Technical note

Anisotropic abdominal aortic aneurysm replicas with biaxial material characterization

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ABSTRACT

An Abdominal Aortic Aneurysm (AAA) is a permanent focal dilatation of the abdominal aorta at least 1.5 times its normal diameter. The criterion of maximum diameter is still used in clinical practice, although numerical studies have demonstrated the importance of other biomechanical factors. Numerical studies, however, must be validated experimentally before they can be clinically implemented. We have developed a methodology for manufacturing anisotropic AAA replicas with non-uniform wall thickness. Different composites were fabricated and tested, and one was selected in order to manufacture a phantom with the same properties. The composites and the phantom were characterized by biaxial tensile tests and a material model was fit to the experimental data. The experimental results were compared with data from the literature, and similar responses were obtained. The anisotropic AAA replicas with non-uniform wall thickness can be used in benchtop experiments to validate deformations obtained with numerical simulations or for pre-intervention testing of endovascular grafts. This is a significant step forward considering the importance of anisotropy in numerical simulations.

1. Introduction

An Abdominal Aortic Aneurysm (AAA) is a permanent dilatation of the abdominal aorta, and its rupture remains a significant cause of death in developed countries among men aged 65–85 [1]. In clinical practice, uncertainty still remains about the correct time to operate, but the criterion of maximum diameter is commonly accepted as a rupture prediction factor, meaning that medical doctors recommend surgical interventions when AAA diameters are greater than 55 mm [2]. When studying AAA rupture, numerical simulations via Finite Element Analysis (FEA) have proved to be very useful in indicating that this rupture criterion needs to be complemented with AAA wall stress data [3–5], meaning that factors such as geometry and biomechanics must also be considered [6,7].

In vitro experiments with AAA phantoms have been shown to be very useful in several applications [8–10]. These phantoms ranged from totally idealized geometries to real AAA geometries generally with uniform [11,12] but also with non-uniform thickness [13]. However, the anisotropy found in the AAA tissue [14–17] is an important property that was not considered in these projects. When using inverse analysis the mechanical properties are not critical [18,19], but the consideration of the anisotropy parameter plays an important role in the results of numerical simulations with a forward approach, and it must be taken into account for further studies [20–22]. Within the context of physical replicas, this consideration points to a step forward in the manufacturing of phantoms with arterial anisotropic behavior.

The purpose of the present work is to describe and apply a new methodology for manufacturing AAA replicas that display anisotropic behavior. To the best of the authors’ knowledge, this is the first time that a methodology is reported for creating arterial replicas with non-uniform wall thickness and defined anisotropy.

2. Materials and methods

2.1. Uniaxial testing of isotropic specimens

Tensile tests were carried out following ASTM D412 Type B. Specimens were manufactured via the vacuum casting technique by using the bi-components PUR SLM 7140, 7160 and 7190 at seven different mixing ratios.

Tensile tests were performed on the specimens to generate force-extension data using an INSTRON MINI 44 (Instron World-Wide, Norwood, MA) tensile test machine. Each specimen was subjected to a cross-head speed of 3.4 m/min until failure with pre-conditioning for 10 cycles to 7.5% of the gauge length. The
force-extension data from the uniaxial tests were converted to strain and Cauchy stress (Eqs. (1) and (2)).

\[
\varepsilon = \frac{\Delta l}{l_0} \quad \text{(1)}
\]

\[
\sigma = \frac{F}{A^*} \quad \text{(2)}
\]

where \(\Delta l\) is the change in specimen length at any time, \(l_0\) is the original length, \(F\) is the force required and \(A^*\) is the area at any instant (Eq. (3) assumes incompressibility).

\[
A^* = \frac{A_0 l_0}{l_0 + \Delta l} \quad \text{(3)}
\]

As the mechanical behavior of the components was quasi-linear, a trend line for each material was fitted to the data \((R^2 = 0.96 \pm 0.04)\) and stiffness was directly derived.

2.2. Biaxial testing of composite specimens

To reproduce the anisotropic behavior, various composite specimens (3 mm-thick 25 x 25 mm\(^2\)) were fabricated, altering the following properties:

- \(f\), proportion of fibers i.e. fiber volume/total volume ratio.
- \(E_m\), matrix elastic modulus.
- \(E_f\), fiber elastic modulus.

Variations of \(f\), \(E_m\) and \(E_f\) were tested and the composite combination with the properties closest to AAA tissue was selected. As these properties were compared with Vande Geest’s data [16], the specimens’ geometries were the same, i.e. squares.

The procedure for obtaining the specimens with fibers inside them was as follows. The specimen was modeled using CREO 2.0 and printed with an OBJET EDEN 330 Additive Manufacturing (AM) printer. The specimen was used as a model for creating a silicone mold that defined the external shape of the specimen (Fig. 1a). The fibers were then attached to the mold (Fig. 1c), the PUR resin was poured to fill the mold, and when cured the silicone mold was opened and the specimen removed (Fig. 1d).

Tests on each specimen were conducted using a custom-made planar biaxial testing system (Fig. 2) similar to the one described by Raghavan et al. [23]. Each sample was loaded with the help of sixteen hooks (four at each side) that were connected to sixteen containers able to hold weights. The load at each point was controlled by gradually placing weights into the containers. Four loading scenarios (240 g, 480 g, 720 g and 960 g) were considered. The strain measurement was calculated through the binocular stereovision technique. Four small markers forming a 5 x 5 mm\(^2\) were placed in the center of the testing specimen for optical tracking. This technique allows the markers’ 3D coordinates to be computed by triangulation from a pair of images, which were captured by a pair of Logitech QuickCam E3500 webcams (resolution ~0.03 mm/pixel) mounted at the top of the device. Before running the biaxial tensile tests, the cameras were calibrated with an opensource code in MATLAB (Mathworks, Natick, MA, USA) language to ensure accuracy [24]. To inspect the stereovision system’s accuracy, the same template used for the calibration was recorded in 6 different positions. For each position, 8 measurements were taken in different directions. The known distances were compared to the ones calculated via stereovision and the errors were calculated as a percentage:

\[
e(\%) = \frac{|RD - MD|}{RD} \quad \text{(4)}
\]

where \(e\) is the error, RD is the real distance between selected points and MD is the distance measured by the stereovision system. The average error (SD) of the stereovision system was equal to 0.58% (0.37%), i.e. a maximum error of 48 \(\mu\)m for 5 mm lengths (distance between markers).

Sample thickness was measured several times with a digital caliper before testing, and the average thickness was used in subsequent stress calculations. The specimen was tested using a stress-controlled protocol, where the first Piola–Kirchhoff stresses (i.e. the engineering stresses) served as a measure. The non-zero components of the first Piola–Kirchhoff stress tensor \(P\) have the form:

\[
P_{00} = f_0/TX_0, \quad P_{11} = f_1/TX_0
\]

where \(f_0\) and \(f_1\) denote the forces in each direction, \(T\) the thickness in the unloaded configuration, and \(X_0\) and \(X_1\) the dimensions between the hooks along the circumferential and longitudinal directions of the square specimen, i.e. 20 mm. Each biaxial specimen was tested in the following order: \(P_{00}:P_{11} = 1:1, 0.75:1, 1.075, 0.5:1, 1.05, 1.1\), keeping the ratio \(P_{00}:P_{11}\) constant for each protocol. The last equibiaxial tension protocol (i.e., \(P_{00}:P_{11} = 1:1\)) was performed to confirm that no structural damage occurred in the specimen. Each specimen was preconditioned through six loading and unloading cycles, and the seventh cycle was used for the subsequent analysis.

From the recorded marker positions, deformation gradient tensor \(F\) was calculated at each measured value of imposed load [25]. Green strain tensor \(E\) was calculated as denoted in Eq. (6). The shear components of deformation gradient tensor \(F\) were found to
be negligible, so the in-plane Green strain tensor components were determined with Eq. (7)
\[ E = \frac{1}{2}(\mathbf{F}^T \mathbf{F} - 1) \]  
(6)
\[ E_{\theta \theta} = \frac{1}{2}(\lambda_2^2 - 1), \quad E_{LL} = \frac{1}{2}(\lambda_1^2 - 1) \]  
(7)
with \( \lambda_2 \) and \( \lambda_1 \) denoting the stretches in both directions.

**Constitutive modeling**

To model the mechanical response of the materials tested, we used strain energy function \( W \) (Eq. (8)), developed by Choi and Vito [26] and used by Vande Geest et al. [16] for both aneurysmal and non-aneurysmal abdominal aortic tissue:
\[ W = b_0(e^{\theta_1/2}b_{\theta \theta} + e^{\theta_2/2}b_{LL} + e^{\theta_3/2}b_{F_{\theta \theta}} - 3) \]  
(8)
where \( b_0, b_1, b_2 \) and \( b_3 \) are the material coefficients to be determined.

From Eq. (8) the in-plane second Piola–Kirchhoff stresses (Eqs. (10) and (11)) can be determined, applying Eq. (9).
\[ S = \frac{\partial W}{\partial E} \]  
(9)
\[ S_{\theta \theta} = b_0(b_1E_{\theta \theta}e^{\theta_1/2} + b_2E_{LL}e^{\theta_2/2} + b_3E_{F_{\theta \theta}}e^{\theta_3/2}) \]  
(10)
\[ S_{LL} = b_0(b_1E_{LL}e^{\theta_1/2} + b_2E_{\theta \theta}e^{\theta_2/2} + b_3E_{F_{\theta \theta}}e^{\theta_3/2}) \]  
(11)

The data from the five biaxial protocols \( P_{\theta \theta}:P_{LL} = 1:1, 0.75:1, 1:0.75, 0.5:1, 1:0.5 \) for each specimen were fitted to this model and the material coefficients were derived for individual samples. In order to derive a single constitutive model, data from each protocol was averaged to obtain a single dataset of the composite.

Additionally, the anisotropy parameter [16,26]:
\[ AI = \sqrt{b_1/b_2} \]  
(12)
was calculated.

### 2.3. Anisotropic AAA phantom

The above process for creating anisotropic specimens was used to manufacture an anisotropic AAA replica. Once the fiber volume fraction \( (f) \) is defined, the dimensions of the fibers need to be calculated. Due to the non-uniformity of the AAA wall thickness, the fiber dimensions should be variable in order to achieve the desired \( f \) along the whole AAA phantom. To that end the following process was followed using MAGICCS v16.02 (Materialise, Leuven, Belgium). The AAA geometry was cut using nine planes normal to the longitudinal direction and spaced 10 mm apart. As a result, 8 different cylindrical slices with non-uniform thickness were obtained. Then each slice was divided into eight parts, and for each part the average thickness was measured. Finally the appropriate fiber dimensions for each slice were designed by considering the selected value of \( f \).

Using these fibers, the process for creating the phantom was based on a previous work that describes how to build isotropic AAAs from medical images [13]. The patient-specific AAA geometry was obtained by segmenting CT images from Allegheny General Hospital (Pittsburgh, PA) using in-house software (AAYASC, University of Texas at San Antonio, San Antonio, TX) capable of identifying the boundaries of the lumen and the inner and outer wall surfaces [27,28]. Based on this virtual geometry, a rigid physical replica was created using an OBJET EDEN 330 AM printer. The printed artery was used as a model to create an outer silicone mold that defined the external shape of the artery and an inner wax mold that defined its internal geometry. The wax mold was placed inside the silicone mold, and the PUR 7140, 7160 or 7190 was poured to fill the gap between the inner and outer molds with the help of a MCP 4/01 vacuum casting machine. When the gap was filled, the vacuum was released and the mold was placed in an oven at 45 °C to cure the resin. After 24 h of curing, the oven temperature was increased to 85 °C to melt the inner wax. At the end of the melting process the silicone mold was opened and the rubber-like artery removed.

To manufacture the anisotropic AAA, the abovementioned procedure was slightly modified to add the fibers into the AAA prior to the vacuum casting process with PUR resin. Each fiber was attached to the external surface of the wax mold by gluing its two ends with cyanacrylate glue, i.e. Superglue 3 (Loctite, Düsseldorf, Germany). Each fiber was fixed along the circumferential direction (Fig. 3). Next, the wax mold with its fibers was placed inside the silicone mold and the process mentioned above was subsequently followed.

The AAA phantom was created with the same properties as the tested composite. From this phantom, two square specimens were cut for subsequent biaxial analysis. Before the tensile tests, sample thickness was averaged by measuring it ten times with a digital caliper. The same protocol was followed for the biaxial analysis.

### 3. Results

#### 3.1. Uniaxial testing of isotropic specimens

A total of 42 specimens were uniaxially tested, six per material. Table 1 shows the average stiffness of each component, together with 95% confidence intervals. The stress–strain curves and the ultimate tensile strength of the materials are included in the Supplementary material.

#### 3.2. Biaxial testing of composite specimens

Considering the results of the uniaxial and biaxial tests (listed in the Supplementary material), six composite specimens with the following parameters were fabricated and biaxially tested: \( f = 0.15, \quad E_m = 0.54 \text{MPa (Component 7)} \) and \( E_f = 1.64 \text{MPa (Component 5)} \). The choice of this composite was made by comparing the overall stiffness and the grade of anisotropy between the AAA tissue [16] and the different composites.

For all tested specimens, the results from the first and last equibiaxial protocol coincided and thus suggested that no structural damage of the tissue occurred as a result of testing. The circumferential and longitudinal experimental results for all the specimens are shown in Tables 2 and 3, respectively. The experimental data was averaged for this composite, and the representative \( \mathbf{S–E} \) plots are displayed in Fig. 4.

In addition, the ratio between the maximum Green strain in the longitudinal and the circumferential \( (E_{LL,\max}/E_{\theta \theta,\max}) \) directions was calculated with an average (SD) equal to 1.77 (0.50). These values are also shown in Table 4.

#### 3.3. Mathematical model of composite and phantom specimens

The material parameters for the composite specimens are reported in Table 4 and shown graphically in Fig. 4. As Fig. 4 illustrates, the material model fit very well to the average composite data \( (R^2 = 0.98) \); it also fits the individual composite specimens \( (R^2 = 0.96) \) and AAA phantom specimens \( (R^2 = 0.96) \) (Table 4).

As a measure of overall stiffness, the strain energy at an equibiaxial nominal stress of 60 kPa was also calculated for each specimen and is reported in Table 4 together with the anisotropy factor \( AI \).

The results derived from the AAA phantom specimens were similar and the model is shown in Fig. 4, with the corresponding
Fig. 3. PUR fibers attached to the wax inner mold (left) and as a part of the final anisotropic AAA physical replica (right).

Table 1
Stiffness average and stiffness extreme values (confidence interval 95%) of the seven components.

<table>
<thead>
<tr>
<th>#</th>
<th>Component</th>
<th>SLM material</th>
<th>A:B mixing ratio</th>
<th>Stiffness mean [MPa] (95% C.I. n = 6)</th>
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<td>100:92</td>
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<td>12.37 (11.50, 13.24)</td>
</tr>
<tr>
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<td>7190</td>
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<td>6.65 (5.81, 7.49)</td>
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<tr>
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</tr>
<tr>
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<td>7160</td>
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</tr>
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</tr>
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Table 2
Nominal Stress–stretch response of specimens in the circumferential direction.

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<th>Aver. stretch</th>
<th>SD</th>
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Table 3
Nominal Stress–stretch response of specimens in the longitudinal direction.

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<th>Aver. stretch</th>
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Fig. 4. S–E plots of the composite average (top) and phantom specimen experimental data with the corresponding material model for the circumferential (left) and longitudinal (right) direction.
material coefficients illustrated in Table 4. The differences in AI, $E_{LL,max}/E_{0,0,max}$ and W between the composite specimens and AAA phantom specimens are not statistically significant, with p-values equal to 0.871, 0.764 and 0.053, respectively.

4. Discussion and conclusions

The present work describes a methodology for manufacturing patient-specific replicas of arteries with regionally varying wall thickness and an overall anisotropic behavior. By varying the composite parameters ($f, E_m$ and $E_f$), different mechanical properties can be obtained for the AAA phantoms. It should be noted that the fibers employed in this study are not intended to imitate the wavy and dispersed distribution of collagen fibers nor their thickness (0.8–2.4 μm); that cannot be achieved even with a 3D printer. The purpose of including the fibers was to provide the AAA phantom with anisotropic behavior at a macro scale, which was verified by the experiments.

Two simplifications were made in this study. The first one was the omission of the thrombus and calcifications, present in 75% of AAAs [29,30], as they are beyond the scope of this study. However, the inclusion of the thrombus in idealized AAA replicas was studied by Corbett et al. [31] and could be implemented in this methodology in an analogous way. The second simplification was that we treated AAA tissue behavior as being quasi linear, while several studies [16,17,32] have revealed the nonlinear behavior of AAA tissue. However, the stress–strain curves reported in those studies were obtained under a zero-stress condition, neglecting the fact that in vivo tissue is exposed to a stressed configuration [33]. The residual strain [34] when tissue is excised was not contemplated either. Thus considering these factors, we believe that a realistic AAA replica should mimic the second region of the curve, which is why the material properties of the manufactured phantoms were contrasted with that region. Furthermore, small strain ranges in a hyperelastic material can be considered linear since the physiological strain ranges due to the pulsatile hemodynamics are small; therefore mimicking the anisotropic range linearly is a good first approach. In order to compare the grade of anisotropy in the AAA tissue [16] and our composites, two parameters were selected: AI and the mean peak Green strain ratio ($E_{LL,max}/E_{0,0,max}$).

As a measure of overall stiffness, the strain energy at an equibiaxial nominal stress of 60 kPa ($W_{60}$) was also compared. As mentioned above, in vivo the realistic material properties correspond to the linear region of the stress–strain curves (we considered it to be above 10 kPa). Hence, in order to estimate $W_{60}$ from Vande Geest’s data, we used Eq. (13).

$$W_{60} = (W_{70} - W_{10}) - \sum_{i=0}^{10} \left( S_i p_{10}\left( E_{i,0,10} - E_{i,0,10} \right) \right)$$

The differences between the AAA samples and our data are small (Table 5).

Comparing our tested composite with Vande Geest’s data, the derived differences are relatively low (Table 5) and acceptable, with a maximum difference equal to 26.40% in the $W_{60}$ parameter. The differences in the factors measuring the grade of anisotropy are lower than 10%. As the manufactured AAA phantom has the patient-specific geometry and non-uniform wall thickness, it is not surprising that the difference between the composite and the AAA replica specimens exists because the experiments were not carried out under the same conditions. That is, while the composite specimens were completely planar and had a uniform thickness, the AAA phantom specimens were not perfectly planar due to curvature, and the thickness varied due to the patient-specific AAA geometry. Both factors influenced the experimental results. Another influential factor is the thickness error of the phantom due to the manufacture process (average dimensional mismatch of 180 microns, 11.4% [13]), which changes the proportion of the fibers and thus the mechanical properties. This is why the main difference between the phantom and composite specimens ($p = 0.053$) is factor $W_{60}$, with an average difference equal to 40.51%. However, AI index and Green strain ratio do not differ significantly between the phantom and composite specimens ($p = 0.871$ and $p = 0.764$), with differences lower than 7%. Apart from the composite shown in this study, other composites have been tested and some of them are shown in Fig. 5 with the corresponding composite parameters, material model, AI and W values. It is worth noting that before the tensile tests, the specimens’ thickness was measured by a digital caliper due to its simplicity, although it is not devoid of measuring errors and a thickness gauge would be a more accurate system [35]. The influence of fiber diameter was also studied by manufacturing two specimens with the same composite parameters but a different number of fibers (2 and 3). They were biaxially tested and similar results were obtained, indicating that fiber diameter is not as critical as the other composite parameters. The results are included in the Supplementary material.
It must be noted that 3D printing is a promising alternative technology, and the considerable evolution over the last decade now makes multi-material 3D printing possible. However, the initial investment for 3D printers is high ($120,000), as is the case for printing flexible materials (approximately 300S/kg). Recently, Cloonan et al. [36] used this technology to manufacture AAAs with a flexible material. The development of the multi-material technology may allow anisotropic AAA phantoms to be printed, but to the authors’ knowledge it has not been done yet, possibly due to the considerable effort and difficulties required to design the application and set process parameters. The limitation in raw materials for 3D printing is another drawback, which means there is a relatively low variety in the mechanical properties of printed AAAs. Other factors that may affect mechanical properties of the resulting AAAs are layering and multiple interfaces, which can cause imperfections in the phantom.

This study represents a step forward in manufacturing more realistic AAA models, presenting the development and application of a novel methodology for making AAA replicas with patient-specific, regionally varying non-uniform wall thickness and anisotropic material properties. However, one limitation should be noted: the anisotropy attained in the AAA models is global, not local. This drawback could be attenuated by increasing the number of fibers and reducing their size, but even using micro fibers would not result in a complete realistic in-vivo local anisotropy. Despite this limitation, the global anisotropy yielded a more realistic behavior of patient-specific AAA phantoms, which will have a positive impact on various clinical applications such as:

- The validation of numerical studies, medical image-based models and inverse characterization methods.
- In vitro experiments (as an alternative to computational modeling) for studying overall aneurysm mechanics coupled with blood flow dynamics or for predicting rupture risk.
- Pre-clinical testing of endovascular grafts where more realistic in vitro models are needed.
- Benchtop testing of endovascular grafts for the detection of type III endoleaks.
- Experimental assessment of new or existing designs of catheter devices in terms of trackability forces, the rigidity of catheter guides, and the deployment of stent grafts.

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Supplementary materials
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References


