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Correlation between age, location, orientation, loading velocity and delamination strength in the human aorta

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Abstract. Aortic dissection is a biomechanical phenomenon associated with a failure of internal cohesion, which manifests itself through the delamination of the aortic wall. The goal of this study is to deepen our knowledge of the delamination strength of the aorta. To achieve this, 661 peeling experiments were carried out with strips of the human aorta collected from 46 cadavers. The samples were ordered into groups with respect to (1) anatomical location, (2) orientation of the sample, and (3) extension rate used within the experiment. The obtained results are in accordance with the hypothesis that delamination resistance is not sensitive to the extension rates 0.1, 1, 10, and 50 mms^{-1}. We arrived at this conclusion for all positions along the aorta investigated in our study. These were the thoracic ascending (AAs), thoracic descending (ADs), and the abdominal aorta (AAb), simultaneously considering both the longitudinal (L) as well as the circumferential (C) orientations of the samples. On the other hand, our results showed that the delamination strength differs significantly with respect to the anatomical position and orientation of the sample. The medians of the delamination strength were as follows, 4.1 in AAs-L, 3.2 in AAs-C, 3.1 in ADs-L, 2.4 in ADs-C, AAb-L in 3.6, and 2.7 in AAb-C case (all values are in $0.01 \cdot Nmm^{-1}$). This suggests that resistance to crack propagation should be an anisotropic property and that the aorta is inhomogeneous along its length from the point of view of delamination resistance. Finally, correlation analysis proved that the delamination strength of the human aorta significantly decreases with age.

Keywords: Aging; Aorta; Crack; Delamination; Fracture; Strength.

1. Introduction

The aorta is the largest artery in the human body and so it is naturally a subject of great interest in the field of arterial biomechanics. It consists of the thoracic and abdominal segment, the thoracic segment being subdivided into the ascending part, the aortic arc, and the descending part. The abdominal segment consists of the suprarenal and infrarenal part. The internal structure of the aortic wall is organized into three layers, which are referred to from the inner to the outer layer as tunica intima, tunica media, and tunica adventitia (Kassab 2006). Their architecture accords with their function, which means that the tunica intima, interacting with blood, contains mechanically sensitive cells (endothelium) that can generate vasodilating molecules of NO. Endothelial cells lie on the collagenous basal lamina which adheres to the internal elastic lamina that separates the tunica intima and media (Gasser et al., 2006). The tunica media consists of so-called musculoelastic fascicles interlaced with elastic and collagenous fibers, and in a healthy artery is responsible for storing most of the elastic energy transferred to the aortic wall by pressure pulse (Clark and Glagov, 1985; Schriefl et al., 2012). On the other hand, the tunica adventitia is responsible for preventing the artery from mechanical failure and thus consists of bundles of collagenous fibers (Holzapfel et al., 2000; Amabili et al., 2021). From a biomechanical point of view, the aorta represents a layered composite structure exhibiting highly nonlinear anisotropic viscoelastic behavior which can, under certain circumstances, be effectively modeled as an elastic and homogenous body (Kassab 2006; Amabili et al., 2019a, 2019b; Franchini et al., 2021). The optimal physiological functioning of the aorta as an elastic conduit for pulsating blood is gradually compromised in aging due to its stiffening and dilation, referred to as arteriosclerosis (Brüel and Oxlund, 1996; Greenwald 2007; Persy and D'Haese, 2009; Horný et al., 2011, 2013, 2014a). The aorta is prone to developing diseases like aneurysms, putting it at risk of a rupture, atherosclerotic plaques which obstruct blood flow, and dissections (Humphrey and Holzapfel, 2012; Amabili et al., 2020a).

Aortic dissection is a life-threatening disease manifested by a tear that separates the aortic wall into two layers (Thubrikar 2007; Golledge and Eagle, 2008; Nienaber and Clough, 2015). It occurs most frequently in the thoracic part of the aorta, but it can spread along its entire length. Aortic dissection is a relatively rare disease, the incidence is typically reported as ranging from 3 to 6 cases per 100 000 per year. This, however, strongly depends on age because in the cohort of individuals aged 65 – 75 years old it reaches up to 35 cases (Golledge and Eagle, 2008; Nienaber and Clough, 2015). On the other hand, the lethality of acute dissection is indeed high. According to Olsson et al. (2006), 37% of patients who are admitted to hospital die within the next 30 days, and approximately 20% of patients die before they receive medical intervention (Mészáros et al., 2000). Besides acute aortic dissection, a chronic type of dissection may be diagnosed if the patient does not develop typical symptoms within 14 days (Erbel et al., 2001; Amabili et al., 2020).

During dissection, blood enters the wall, which causes the delamination. Further separation often leads to the creation of a new false lumen which can extend longitudinally (cf. for example Figure 2 in Amabili et al., 2020). This shows that the dissection is a biomechanical phenomenon associated with an internal cohesion of the arterial wall and that crack propagation is a basis of its mechanical manifestation. The number of studies dealing with the delamination of the arterial wall has increased significantly in the last fifteen years, which shows that questions regarding this form of damage and discontinuity have become a focus of current cardiovascular biomechanics (Sherifova and Holzapfel, 2019; Brunet et al., 2021).

From the mechanical point of view, there are two essential events in the development of the dissection disease, namely it is an onset of the dissection by means of the initial tear and the subsequent spreading of the dissection within the delamination process. Various mechanisms like injuries, excessive blood pressure elevation, stress concentration inhomogeneities, or percutaneous interventions are suspected to be the causes of the dissection initiation (Sherifova and Holzapfel, 2019; Brunet et al., 2021).

With regard to the dissection spreading, a discontinuity propagation requires internal forces to exceed the delamination resistance of the tissues. M. R. Roach and colleagues carried out experiments to simulate dissection propagation (van Baardwijk and Roach 1987; Carson and Roach 1990; Tiessen and

Roach 1993). In their experiments, which were based on pumping a pressurized liquid into the blood vessel wall, it was revealed that pressure gradient, rather than peak pressure, is correlated with the dissectioning, which is in accordance with the results of Prokop et al. (1970). It was also found that dissections propagated more easily between the elastic lamellae than across them. Arterial wall cohesion can also be studied by means of the peeling experiment that has been, within the context of arterial delamination, introduced by Sommer et al. (2008). It resembles the mode I crack opening that is well known from fracture mechanics. As indicated in Figure 1, the forces induced by clamps, which are moving apart, exert a load upon a T-shaped specimen which tears longitudinally in the delamination process, which resembles the peeling of a layered structure.

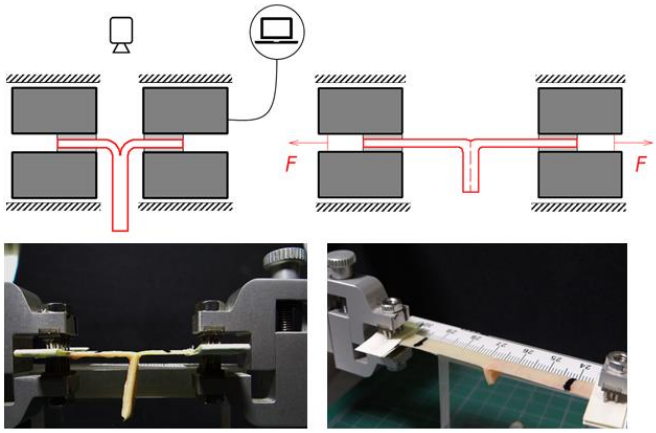

Figure 1. Peeling experiment. Upper sketches depict the arrangement of the peeling experiment in our experimental setup where the extension of the sample is recorded by videoextensometer, and loading force, *F*, is recorded into a PC. Photographs in the lower row show a sample within a real experiment.

Sommer et al. (2008) employed this technique to determine the delamination strength and the areal density of the fracture energy in the human abdominal aorta. Tong et al. (2011) used this method in a similar way in the research into human carotid bifurcations, and Pasta et al. (2012) in the investigation of aneurysms in the ascending aorta. Angouras et al. (2019) and Chung et al. (2020) also carried out delamination experiments with samples of the ascending aortic aneurysms. Tong et al. (2014) used peeling experiments in the study of the delamination properties of the abdominal aortic aneurysm thrombi. The delamination properties of the human coronary arteries were studied by Wang et al. (2014) and the same research group adapted this technique in order to measure the adhesive strength and stability of atherosclerotic plaques in a mouse model (Wang et al., 2011, 2013).

These experiments have suggested that delamination strength is a site-specific property, i.e. that the internal cohesion of the arterial wall depends on the location in the arterial tree (Tong et al., 2011). A locally varying delamination strength is also in accordance with the results yielded by studies working with animal tissues (porcine abdominal aortas in Roach and Song 1994; porcine thoracic aortas in Myneni et al., 2020). It was found that delamination resistance is anisotropic because longitudinally oriented strips usually exhibit a higher delamination force than circumferential strips (Sommer et al., 2008; Tong et al., 2011; Kozuń et al., 2016). Studies by Pasta et al. (2012), Angouras et al. (2019), Chung et al. (2020), and Kozuń et al. (2018) have, by means of the peeling experiment, shown that pathologies like ascending aortic aneurysm or atherosclerosis are associated with a decreased delamination resistance of the aorta. On the other hand, the present literature does not include any studies which have carried out peeling experiments designed to simultaneously reveal delamination anisotropy and heterogeneity in tissue obtained from the same donor. A detailed description of age-related changes of delamination strength is also lacking in the literature.

In order to fill this gap, our study yields the results of the peeling experiments carried out with samples that were obtained along the entire length of the human aorta, i.e. from the thoracic ascending (AAs), the thoracic descending (ADs), and the abdominal (AAb) part of the aorta. The results are used to document site-specific differences in the delamination strength, the anisotropy of the delamination

strength, and to show how the delamination strength correlates with age in each of these locations considering tissue anisotropy. For all of these factors, our study also shows whether extension rate plays a significant role in the determined delamination strength, and thus whether we should regard delamination strength as a rate-dependent property or not, a question which, to the best of our knowledge, has so far remained rather outside of scientific attention (Prokop et al., 1970; van Baardwijk and Roach 1987; Tong et al., 2016).

2. Materials and Methods

Specimens. Segments of human aortas were obtained during regular autopsies carried out in the Department of Forensic Medicine and Toxicology at the Regional Hospital, Liberec. The post-mortem use of human tissue in our project was approved by the Ethics Committee of the Regional Hospital, Liberec. Tubular segments of the thoracic ascending, thoracic descending, and abdominal part of the aorta were excised from a cadaver and transported to the laboratory. In all steps preceding the experiment (autopsy room, post-autopsy storage, and transport), tissues were kept in the cold (4 – 6 °C). Only cadavers with no putrefaction changes and with a known post-mortem interval (PMI) were involved as tissue donors.

In the laboratory, rectangular samples, approx. 8 x 60 mm, were cut from each aortic segment. These rectangular strips were aligned with both the longitudinal (L) and circumferential (C) direction of the vessel. Every sample was photographed in order to determine its exact width. An incision was made with a scalpel to the medial layer to create an initial separation, which was extended to approx. 3 cm in length. These arms of the T-shaped sample were used when mounting the sample to the clamps of the experimental machine. To prevent the samples from tearing in the needle-based clamps, the ends of the arms of the T-shaped samples were reinforced by gluing small pieces of sturdy paper. The mounted specimen is depicted in Fig. 1.

Testing machine, experimental protocol, and delamination strength. The method adopted to characterize the delamination properties of the aorta was the aforementioned peeling test. Figure 1 illustrates how it is arranged. The experiments were carried out with the help of the multipurpose tensile testing machine Zwick/Roell (Messphysik). Both the delamination force F (the force that is necessary to increase a tear length) and the tear length itself were recorded on a PC (at a sampling frequency of 50Hz). The delamination force was measured by HBM U9C +/- 25N (accuracy class 0.2) force transducers. The tear length was determined from the movement of the clamps, which was recorded at 1 μm resolution. This data was complemented by the recordings carried out by a built-in video-extensometer (5MPx camera IDS uEye 3.0), which measured the distance between the marks (black liquid eyeliner lines) made on the surface of the samples. In order to determine whether delamination strength depends on loading rate, the experiments were carried out with the clamps' speed set to 0.1, 1, 10, 50 mms^{-1}.

Delamination strength S_d in our study is considered as the ratio of the recorded force F to the reference width of the sample. To this end, F measured in the last 20 mm of the delamination process in each experiment was used. To obtain point-wise characteristics, the median of the recorded force was used.

Statistical methods. Standard descriptive statistics were used to characterize the collected data. Normality was checked by means of the *Shapiro-Wilk test* (*SW-test*). Comparisons which aimed to show differences in groups are graphically presented with the help of box-plots. Data arranged into groups to determine whether results support or contradict the hypotheses that the delamination strength depends (1) on location, (2) on sample orientation, and (3) on extension rate, were tested with the help of the *Kruskal-Wallis test* (*KW-test*; non-parametric equivalent of ANOVA comparing medians in groups that may not have the same dimensions and variances) which was complemented with *Dunn's test* (*D-test*) to reveal significant pairwise differences. In the case that two specific groups were compared, it was based on the *Kolmogorov-Smirnov test* (*KS-test*; a comparison of distribution functions) and the *Mann-Whitney test* (*U-test*; a comparison of medians). The correlation between age

and delamination strength was expressed by means of the Pearson correlation coefficient R and its significance was verified with the *T-test*. The linear regression model was used to capture age-related changes in S_d. Correlation analysis was also used to reveal whether the resulting data are biased by post mortem autolysis. To this end, the correlation between PMI and S_d for each data set was computed in order to exclude possible bias of the results by post mortal autolysis. Within the entire study, a significance level of $\alpha = 0.05$ was considered.

3. Results and Discussion

The results presented here cover approximately two years of data collection. During this time, 46 cadavers were utilized as tissue donors, and a total of 661 delamination experiments were carried out. In the first year of the study, only experiments at extension rate of 0.1 and 1 mms^{-1} were conducted. After the annual data evaluation, it was decided to also include experiments at 10 and 50 mms^{-1}. This decision was motivated by the uncertainty over what is a typical speed at which a dissection usually spreads along the aorta *in vivo*, and was also an attempt to extend the loading speed to magnitudes that would be closer to traumatic events, for example the sudden impacts that the human body would experience in car accidents. The second factor was a natural uncertainty associated with the unknown sensitivity of the delamination strength to the extension rate. Both are factors which contributed to our decision to extend the range of experimentally observed extension rates.

Hence, from a total number of 46 cadavers, tissues from approximately 20 of them were subjected to experiments carried out at 0.1, 1, 10, and 50 mms^{-1}, and the rest were tested at 0.1 and 1 mms^{-1}. Table 1 summarizes the ranges of data samples reached in our study. Table 2 complements the numbers of conducted experiments with descriptive statistics of the gained data. Since normality checking was inconclusive (some groups corresponded to the normal distribution but others did not), rather than an arithmetic mean and sample standard deviation, a median and lower and upper quartile are used to describe a position and a variability in the data.

Table. 1 Summary of tested specimens.

Location	Extension rate				Sum
	0.1 mms^{-1}	1 mms^{-1}	10 mms^{-1}	50 mms^{-1}	
AAs-L	33	36	20	19	108
AAs-C	33	36	20	18	107
ADs-L	44	36	21	21	122
ADs-C	46	36	21	21	124
AAb-L	31	31	17	14	93
AAb-C	34	36	19	18	107
Sum	221	211	118	111	661

AAs = ascending part of the thoracic aorta,
ADs = descending part of the thoracic aorta,
AAb = abdominal aorta,
L = strip aligned with longitudinal axis of the vessel,
C = strip aligned with circumferential axis of the vessel.

Table. 2 Summary of resulting delamination strengths. Data has the form median [minimum, lower quartile, upper quartile, maximum]. Data are in $0.01 \cdot \mathrm{Nmm^{-1}}$.

Location	Extension rate				Pooled
	0.1 $\mathrm{mms^{-1}}$	1 $\mathrm{mms^{-1}}$	10 $\mathrm{mms^{-1}}$	50 $\mathrm{mms^{-1}}$	
AAs-L	4.3 [1.8, 3.3, 5.8, 8.8]	3.8 [1.9, 3.2, 5.3, 8.1]	3.5 [2.3, 3.2, 4.8, 7.5]	4.1 [2.6, 3.2, 4.8, 7.1]	4.1 [1.8, 3.3, 5.3, 8.8]
AAs-C	3.0 [1.4, 2.2, 4.2, 6.4]	2.8 [1.6, 2.4, 4.2, 5.4]	3.4 [1.6, 3.0, 4.6, 7.8]	3.5 [2.3, 2.9, 4.6, 7.8]	3.2 [1.4, 2.5, 4.3, 7.8]
ADs-L	3.0 [1.3, 2.2, 3.7, 6.0]	3.0 [1.8, 2.5, 4.1, 6.2]	3.4 [2.1, 2.9, 3.6, 5.0]	3.5 [1.8, 2.8, 4.5, 5.4]	3.1 [1.3, 2.4, 4.0, 6.2]
ADs-C	2.3 [1.2, 1.8, 3.1, 3.9]	2.2 [1.2, 1.9, 2.9, 4.1]	2.1 [1.6, 1.9, 2.7, 3.9]	2.6 [2.0, 2.5, 3.3, 4.0]	2.4 [1.2, 1.9, 2.9, 4.1]
AAb-L	2.1 [0.5, 2.1, 3.9, 7.7]	3.7 [0.9, 2.6, 4.9, 6.5]	4.3 [1.1, 2.8, 5.1, 6.4]	3.6 [1.0, 2.8, 4.3, 6.5]	3.6 [0.5, 2.4, 4.4, 7.7]
AAb-C	2.1 [0.9, 1.8, 3.2, 3.9]	2.8 [0.8, 2.3, 3.5, 4.4]	2.9 [0.4, 2.3, 3.4, 5.0]	3.1 [1.7, 2.1, 3.4, 4.6]	2.7 [0.4, 2.0, 3.4, 5.0]

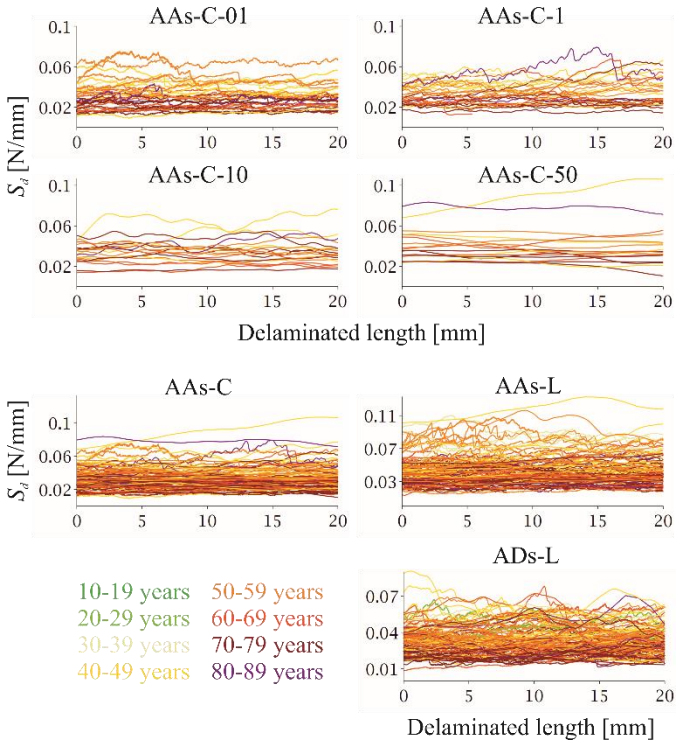

Figure 2. Examples of recorded delamination forces. Upper four panels show the differences associated with the extension rate (all data are for circumferentially oriented samples cut from the ascending aorta). Differences between groups of medians were not found to be statistically significant. Panels for AAs-C and AAs-L demonstrate that the groups of curves gained in the same location suggest dependence on the sample orientation (data were pooled with respect to the extension rate). Panels AAs-L and ADs-L indicate that the delamination force depends on the position along the aorta. Color of every single force curve highlights the age of a donor according to the legend in the image.

Fig. 2 illustrates signals recorded in experiments as the dependence of S_d on the delaminated length. Its four upper panels offer mutual comparison between the delamination forces recorded at different extension rates with the samples of the ascending aorta oriented in the circumferential direction. Most of the signals lie in the interval from 0.02 to 0.06 $\mathrm{Nmm^{-1}}$ which suggests an insignificant effect of the extension rate. On the other hand, AAs-C and AAs-L panels in Fig. 2 suggest that the orientation of

samples is important. Finally, when signals on AAs-L and ADs-L panels are compared visually, one can clearly observe that the delamination strength is different at different locations. All these results are described in deeper detail in what follows. However, the graphical presentation of the further results is based on the box-plots of the sets of mean values, which we consider to be clearer than the images depicting the recorded force signals. In Fig. 2, readers can notice a flattening of the curves corresponding to a high extension rate which is the effect caused by the sampling frequency and presentation method based on the constant delamination length.

3.1 Loading velocity

The *KW-test* did not reveal any significant differences between groups of data gained at speeds of 0.1, 1, 10, and 50 mms^{-1} in any of the considered locations and orientations (*KW-test*: AAs-L p = 0.77, AAs-C p = 0.32, ADs-L p = 0.32, ADs-C p = 0.13, AAb-L p = 0.41, AAb-C p = 0.11; for the specific values of compared medians see Table 2). Box-plots of these six quadruplets are in Fig. 3. Interestingly, pairwise comparisons based on *D-test* suggested that in the descending thoracic aorta results obtained for samples oriented in the circumferential direction at 1 mms^{-1} could significantly differ from those gained at 50 mms^{-1}, and the same was found in the abdominal aorta for 0.1 and 1 mms^{-1} again in the circumferential direction (ADs-C1 vs. ADs-C50 at p = 0.02, AAb-C01 vs. AAb-C1 at p = 0.03). Although *D-test* in these two cases contradicts the suggestion obtained by the *KW-test*, Fig. 3 does not indicate any unequivocal trend (increasing or decreasing S_d with an increasing extension rate) and thus we accept the hypothesis that the mean values of the delamination strength in the investigated groups do not significantly differ.

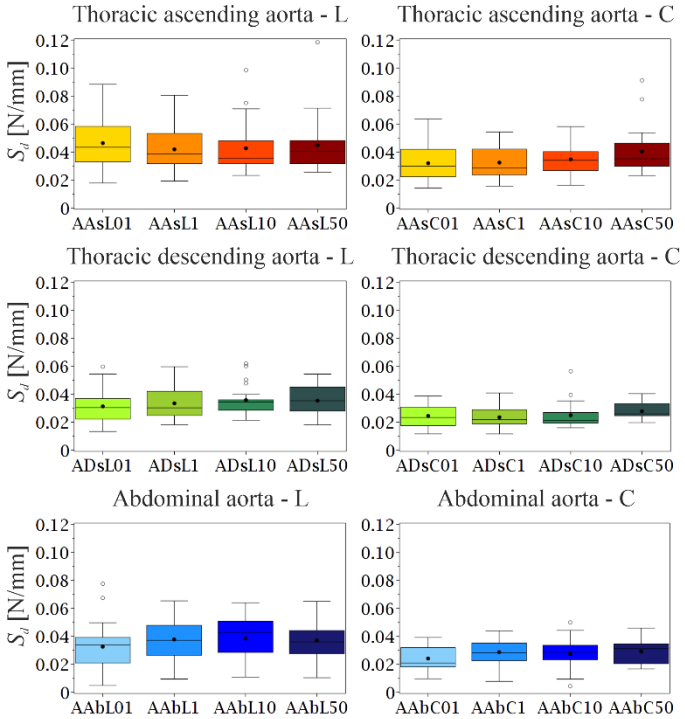

Figure 3. Delamination strength and its sensitivity to the extension rate, sample orientation, and anatomical location. *KW-test* did not reveal significant differences between medians in any quadruplet of groups (AAs-L p = 0.77, AAs-C p = 0.32, ADs-L p = 0.32, ADs-C p = 0.13, AAb-L p = 0.41, AAb-C p = 0.11). *D-test* suggested that two pairs are suspected to be different (ADs-C1 vs. ADs-C50 at p = 0.02, AAb-C01 vs. AAb-C1 at p = 0.03). Since the definition of box-plot construction varies in the literature, let us note that the horizontal lines of boxes indicate 25th, 50th, and 75th percentile, and open circles indicate outliers, which are considered to be points that are farther than 3/2 times the interquartile range away from the upper and lower quartiles (3/2 times the interquartile range distance is indicated by whiskers which, however, always end in a datapoint). Black circles indicate arithmetic mean. This method of box-plot construction is used within the entire article.

To the best of our knowledge, this is the first study evaluating the effect of the extension rate on the delamination strength in the human aorta in detail. The only study known to us which has dealt with the effect of the loading rate on the delamination properties in the peeling experiment thus far, is Tong et al. (2014) where peeling experiments with an abdominal aortic aneurysm and its thrombus at extension rates 1 mms^{-1} and 1/60 mms^{-1} were investigated. Tong et al. (2014) concluded that the delamination strength in an aneurysmatic abdominal aorta is sensitive to the extension rate. On the contrary, our data suggest that a (non-aneurysmal) human aorta does not exhibit a significant dependence of the delamination strength on the extension rate, at least within the range applied in our experiments (0.1 – 50 mms^{-1}). This is in agreement with the general rate-insensitivity in the mechanical response of arteries (Fung, 1993). In contrast, rate-sensitivity in the delamination resistance of aneurysms and thrombi could have its origin in the decreased content of the elastic lamellae, in their disintegration by enzymatic degradation, and in the general accumulation of a gel-like substance in the wall which could theoretically amplify viscous phenomena in their mechanical response (Cocciolone et al., 2018). On the other hand, studies by Prokop et al. (1970), and van Baardwijk and Roach (1986) have documented the dependence of dissection resistance on the loading rate. We should, however, take into account important differences between applied experimental methods. Although one can always expect a complex stress state at the delamination interface, in the peeling test is a rest of the sample predominantly in the uniaxial stress state or even without stress. This is in contrast to the van Baardwijk and Roach (1986) method, where the whole sample experienced complex loading when pressurized. These methodological differences could contribute to the different conclusions derived in the studies.

Since the hypothesis of the insensitivity of S_d to the extension rate has been accepted, in what follows, data gained at different speeds are pooled, and only sorting with respect to the orientation of samples and with respect to their positions along the aorta is kept.

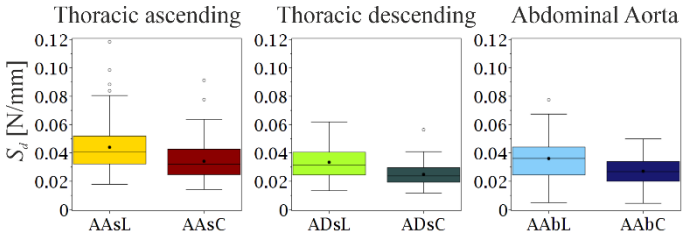

Figure 4. Anisotropy of the delamination strength. Data were pooled with respect to the extension rate. *U-test* as well as *KS-test* suggest that significant differences between the delamination strengths of longitudinally and circumferentially oriented samples exist in all studied locations (*U-test*: $p << 0.01$ for AAsL vs. AAsC, ADsL vs. ADsC, and AAbL vs. AAbC; *KS-test*: $p << 0.01$ again for all compared doublets).

3.2 Anisotropy of the delamination strength

The pooled data gives two groups of orientations (L, C) at three different locations (AAs, ADs, AAb). The effect of orientation is shown in Fig. 4 and the fact that the results strongly depend on the direction in which the delamination propagates is clear. In all three positions, delamination resistance is always higher in the longitudinal direction. That was confirmed by *U-test* ($p << 0.01$ for AAsL vs. AAsC, ADsL vs. ADsC, and AAbL vs. AAbC). *KS-test* suggested the same conclusion. The expression $p << 0.01$ is used in our study to indicate that the attained *p-value* is less than 0.001.

Our result showing that delamination strength is orientation dependent is in agreement with previous results found by Kozuń (2016) and Kozuń et al. (2018) within experiments carried out with samples harvested from the human thoracic aorta, and by Sommer et al. (2008) who observed the anisotropy in the case of abdominal aortic tissue. From our study one can conclude that the dependence of delamination resistance on the orientation of the sample is confirmed for the entire length of the human aorta (the ascending part of the thoracic aorta, its descending part, and also for the abdominal aorta).

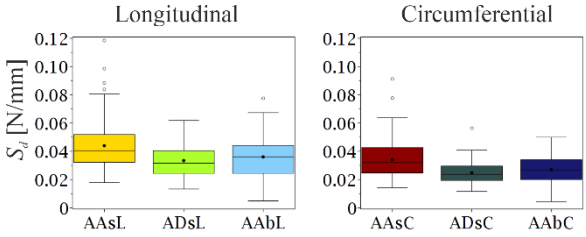

Figure 5. Inhomogeneity of the delamination strength along the aorta. Data were pooled with respect to the extension rate. *KW-test* suggests that delamination strength depends on the position along the aortic length (longitudinal as well as circumferential orientation attained $p << 0.01$). With regard to the longitudinal direction, *D-test* revealed that AAsL significantly differs from ADsL and AAbL, whereas there is a lack of evidence that ADsL and AAbL differ (p(AAsL,ADsL) << 0.01, p(AAsL,AAbL) << 0.01, p(ADsL,AAbL) = 0.13). For samples aligned with the circumferential direction, *D-test* suggested that medians in all groups significantly differ from each other (AAsC vs. ADsC and AAsC vs. AAbC attained $p << 0.01$, p(ADsC,AAbC) = 0.04).

3.3 Location

Since direction dependence can be considered as confirmed, Fig. 5, depicting site-specific differences, is divided into two panels with respect to the longitudinal and circumferential orientation. The positions of the medians in the boxes suggest that delamination resistance is highest in the ascending part of the aorta (AAsL 0.041 Nmm^{-1}, AAsC 0.032 Nmm^{-1}). In contrast, the lowest values were found in the descending thoracic aorta (ADsL 0.031 Nmm^{-1}, ADsC 0.024 Nmm^{-1}). Finally, the decline in the descending thoracic aorta is followed by an increase of the delamination strength in the abdominal aorta (AAbL 0.036 Nmm^{-1}, AAbC 0.027 Nmm^{-1}). Our results suggesting that delamination resistance is a site-specific property are in accordance with previous findings obtained with animal models (Roach and Song 1994; Myneni et al., 2020). They are also consistent with the conclusions obtained if one compares typical results found across different studies of the human aorta (Pasta et al., 2012, arrived at 0.126 Nmm^{-1} as a typical value of S_d for AAs-C, and 0.146 Nmm^{-1} for AAs-L, in contrast to e.g. Sommer et al., 2008, who determined 0.035 Nmm^{-1} as typical for AAb-C, and 0.035 Nmm^{-1} for AAb-L). The decrease in the delamination strength along the aortic length could be attributed to the decreasing number of elastic lamellae (Kassab, 2006; Cocciolone et al., 2018). On the other hand, the increase from the descending thoracic aorta to the abdominal aorta could theoretically be explained by the decreasing density of *vasa vasorum*, which are very rare in the abdominal part of the aorta and which could theoretically introduce a local weakening of the delamination strength because they create local voids in the delamination interface and thus provide no cohesion between arterial layers (Sokolis et al., 2002). A link between vasa vasorum and a susceptibility to dissection, and therefore reduced delamination resistance, was suggested by Angouras et al. (2000) who reported that the thoracic aorta of pigs with an impaired vasa vasorum blood flow developed histologically apparent borderline between sufficiently vascularized and the avascular part of the aortic media. Our own histological observations are unfortunately unavailable in the present study.

3.4 Correlation between S_d and age

It is well known that the mechanical properties of arteries exhibit significant age-related changes (Greewald 2007; Horný et al., 2013, 2014b; Horný 2019). Due to a combination of several factors, such as overall calcium accumulation, fragmentation of the elastic membranes with a subsequent transfer of the load carrying function from these membranes to collagen fibers, increased collagen content, additional cross-linking by advanced glycation end-products, as well as due to atherosclerotic and non-atherosclerotic wall thickening, arterial walls become stiffer with increased age (Greenwald 2007; Horný 2019; Amabili et al., 2020b, 2021; Jadidi et al., 2020, 2021).

However, previous studies of delamination strength in the human aorta have, to the best of our knowledge, focused their attention on subjects other than the quantitative description of the mutual relationship between age and S_d. Although, from the aforementioned it is clear that one can expect that delamination properties will depend on age similarly as other mechanical properties. Exceptions are works by Angouras et al. (2019) where a significant correlation between age and S_d was found for ascending thoracic aneurysms, and Chung et al. (2020) who investigated the same part of the aorta and also found a significant decrease in delamination strength in aging.

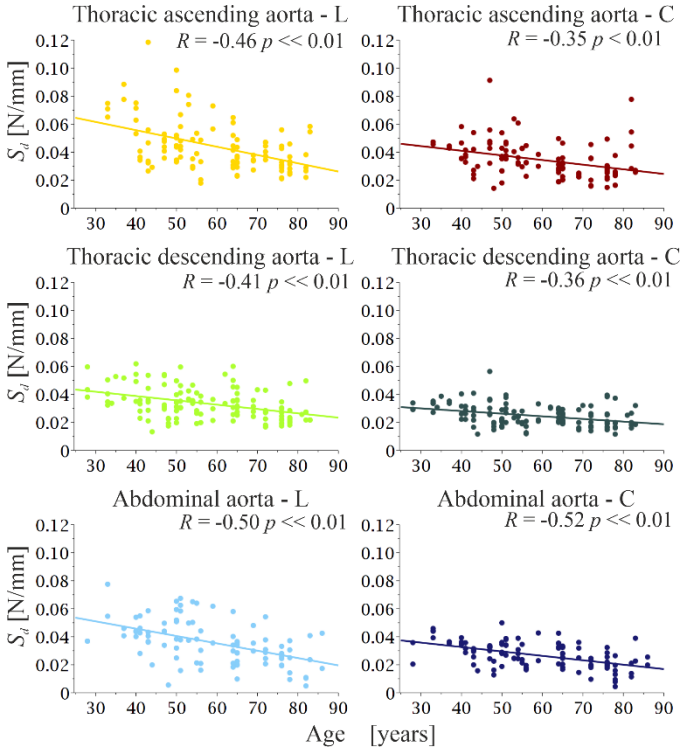

Figure 6. Delamination strength significantly depends on age. Data were pooled with respect to the extension rate.

Our data confirms the hypothesis that the delamination strength in the human aorta depends on age. Figure 6 clearly shows that S_d decreases with age in all studied groups irrespective of the sample orientation and the location from which samples were obtained. Correlation coefficients fell into the interval [-0.52,-0.35] and according to the *T-test* of the hypothesis $R = 0$, they have to be considered as highly significant ($p < 0.001$ in all cases). Figure 6 also shows the lines of the linear regression models $S_d = a \cdot Age + b$. Parameters a and b, including their 95%-confidence intervals, are given in Table 3.

The results suggest that age, since the correlation coefficient attained statistical significance, should be considered as a risk factor for dissection because the higher the age, the lower the delamination strength. Future studies should focus on clarifying why this is observed, because the aforementioned age-stiffening mechanisms cannot be, at the first sight, associated with decreasing strength. Previous works linked delamination strength with radially running collagen fibers (Pal et al., 2014). One possible explanation could be that age-related changes in the chemical composition of the wall lead to a weakening of the bonds between these collagen fibers and other components of the extracellular matrix, like elastic lamellas.

Table 3 Regression of the dependence of delamination strength on age. Model equation: $S_d = a \cdot Age + b$, *Age* [year], a [N/(year·mm)], b [N/mm]. Estimated parameters are completed with 95%-confidence intervals based on the assumptions of the classical linear model.

	a	*b*
AAsL	-5.9E-4 ± 2.2E-4	7.9E-2 ± 1.3E-2
AAsC	-3.3E-4 ± 1.8E-4	5.4E-2 ± 1.1E-2
ADsL	-3.1E-4 ± 1.3E-4	5.1E-2 ± 7.5E-3
ADsC	-1.9E-4 ± 8.6E-5	3.6E-2 ± 5.2E-3
AAbL	-5.2E-4 ± 1.9E-4	6.7E-2 ± 1.1E-2
AAbC	-3.2E-4 ± 9.9E-5	4.5E-2 ± 6.0E-3

3.5 Post mortem interval

Our study involved cadavers as tissue donors. The mean PMI length was 64 ± 29 hours (employing the descriptive statistics used in Table 2, one obtains 64 [14, 45, 84, 156] hours). To show that PMI did not affect our results, correlation analysis was carried out. The correlation coefficient for the S_d and PMI was calculated in each studied group. No group exhibited a significant correlation between delamination strength and post mortem interval (mean $|R| = 0.12 \pm 0.08$, mean $p = 0.57 \pm 0.25$). It was concluded that the observed S_d were not significantly affected by the length of the post mortem interval.

3.6 Limitations

There are several limitations which should be born in mind when our results are compared with those determined by other research groups. Our experiments were carried out in air at room temperature. It is generally recommended to conduct mechanical tests with samples of soft tissues immersed in a liquid environment at body temperature, however our experimental setup did not allow it. This theoretically could have affected the results. Nevertheless, our study did not reveal significant differences in the mean delamination strength between the four groups of extension rates (0.1, 1, 10, and 50 mms^{-1}). Since the experiments conducted at 50 mms^{-1} were typically completed within several seconds, whereas those conducted at 0.1 mms^{-1} lasted for several minutes and the differences were not found to be significant, it suggests that the experimental environment probably did not play a decisive role.

Another limitation is associated with the exact locations of the samples and the exact positions of the initial incisions. AAs samples were obtained the from proximal part of the ascending aorta and ADs and AAb samples were cut approximately from the middle of the descending thoracic part and the abdominal part. The exact positions, however, were not described within the sample preparations. As far as the initial incision, we cannot be more precise than that it was made in the media of the wall. It was created approximately in the middle of the thickness, but again the exact depth was not measured. Previous studies have shown that delamination resistance can vary along the entire length of the aorta, and with respect to the depth at which delamination extends (van Baardwijk and Roach 1987; Roach and Song 1994; Tong et al., 2011; Kozuń et al., 2016, 2018; Angouras et al., 2019). These uncertainties could be sources of inter-sample and inter-donor variability. On the other hand, the differences found in our data were statistically significant irrespective of it.

4. Conclusion

Our study yielded the results of 661 peeling experiments carried out with strips of the human aorta harvested from 46 cadavers. The samples were arranged into groups according to (1) their position along the aorta, (2) the orientation of the sample, and (3) the extension rate used within the experiment. It was found that the collected data is in agreement with the hypothesis that delamination resistance is not sensitive to loading rate. In other words, we did not find any statistical evidence which contradicted the hypothesis that the medians of the delamination strength measured at 0.1, 1, 10, and 50 mms^{-1} of the

extension rate are equal. We arrived at this conclusion for all positions along the aorta (thoracic ascending, thoracic descending, abdominal) and when considering both the longitudinal and the circumferential orientation of the samples. On the other hand, our results showed that delamination strength differs significantly with respect to anatomical position and sample orientation. This suggests that resistance to crack propagation should be an anisotropic property and that the aorta is inhomogeneous along its length, from the point of view of delamination resistance. Finally, correlation analysis proved that the delamination strength of the human aorta significantly decreases with age.

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