and clinical performance, and may need to be investigated in combination with the longitudinal pre-stretch.

Analysis based on idealized geometry allowed its easy parametrization, but real geometries may be significantly more complex and include tortuous aortas with acute arch

angulations (Wolf et al. 2001; Sugawara et al. 2008; MacTaggart et al. 2016). These local geometric effects, along with the design of the stent-graft, may affect device apposition, which warrants further studies using patient-specific geometries and other stent-graft types. Such studies should also include a wider range of mechanical properties as biological tissues are known to have high variability, should preferably use pre-stretch values obtained for the thoracic, rather than the abdominal aorta, and include the effect of surrounding tissues and perivascular tethering (Ferruzzi et al. 2018). Finally, it is always important to remember that all computational models need to be verified and validated experimentally. Since our main goal was to introduce a new approach to simulate pre-stretch and determine the associated intramural stresses, validation of these results is not trivial and may require a combination of *ex vivo* and *in vivo* testing, and a mix of large animal models and patient clinical data. While these limitations are being addressed, the described method can be used to help determine more accurate stress distributions and stress values in young aortas before and after TEVAR. With proper validation, these values can in the future help determine the stress thresholds associated with TEVAR complications in younger subjects.

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Figure 1.

Parametric Finite Element model of the thoracic aorta before (A) and after (B) applying pressurization and longitudinal pre-stretch. Springs represent aortic arch branches and three upper intercostal branches.

Figure 2.
GORE C-TAG (A) and its finite element model (B).

Figure 3. Deployment of the GORE C-TAG stent-graft into the thoracic aorta. The device (A) is simultaneously crimped and bent into a catheter (B,C), and then released from the catheter starting from the center (D), which mimics the actual deployment procedure (E).

Figure 4.

Equibiaxial stress-stretch curves for human thoracic aortas stretched in the (A) longitudinal and (B) circumferential directions. Legend refers to specimen age. Dots represent experimental data, while solid lines are HGO model fits. Constitutive parameters are summarized in Table 5.

Figure 5.

Effect of longitudinal pre-stretch on Von Mises stress distribution in thoracic aortas of different ages. Top row illustrates aortas without longitudinal pre-stretch, while bottom row depicts pre-stretched thoracic aortas. Internal pressure is 80 mmHg.

Figure 6. Change in mean intramural stresses with age plotted for the longitudinally pre-stretched (red) and non-pre-stretched (blue) aortas. Error bars mark one standard deviation.

Figure 7.

Von Mises stress distributions in thoracic aortas of different ages after TEVAR. Top row represents aortas without pre-stretch, while bottom row depicts pre-stretched aortas. Internal pressure is 80 mmHg.

Figure 8.

Mean intramural stresses in the aorta behind the stent-graft. Red line represents pre-stretched aortas, while blue refers to non-pre-stretched aortas. Error bars mark one standard deviation.

Figure 9.

Von Mises stress distributions in the stent-graft skeleton and fabric in models of thoracic aorta from different ages. Top row represents aortas without pre-stretch, while bottom row depicts pre-stretched aortas.

Table 1.

Geometric parameters of the thoracic aorta in different age groups

Geometric parameters and pre-stretch	Age groups, years					
	10–19	20–29	30–39	40–49	50–59	60–69
R_{arch} , mm (Kamenskiy et al. 2015)	26.0	27.5	31.3	33.5	39.3	38.5
D_{dLSA} , mm (Kamenskiy et al. 2015)	18.6	19.4	22.7	21.9	25.0	26.1
$D_{at\ xiphoid}$, mm (Kamenskiy et al. 2015)	16.2	16.6	19.2	19.8	22.3	23.5
λ_z^{aorta} (Horný et al. 2013)	1.42	1.28	1.20	1.14	1.10	1.06
λ_z^{br} (Horný et al. 2016)	1.38	1.33	1.28	1.22	1.17	1.11
$L_{xiphoid-BA}$, mm (MacTaggart et al. 2016)	152.0	166.0	178.0	183.0	210.0	199.0
$L_{xiphoid-LCCA}$, mm (MacTaggart et al. 2016)	147.0	158.0	171.0	181.0	206.0	195.0
$L_{xiphoid-LSA}$, mm (MacTaggart et al. 2016)	135.0	147.0	158.0	161.0	189.0	179.0
$L_{xiphoid-center}$, mm	141.1	153.0	160.6	158.9	179.4	172.3
Aortic wall thickness, mm (V.K. Goyal 1982)	1.77	2.19	2.35	2.56	2.78	3.03

Table 2.

Subject demographics. Here BMI=body mass index, HTN=hypertension, DM=diabetes mellitus, CAD=coronary artery disease, (*) indicates past history.

Age, years	Sex	BMI	HTN	DM	Dyslipidemia	CAD	Smoking (pack years)
16	M	25.2	N	N	N	N	N (0)
24	M	25.1	N	N	N	N	Y (5)
39	M	32.1	N	N	N	N	Y (*)
49	M	27.3	N	N	N	N	Y (32)
59	M	38.5	Y	Y	N	N	Y (*)
66	F	30.5	N	N	N	N	Y (60)

Table 3.

Parameters of the GORE C-TAG stent skeleton

Size	21 mm	26 mm
Amplitude, A, mm	3.1	3.65
Longer link, l_1 , mm	7.5	9.1
Shorter link, l_2 , mm	6.65	8.05
Graft length, mm	94.9	97.6

Table 4.

Nitinol material properties used in simulations(Kleinstreuer et al. 2008)

Austenite elastic modulus E_A , MPa	51700
Austenite Poisson's ratio ν_A	0.3
Martensite elastic modulus E_M , MPa	47800
Martensite Poisson's ratio ν_M	0.3
Transformation strain ϵ^L	0.063
Start of transformation loading σ_L^S , MPa	600
End of transformation loading σ_L^E , MPa	670
Start of transformation unloading σ_U^S , MPa	288
End of transformation unloading σ_U^E , MPa	254
Start of transformation stress in compression σ_{CL}^S , MPa	900
Volumetric transformation strain ϵ_V^L	0.063
Density ρ , g/cm ³	6.5

Table 5.

HGO constitutive parameters for human thoracic aortas plotted in Figure 4.

Age, years	C_0 , kPa	C_1^{col} , kPa	C_2^{col}	γ°	R^2
16	26.2	13.7	0.23	45.81	0.97
24	32.5	8.95	1.02	50.39	0.97
39	33.7	4.15	2.89	43.21	0.97
49	30.2	7.8	3.14	51.58	0.96
59	36.3	7.55	3.74	39.99	0.96
66	31.3	5.9	5.14	43.89	0.95