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Characteristics of thoracic aortic aneurysm rupture *in vitro*

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ABSTRACT

Ascending thoracic aortic aneurysms (ATAAs) are focal dilatations in the aorta that are prone to rupture or dissection. To accurately evaluate the rupture risk, one must know the local mechanical conditions at the rupture site and understand how rupture is triggered in a layered fibrous media. A challenge facing experimental studies of ATAA rupture is that the ATAA tissue is highly heterogeneous; experimental protocols that operate under the premise of tissue homogeneity will have difficulty delineating the location conditions. In this work, we employed a previously established pointwise identification method to characterize wall stress, strain, and property distributions to a sub-millimeter resolution. Based on the acquired field data, we obtained the local mechanical properties at the rupture site in nine ATAA tissue samples. The rupture stress, ultimate strain, energy density, and the toughness of the tested samples were also reported. Our results show that the direction of the rupture is aligned with the direction of maximum stiffness, indicating that higher stiffness is not always related to higher strength. It was also found that the rupture generally occurs at a location of highest stored energy. As a higher stiffness and higher strain energy indicate a larger recruitment of collagen fibers in the tissue at the location and along the direction of rupture, the recruitment of collagen fibers in the deformation of the tissue is probably essential in ATAA rupture.

Statement of Significance

A major challenge in the experimental study of aneurysm properties is that the tissues are heterogeneous. When the specimens are not reasonably homogeneous, traditional tests that work under the premise of tissue homogeneity cannot reliably delineate the local conditions at the rupture site. In this work, we investigated the local characteristics of rupture of human ascending aortic aneurysm tissue. We identified the stress, strain, and elastic properties to a submillimeter resolution. Based on the field values, we determined the local conditions – elastic properties, direction of maximum stiffness, stress, strain, energy consumption – at the rupture site. It was found that the tissues consistently cleave in the direction of the maximum stiffness, and generally occurs at the location of highest energy. Since a higher stiffness and higher strain energy indicate a larger recruitment of collagen fibers in the tissue at the location and along the direction of rupture, the work suggests that the recruitment of collagen fibers in the deformation of the tissue is probably essential in aneurysm rupture.

1. Introduction

Ascending thoracic aortic aneurysms are focal dilatations of the aortic wall [6,11]. They may grow silently or may suddenly rupture or dissect, causing life-threatening internal bleeding. Studies have shown that the likelihood of rupture or dissection is greater than 30% when an aneurysm's diameter exceeds 6.0 cm [11]. The mortality rate of ruptured thoracic aortic aneurysms is nearly 100% [6,17]. Currently surgical intervention is indicated when the diameter of ATAAs is greater than 5.5 cm [4]. While size is a common criterion, there is a need for identifying better indicators

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in monitoring and evaluating ATAAs. From the standpoint of biomechanics, rupture propensity hinges on local mechanical conditions and micromechanical events leading to fracture initiation. However, our current knowledge on these subjects remains poor.

Several studies have investigated the mechanical properties, including rupture strength, of ATAA tissues. Vorp et al. [34], Iliopoulos et al. [16], Choudhury et al. [5] and Khanafer et al. [19] measured the tensile properties using uni-axial tensile tests. They examined the regional and directional differences using specimens harvested from different locations and orientations, and reported moderate to significant differences in both stiffness and strength. Okamoto et al. [24], Matsumoto et al. [23], Azadani et al. [1] and Pham et al. [25] investigated the bi-axial properties using bi-axial tension tests. They also reported regional and directional properties, and compared the properties of ATAAs caused by various diseases [23] or of different age groups [24]. Martin et al. [22] developed a predictive model to assess the *in vivo* rupture risk of ATAAs based on the measured strength and estimated wall stress. Sugita et al. [31] used an inflation test to measure the bi-biaxial properties, and reported a strong correlation between strength and a characteristic stiffness modulus [30]. On the related subject of abdominal aortic aneurysm (AAA) strength, Vorp's group [28,33] measured the tensile strength of AAA tissues. Vande Geest et al. [32] developed a statistical model for estimating the distribution of AAA wall strength considering aneurysm size, local diameter, and local intraluminal thrombus thickness as well patient's age, gender, family history of AAA, smoking status. Regional variability of AAA tensile strength was reported in AAAs [27]. It was found that the strength of specimen strips at or close to rupture sites was mostly low.

One of the challenges in the experimental study of ATAA properties is that the ATAA tissues are heterogeneous. ATAAs undergo continuous remodeling, and the properties are modulated by the local cellular activities underneath the pathological development [2,18]. Recent studies [7,8] by the authors indicated that there is a significant level of heterogeneity in ATAA samples of centimeter dimension, a typical size used in the aforementioned mechanical tests. When the material is not reasonably homogeneous, these tests no longer generate a uniform stress field in the center region of specimen. Thus, the measured stress and strain, which are homogenized values, may not truly reflect the local values at the rupture site. For this and other reasons, it is not surprising that conflicting results were reported on the regional and directional stiffness and strength. In this regard, a fundamental limitation of the previous studies is the underlying assumption of tissue homogeneity. The assumption may be appropriate for estimating the global elastic properties, but not the local rupture conditions.

Motivated by the need of delineating the local conditions, our laboratories have developed a method that can identify the tissue properties to a sub-millimeter resolution [7,8]. This method integrated Digital Image Correlation (DIC), inflation test and an inverse stress analysis methodology [21], enabling the identification of full-field stress, strain and mechanical properties without being limited by the complexity of the tissue heterogeneity. In a parallel study along the same line, a different analysis approach was employed [29]. We have characterized the heterogeneous anisotropic properties of ten ATAA samples [8]. The peak tension was also determined in all these tests. The availability of the field data enabled the investigation of the local conditions at the rupture sites and the exploration of possible link between elastic properties and rupture. In this paper, we report these findings.

2. Methods

2.1. Experiment

Nine ATAA sections were collected from seven patients undergoing elective surgery to replace their ATAA with a graft in accordance with a protocol approved by the Institutional Review Board of the University Hospital Center of St. Étienne and then tested according to our previously developed protocol for identifying the pointwise distribution of the mechanical properties of soft tissues using bulge inflation tests [7]. Patients' information is briefly summarized in Table 1.

Specimens of approximately $4 \times 4\,cm^2$ cut from the excised sections were clamped to an inflation device and inflated using water at a constant rate until rupture. Images of the outer surface were recorded every 3 kPa. Three dimensional displacement of the tissue surface was extracted using a commercial DIC software, ARAMIS (GOM, v. 6.2.0). A deforming NURBS surface that corresponds through all pressure states were derived from the DIC point clouds for the center region of each specimen. The size of mesh region is approximately $2.5 \times 2.5\,cm^2$. The surface deformation tensor, **C,** and the Cauchy-Green strain, **E,** were computed from the deforming NURBS meshes. The surface tension (the resultant stress over the wall thickness) at every Gauss point was computed using the inverse method in [21], which solved the equilibrium problem directly on a deformed configuration. Having obtained the stress and strain distributions at every pressure steps, the stress-strain curves at every Gauss point were collected. The stress-strain data were then fitted to a hyperelastic constitutive equation to identify the material parameters. The theoretical underpinnings and additional details of this pointwise identification approach can be found in [13,20,35,36].

A material model was adopted from the work of Gasser, Ogden, and Holzapfel (GOH) [12,14] to describe the planar response of the ATAA tissue:

$$W = \frac{\mu_1}{2}(I_1 - \ln I_2 - 2) + \frac{\mu_2}{4\gamma}\left(e^{\gamma(I_\kappa - 1)^2} - 1\right) \quad (1)$$

The tissue is modeled as a single layer composite material consisting of a matrix and angularly distributed fibers. The first term represents the response of elastin network and ground substances, and $I_1 = \mathrm{tr}\,\mathbf{C}$ and $I_2 = \det \mathbf{C}$ are the principal invariants of the deformation tensor. The second term, which dominates the energy, represents the contribution of collagen fibers, with I_κ being an anisotropic strain invariant

$$I_\kappa = \kappa I_1 + (1 - 2\kappa)\mathbf{M} \cdot \mathbf{CM} \quad (2)$$

In obtaining this invariant the fibers are assumed symmetrically distributed with respect to two mutually perpendicular directions. The parameter κ represents the dispersion of the angular distribution. The value of κ varies from 0 to 0.5. When $\kappa = 0$ all of the collagen fibers are perfectly aligned in the direction of **M** and when

Table 1
Sample information.

Patient	Gender (M/F)	Age	Diameter (mm)	Thickness (mm)
1	M	55	55	2.35
2	F	65	49	1.82
3	F	80	52	1.68
4	M	79	52	1.76
5(a) & (b)	M	76	58	1.82
6	M	72	51	1.90
7(a)	F	76	65	2.38
7(b)	F	76	65	2.51