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The biaxial mechanical behaviour of abdominal aortic aneurysm intraluminal thrombus: Classification of morphology and the determination of layer and region specific properties

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ABSTRACT

Intraluminal thrombus (ILT) is present in 75% of clinically-relevant abdominal aortic aneurysms (AAAs) yet, despite much research effort, its role in AAA biomechanics remains unclear. The aim of this work is to further evaluate the biomechanics of ILT and determine if different ILT morphologies have varying mechanical properties.

Biaxial mechanical tests were performed on ILT samples harvested from 19 patients undergoing open surgical repair. ILT were separated into luminal, medial and medial/abluminal layers. A total of 356 tests were performed and the Cauchy stress (σ) and tangential modulus (TM) at a stretch ratio (λ) of 1.14 were recorded for each test in both the circumferential (θ) and longitudinal (L) directions.

Our data revealed three distinct types of ILT morphologies, each with a unique set of mechanical properties. All ILT layers were found to be isotropic and inhomogeneous. Type 1 ($n=10$) was a multi-layered ILT (thick medial/abluminal layer) whose strength and stiffness decreased gradually from the luminal to the medial/abluminal layer. Type 2 ($n=6$) was a multi-layered ILT (thin/highly degraded medial/abluminal layer) whose strength and stiffness decreased abruptly between the luminal and medial/abluminal layer and Type 3 ($n=3$) is a single layered ILT with a lower strength and stiffness than Types 1 and 2. In a sub-study, we found the luminal layer to be stronger and stiffer in the posterior than the anterior region.

This work provides further insights to the biomechanical behaviour of ILT and the use of our ILT classification may be useful in future studies.

1. Introduction

Abdominal aortic aneurysm (AAA) is the gradual expansion of the distal region of the aorta. The total number of people with AAA is estimated to be 1.1 million (prevalence 1.4%) between the ages of 50 and 84 years old in the United States (Kent et al., 2010). If undetected, AAAs can continue to expand until eventual rupture, with the risk of rupture for AAAs with diameter >6 cm estimated to be 10–20% (Brown et al., 2003). Rupture of AAA is a catastrophic event and accounts for 1.3% of all deaths among men aged between 65 and 85 years old and represents the 14th leading cause of death in the United States (Lederle, 2009). Prediction of AAA rupture is non-trivial and while endovascular aortic repair (EVAR) has greatly improved the standards of AAA treatment (Schermerhorn et al., 2008; Lederle et al., 2009); pre-emptive surgical intervention is still considered high risk. Current clinical risk assessment is typically based on maximum AAA diameter and growth rate. To improve rupture risk assessment, it has been hypothesised that rupture occurs when the intramural stress exceeds the strength of the AAA wall and by utilising the finite element method (FEM) it has been shown that regions of elevated

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wall stress correlate with an increased rupture risk (Maier et al., 2010; Doyle et al., 2010; Fillinger, 2007).

The prediction of AAA wall stress and hence rupture risk, is largely influenced by its material model, which is defined by its mechanical properties, and the AAA geometry. The inclusion of anisotropy has been found to increase wall stress (Vande Geest et al., 2008; Rodríguez et al., 2008, 2009), while AAA length (Rodríguez et al., 2008), degree of asymmetry (Doyle et al., 2009) and tortuosity (Pappu et al., 2008) have also been linked to an increased rupture risk. Furthermore, it has been shown that failure to compensate for the effects of preloaded geometries (CT images acquired at one instant within the cardiac cycle), may lead an overestimation of the wall stress (Raghavan et al., 2006; de Putter et al., 2007; Lu et al., 2007; Speelman et al., 2009). It is important to note that there is currently no 'gold standard' with regards to the computational modelling approach (Doyle et al., 2011), however, it is generally agreed that the intraluminal thrombus (ILT) must be included in the computational model.

ILT is a complex fibrin structure, infiltrated by a continuous network of canalculi, platelets, red blood cells and other hematopoietic cells (Adolph et al., 1997). It is located within the sac of 75% of clinically-relevant AAAs (Harter et al., 1982) yet its role in AAA rupture risk is much disputed and not entirely understood. It has been reported that the ILT allows transmittance of the entire mean arterial pressure to the AAA wall (Schurink et al., 2000) while at the same time significantly reducing the stress at the wall (Mower et al., 1997; Di Martino et al., 1998; Wang et al., 2002; Di Martino and Vorp, 2003). Thubrikar et al. (2003) proposed that although the ILT may not reduce pressure at the wall, its complex fibrous structure may reinforce the wall thus, reducing AAA strain and overall rupture risk. This hypothesis was also supported by Polzer et al. (2012) who after modelling the ILT as a poroelastic material, capable of transmitting the blood pressure to the wall, reported a reduction in the stress at the wall. Aside from ILT's role in pressure transmission, its complex biological structure is thought to be responsible for the proteolytic (Swedenborg and Eriksson, 2006; Kazi et al., 2005) and hypoxic (Vorp Lee et al., 2001) degradation of the wall, resulting in a thinner wall of diminished strength. These effects coupled with reports implicating ILT failure as a predecessor of AAA rupture (Roy et al., 2008; Polzer et al., 2011) may outweigh any potential protective benefits of the presence of the ILT structure.

It is therefore unclear whether ILT increases or decreases the rupture risk of AAA. A recent review of AAA biomechanics highlighted the lack of mechanical ILT data; '*there have been limited studies on the mechanical properties of intraluminal thrombus*' as a specific need to improve our understanding of the influence of ILT in vivo (Humphrey and Holzapfel, 2012). However, due to the recent popularity of EVAR, the opportunities to harvest and conduct mechanical tests on this tissue are becoming rare. Utilising uniaxial test methods, it was found that the failure strength and stiffness was lower than that of the AAA wall (Di Martino et al., 1998), decreased radially throughout the thickness of the ILT (Wang et al., 2001, Gasser et al., 2008), the material was isotropic (Wang et al., 2001), may be susceptible to fatigue failure (Gasser et al., 2008) and the properties may be region specific (Celi et al., 2012). Studies using biaxial tests, which are considered a better representation of the in vivo loading conditions and can investigate mechanical anisotropy, were also employed. However, there was little agreement regarding the anisotropy of the luminal layer; reported as isotropic by Vande Geest et al. (2006b) and partially anisotropic by Tong et al. (2011). Despite these findings, FE models which have been used to assess the influence of ILT on AAA wall stress, have in most cases assumed the ILT is isotropic and homogeneous (Vande Geest et al., 2008; Li et al., 2008; Georgakarakos et al., 2009; Doyle et al., 2013).

The aim of this study is to further evaluate the mechanics of different ILT morphologies utilising biaxial test methods. In particular, we aim to investigate if properties are: (a) directionally dependent and (b) homogeneous – radially (throughout its thickness) and where possible, regionally (around the circumference of the lumen).

2. Methods

2.1. Tissue specimens

This study was approved by the Hospital and University Ethics Committees and patient consent was granted. ILT was harvested, in its entirety where possible, from 19 patients undergoing open AAA repair at the HSE Midwestern Regional Hospital, Limerick. We identified three distinct types of ILT based on visual inspection of the morphology (Fig. 1).

- Type 1 ($n=10$): Multi-layered structure with a distinct luminal layer and thick underlying medial and abluminal layers.
- Type 2 ($n=6$): Multi-layered structure similar to Type 1 however; medial and abluminal layers were either very thin or highly degraded.
- Type 3 ($n=3$): Single-layered, homogenous and fluid like structure thought to be fresh or newly developed thrombi.

Upon excision, all samples were stored frozen at −20 °C until further analysis (van Dam et al., 2006; Hinnen et al., 2007; Gasser et al., 2008).

2.2. Tissue preparation

ILT samples were thawed at 4 °C overnight, allowed to equilibrate at room temperature (~20 °C) and then immersed in warm (37 °C) isotonic saline. As ILT typically encircles the lumen in vivo (Fig. 2(A)), we could easily identify the circumferential and longitudinal directions of the structure, with the longitudinal

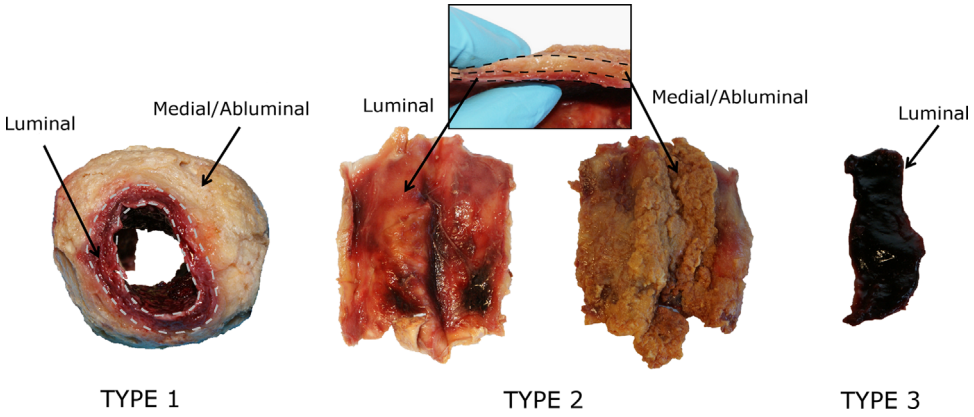

Fig. 1. Photographic images of the morphologies of ILT Types 1, 2 and 3. Type 1 has a distinct luminal layer and thick underlying medial/abluminal layers. Type 2 has a distinct luminal layer and thin/degraded underlying medial/abluminal layers. Type 3 has a single homogenous, fluid like layer.