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Variations of dissection properties and mass fractions with thrombus age in human abdominal aortic aneurysms

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ABSTRACT

Introduction: Thrombus ages, defined as four relative age phases, are related to different compositions of the intraluminal thrombus (ILT) in the abdominal aortic aneurysm (AAA) (Tong et al., 2011b). Experimental studies indicate a correlation between the relative thrombus age and the strength of the thrombus-covered wall.

Methods: On 32 AAA samples we performed peeling tests with the aim to dissect the material (i) through the ILT thickness, (ii) within the individual ILT layers and (iii) within the aneurysm wall underneath the thrombus by using two extension rates (1 mm/min, 1 mm/s). Histological investigations and mass fraction analysis were performed to characterize the dissected morphology, to determine the relative thrombus age, and to quantify dry weight percentages of elastin and collagen in the AAA wall.

Results: A remarkably lower dissection energy was needed to dissect within the individual ILT layers and through the thicknesses of old thrombi. With increasing ILT age the dissection energy of the underlying intima–media composite continuously decreased and the anisotropic dissection properties for that composite vanished. The quantified dissection properties were rate dependent for both tissue types (ILT and wall). Histology showed that single fibrin fibers or smaller protein clots within the ILT generate smooth dissected surfaces during the peeling. There was a notable decrease in mass fraction of elastin within the thrombus-covered intima–media composite with ILT age, whereas no significant change was found for that of collagen.

Conclusions: These findings suggest that intraluminal thrombus aging leads to a higher propensity of dissection for the ILT and the intima–media composite of the aneurysmal wall.

1. Introduction

An abdominal aortic aneurysm (AAA) is a vascular pathology associated with permanent and irreversible localized dilations. Rupture of an AAA is a mechanical failure of the aneurysm wall, which occurs when the peak wall stress exceeds the local strength of the aortic tissue. In order to seek a more reliable criterion for the AAA rupture assessment, the majority of recent studies have focused on the development of non-invasive methods to predict the rupture risk of patient-specific AAA models on a computational basis. Detailed information of patient-specific geometries of intraluminal thrombi (ILT) and walls, advanced anisotropic constitutive models for AAA walls and the interaction between the fluid and the structure have improved the reliability of finite element simulations to a great extent (Wang et al., 2002; Vande Geest et al., 2006b; Rissland et al., 2009; Maier et al., 2010; Xenos et al., 2010). Aneurysmal degeneration, from a pathohistological point of view, is mainly attributed to loss of elastin and collagen remodeling within the aortic wall (Dobrin et al., 1984; Carmo et al., 2002; Schriefl et al., 2012a). As a key issue, rupture locations of AAA have been identified by several studies (Golledge et al., 1999; Doyle et al., 2009, 2010) using experimental techniques and computational validations. For example, Doyle et al. (2009) reported the rupture site of a silicon rubber AAA model, i.e. at the inflection point, which is in agreement with the peak stress regions as numerically predicted. In addition to that, they continuously measured the internal rupture pressures of

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experimental AAA models manufactured by different silicon materials (Doyle et al., 2010). Another representative work in characterizing rupture sites was conducted by Raghavan et al. (2011). Based on whole ruptured AAA specimens harvested from fresh cadavers, they suggested that primary rupture sites were on the lateral quadrants and were longitudinally oriented.

Despite these new findings, understanding of the intrinsic AAA rupture mechanisms and patterns remains poor. It has long been suggested that bleeding into the ILT caused by fissures is frequently associated with AAA rupture (Mehard et al., 1994; Arita et al., 1997; Roy et al., 2008) and fissure creation is most probably a consequence of ILT dissection during the AAA expansion (Roy et al., 2008). Recently, Pasta et al. (2012) reported a set of mechanical dissection data of ascending thoracic aortic aneurysm; relevant experimental tissue data within the AAA are not yet available in the literature. Although, dissection associated with AAA is clinically rare compared with dissection of the thoracic aortic aneurysm, AAA dissection data can be used as a surrogate measure for the propensity to rupture. ILT may influence AAA remodeling, expansion, and rupture risk in addition to the AAA wall microstructure (Vorp et al., 1998, 2001; Adolph et al., 1997; Kazi et al., 2003; Holzapfel et al., 2011). Hence, there is also a need to explore how much ILT aging can potentially affect the dissection properties of aneurysmal tissues. An advanced understanding of the underlying relationships is of essential importance for gaining more insights in pathological progressions and rupture mechanisms of AAAs.

In the present study, we quantitatively assess the dissection properties of the degenerated thrombus-covered aortic tissues and the related ILTs. Since the ILT is heterogeneous (Tong et al., 2011b; Wang et al., 2001; Vande Geest et al., 2006a) we investigate the dissection properties of the three individual ILT layers (luminal, medial, and abluminal). Peeling tests (Sommer et al., 2008; Tong et al., 2011a) were performed to measure the dissection energy that is needed to propagate a dissection within the tissue. In addition, the relative thrombus age was histologically determined according to the methodology proposed in our recent study (Tong et al., 2011b), and was then correlated with the changes in the dissection properties of the ILT and the aortic wall tissue covered by the thrombus. Finally, mass fraction analyses were performed to quantify the corresponding dry weight percentages of elastin and collagen within the thrombus-covered walls and to explore their variations with the ILT age.

2. Methods

2.1. Material and specimen preparation

In total, 32 AAA samples (patients' mean age 70 ± 10 yr) consisting of ILTs and AAA walls were harvested from open surgical aneurysm repairs. Use of the material was approved by the Ethics Committee, Medical University Graz, Austria. All samples were procured from the anterior portion of the aneurysm and stored in Dulbecco's Modified Eagle's Medium (DMEM). The ILT heterogeneity has been reported by previous studies (Tong et al., 2011b; Wang et al., 2001; Vande Geest et al., 2006a), in which three individual ILT layers, i.e. luminal, medial and abluminal, were introduced.

For executing peeling tests through the ILT thickness a prismatic-shaped specimen was first cut from the thickest part of the ILT sample, as shown in Fig. 1. In addition, circumferential and longitudinal rectangular strips through the thickness of the ILT (two pieces in each direction, illustrated by the dashed lines in Fig. 1) were obtained by gently cutting them from the prismatic-shaped specimen. The lengths of the rectangular strips varied a lot due to the different thicknesses of the ILT. For the remaining part of the ILT sample, the individual layers were separated, and strips were then cut from the separated ILT layers in the circumferential and longitudinal directions, respectively (see also Fig. 1). The dimension of each rectangular strip was about 18.0×6.0 mm^2 (length $\times$ width).

Due to the size of the thrombus-covered wall specimens, two adjacent rectangular strips were cut in the circumferential and longitudinal directions, respectively (see specimens 1 and 2 in Fig. 1). Further separation was performed to remove the adventitia from the intima–media composite for each strip. Finally, we cut a small (rectangular) piece of aortic wall tissue from the remaining material as representatively shown by specimen 3 in Fig. 1, on which we performed the mass fraction analysis.

Details of the specimen preparation for the peeling test have been described in previous studies by our lab (Sommer et al., 2008; Tong et al., 2011a). In brief, each rectangular strip was given an initial cut (incision of about 2.0–3.0 mm in length)

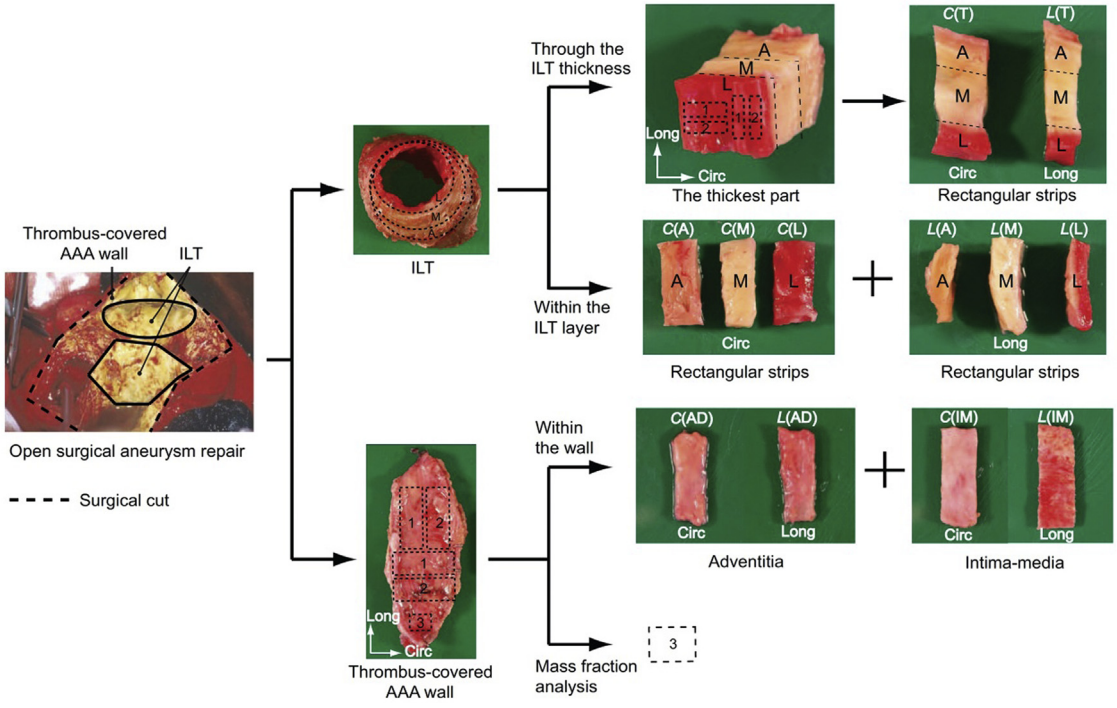

Fig. 1. Schematic illustration of specimen cutting and anatomical separation of the ILT and the thrombus-covered wall. Test samples for peeling through the ILT thickness, within the ILT layer and within the wall; one sample for mass fraction analysis. Circ and Long represent circumferential and longitudinal directions, respectively; L, M, A denote the three layers of the ILT, which are luminal (L), medial (M) and abluminal (A); the labeling of the individual samples is stated in Section 2.2.