Estimation of wall properties and wall strength of aortic aneurysms using modern imaging techniques. One more step towards a patient-specific assessment of aneurysm rupture risk

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Abstract
Abdominal aortic aneurysmal disease is a major health problem with rupture representing its main complication accompanied by great mortality. Elective repair is currently performed with mortality rates <3%, based upon size or expansion rate, with a recommended threshold of 5.5 cm maximum diameter or >1 cm/year enlargement. It is well established that even small AAAs without indication for surgical repair can experience rupture with catastrophic outcomes whereas larger aneurysms often remain intact for a long period. It is recognized, therefore, that the currently used, maximum diameter criterion can not accurately predict AAAs evolution.

There is increasing interest in the role of patient-specific biomechanical profiling of AAA development and rupture. Biomechanically, rupture of a vessel occurs when intravascular forces exceed vessel wall structural endurance. Peak Wall Stress (PWS) has been previously shown to better identify AAAs prone to rupture than maximum diameter, but currently stress analysis takes into account several assumptions that influence results to a large extent and limit their use. Moreover stress represents only one of two determinants of rupture risk according to the biomechanical perspective. Wall strength and mechanical properties on the other hand cannot be assessed in vivo but only ex vivo through mechanical studies with mean values of these parameters taken into account for rupture risk estimations. New possibilities in the field of aortic imaging offer promising tools for the validation and advancement of stress analysis and the in vivo evaluation of AAAs' wall properties and wall strength. Documentation of aortic wall motion during cardiac cycle is now feasible through ECG-gated multi-detector CT imaging offering new possibilities towards an individualized method for rupture risk and expansion-rate predictions based on data acquired in vivo.

Introduction
Abdominal aortic aneurysm (AAA) represents a focal dilatation of the vessel exceeding 1.5 times its normal diameter, leading to a threshold of 3 cm to define aortic aneurysms [1]. AAA is encountered in 4–8% of male and 0.5–1% of female population over 50 years of age [2,3]. The most catastrophic complication of this condition is rupture accompanied by increased mortality [4–6]. On the other hand, elective AAA repair is currently associated with mortality rates <3% and is performed based upon the size or growth rate of the aneurysm with a threshold of 5.5 cm maximum diameter and >1 cm/year enlargement, respectively [7]. While rupture risk is associated with size, some small AAAs, well under the critical threshold for surgical repair, rapidly progress and rupture can occur between scanning intervals. Specifically, it has been reported that 10–24% of ruptured aneurysms, present with maximum diameter of 5.0 cm or less, and the annual rupture rate for aneurysms 4–5 cm is 0.5–5% and 5–15% for aneurysms 5–6 cm [1,8]. On the other hand physicians often come across very large aneurysms that remain intact for many years, despite having a theoretical annual rupture risk of 40% [1,7].

It is now well understood that aneurysms due to their complex geometry are subject to mechanical forces (stress) resulting from systolic pressurization, counteracting the mechanical strength of the wall that resists to rupture. From a biomechanical point of view, rupture of AAA occurs when the mechanical stress exceeds the ability of the wall tissue to withstand this stress. Therefore,
the use of maximum diameter as a “one-size-fitting-all” criterion for the estimation of rupture risk is often inaccurate, since it cannot predict thoroughly the balance between the aforementioned factors. In an effort to move towards a patient-specific rupture risk assessment based on physical principles, AAA wall stress distribution has been estimated using Finite Element Analysis (FEA) and related to risk of rupture. Peak Wall Stress (PWS) has been suggested by many investigators to be superior to maximum diameter in rupture risk estimation and has been extensively studied in the literature [9–13].

**The problem**

Although the significant contribution of PWS in predisposition for AAA rupture is well established, one should identify that it is not the sole determinant of rupture risk, since it is one of two variables that define rupture from a biomechanical point of view [14]. It is logical that no matter how low the intravascular pressure and forces may be, rupture may occur if structural integrity of the vessel wall has been compromised. In regard it has been postulated that not only small AAAs with different PWS values can present similar growth rates but also low PWS can be accompanied by rapid expansion [15,16]. At the same time a variance in mechanical forces may be, rupture may occur if structural integrity of the vessel wall has been compromised. In this regard it has been postulated that not only small AAAs with different PWS values can present similar growth rates but also low PWS can be accompanied by rapid expansion [15,16]. At the same time a variance in mechanical forces may be, rupture may occur if structural integrity of the vessel wall has been compromised. In this regard it has been postulated that not only small AAAs with different PWS values can present similar growth rates but also low PWS can be accompanied by rapid expansion [15,16]. At the same time a variance in mechanical forces may be, rupture may occur if structural integrity of the vessel wall has been compromised. In this regard it has been postulated that not only small AAAs with different PWS values can present similar growth rates but also low PWS can be accompanied by rapid expansion [15,16]. At the same time a variance in mechanical forces may be, rupture may occur if structural integrity of the vessel wall has been compromised. In this regard it has been postulated that not only small AAAs with different PWS values can present similar growth rates but also low PWS can be accompanied by rapid expansion [15,16].

Additionally, there is a need to identify those large AAAs at low risk for rupture, despite high stress values, since clinicians often come across cases of gigantic AAAs in elderly people that have not ruptured and, therefore, could theoretically avoid an unnecessary intervention with its consequent complications. Taking the aforementioned data into consideration, there is a need to evaluate the critical role of wall mechanical properties and strength.

Moreover, wall stress analysis is not without limitations. Several assumptions that are being taken into account by FEA, may influence obtained results. Specifically it has been reported that differences of model assumptions are more important for simulation results than differences between patient-specific morphologies [18]. Therefore, the results of finite element model simulations are highly dependent on the quality and complexity of the underlying finite element models. As a consequence, interpretation of results in many publications is difficult and the results are often not comparable.

**The hypothesis**

Since ECG-gated multi-detector CT has been recently exploited for objective determination of crucial biomechanical properties of AAA wall, it can be used in order not only to identify those small ones at risk for sudden great expansion making them amenable to operation, but also those large AAAs that do not share a high mechanical rupture profile. Documentation of regional elastic properties and wall stress variations throughout the AAA wall may become feasible with the use of this imaging modality. Furthermore, validation of finite element models being used for wall stress estimation, comparing the in vivo observed vessel deformation with that calculated by strain analysis with FEA could be possible. Such data could be exploited to advance finite element analysis in order to obtain more realistic and reproducible results of wall stress distribution.

**Evaluation of the hypothesis**

**Feasibility of ECG-gated CT scan in AAAs’ evaluation**

Late advances in aortic imaging with the development of ECG-gated multi-detector CT have managed to capture wall motion throughout the cardiac cycle and subsequently introduced new possibilities in the study of AAAs.

Klein et al. suggested that ECG-gated CTA is a suitable technique for studying the expected motions of the vessel wall in AAAs [19]. Others managed to measure Pulse Wave Velocity using this state-of-the-art technique and proposed that it allows noninvasive mapping of vascular disease in vivo [20]. Manduca et al. applied ECG-gated CT imaging in patients with AAAs claiming that automated segmentation, centerline generation, and registration of temporally resolved CTA datasets permit measurements of regional changes in cross-sectional area over the course of the cardiac cycle (i.e., regional aortic pulsatility). Their measurements were reproducible between scans 6–12 months apart, with differences in aortic areas reflecting both aneurysm remodeling and changes in blood pressure. Regional pulsatility ranged from 2% to 13% but were reproducible at the 1% level [21]. AAAs segmentation process has been reported to require as low as 5–10 min while post-processing of AAA surfaces does not take longer [22,23]. Ganet et al. measured changes of cross sectional areas from CT slices and along with blood pressure measurements managed to calculate distensibility of the vessel wall [24]. They also estimated AAA distensibility suggesting a significant reduction compared to the unaffected aorta that applies to both small and large aneurysms [25]. Others report no significant correlation between aneurysm diameter and distensibility of aneurysm lumen, aneurysm wall and normal aorta [26]. Moreover, using ECG-gated CT scan to study the compressibility of thrombus of AAAs Trujers et al. concluded that in vivo thrombus compressibility varied from patient to patient, and this variation was irrespective of aneurysm size, pulse pressure, and thrombus volume. Therefore, thrombus might act as a biomechanical buffer in some, while it has virtually no effect in others [27].

The above mentioned studies highlight the value of ECG-gated CT scan in the examination of patients bearing AAAs underscoring reproducibility and accuracy of measurements.

**AAA wall elasticity and strength estimation using ECG-gated CT derived data**

Documentation of aortic expansion during the cardiac cycle when related to pressure data provides an analogue of the ex-vivo mechanical testing of aortic tissue where deformation is related to driving forces in order to determine elastic material properties [28]. Specifically pressure strain elastic modulus (Ep) and aortic stiffness (β) could be calculated using strain data derived from ECG-gated CT imaging and blood pressure measurements from the following equations [29]:

\[
Ep = \frac{(133.3) \times (BP_{systolic} - BP_{diastolic})}{(D_{maxSystolic} - D_{maxDiastolic})/D_{maxSystolic}}
\]

(1)

\[
\beta = \frac{\text{natural logarithm} (BP_{systolic} - BP_{diastolic})}{D_{maxSystolic} - D_{maxDiastolic}}
\]

(2)

Currently using dedicated software, following vessel three dimensional reconstruction, the AAA surface can be divided in continuous cross-sections (i.e. 0.1 mm apart) perpendicular to the corresponding centerline and for each cross-section the expansion during the cardiac cycle can be calculated by means of area or diameter change [30]. Therefore recording the AAA wall deformation between peak-systole and end-diastole throughout the entire aneurysmal surface, also taking into account the pulse pressure that caused this deformation and using Eqs. (1) and (2), could result in a detailed map of aortic elasticity along the AAA wall. Since such properties could also be obtained for the adjacent non-aneurysmal aorta, the direct comparison of elastic properties between
non-aneurysmal and aneurysmal aortic segments could display the degree of AAA wall degeneration providing useful information in assessing susceptibility to rupture.

Moreover, since the prompt relation of such properties with wall strength has been suggested by mechanical testing, postulations of wall strength distribution on the AAA wall could be made. Specifically, it has been indicated that there is a significant positive correlation of wall strength with tissue elastic modulus ($R = 0.76; P < .05$) [31]. Taking into account that the latter can be directly calculated from imaging derived data as explained before, this could be exploited to estimate wall strength distribution throughout the AAA surface.

### Validation of stress analysis using in vivo acquired data from ECG-gated CT scan

Stress analysis is performed to determine wall stress distribution. This takes into account the specific AAA geometry to which an internal pressurization is applied. Considering constitutive parameters of the aortic wall derived from mean population data, the deformation of the vessel is computed as well as the stress exerted on the aneurysm wall using a means to solve the resultant system of partial differential equations. Varying model assumptions influence results to a large extent and specifically alterations in displacements due to the different model assumptions are up to 60% while differences in peak wall stress present an average 170% [18]. On the other hand, ECG-gated CT scan can capture AAA wall displacement during the cardiac cycle in vivo. Comparing the latter with the numerically calculated deformation using FEA could provide a measure of the accuracy of the computational analysis and obtained stress values. Moreover, discrepancies between in vivo and numerically acquired data could lead to modifications in material and model assumptions of FEA for its results to be consistent with those obtained from EGG-gated CT scan. This would improve accuracy of stress analysis to provide results that are likely to display actual values [32].

### Discussion

Mechanical forces and deformations along with mechanical properties and strength of aneurysmal wall are considered to be of paramount importance in the maintenance of structural wall integrity which may determine the natural history of AAAs [28]. Wall stress has been extensively studied in the literature and its value in the evaluation of rupture risk has been indicated by various research groups. Fillinger et al. indicated a higher PWS for ruptured and emergent symptomatic than for electively repaired aneurysms without any significant differences in maximum diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9]. The same research group proposed that for AAAs under observation, PWS seems superior to diameter or blood pressure [9].

With regard to AAA wall elastic properties many studies attempted to estimate AAA wall deformation and elastic properties and examine their possible predictive role in rupture risk estimations. Wilson et al. considered 210 patients with AAA indicating that there was a decrease in AAA distensibility and a subsequent increase in stiffness along with the progression of aneurysmal disease. On the other hand, a significant relation between increased distensibility at baseline, defined by ultrasound scan based echotracking technique and risk of rupture was found [33]. Moreover, Sonesson et al. used ultrasonography to investigate the stiffness of the abdominal aorta as well as the common carotid artery in patients with AAA and reported an increase in stiffness in both, when compared with data reported for healthy subjects [34]. Others suggest that the baseline aortic wall distensibility can be predictive for later aneurysmal expansion rate and indicate that this may provide an additional parameter for monitoring small asymptomatic AAAs to optimize the indication and time for elective repair [35]. Furthermore, Mojacek et al. in a recent study not only found a decreased distensibility in the affected AAA wall compared to normal aorta but also a significant increase of the same parameter in aneurysms presenting a rapid expansion [24]. Data from invasive pathologic studies have significantly correlated the above-mentioned elastic properties of the arterial wall with its strength underlining the importance of these variables in the progression of aneurysmal disease. Vorp et al. measured wall strength through mechanical testing of aneurysmal and non-aneurysmal aorta and demonstrated a reduction by nearly 50% in tensile strength of the aorta due to aneurysm while an increased stiffness was also found [36]. Di Martino et al. measured wall strength of ruptured and electively repaired AAAs and attempted to correlate the later with wall properties. They were able to demonstrate a strong positive correlation of wall strength with aortic wall stiffness whereas no such correlation of strength with aortic diameter was found. They suggested that aortic wall strength and stiffness are decreased in AAAs approximating rupture [29]. Based upon mechanical testing, models for the estimation of the wall strength have been developed and represent an effort towards an individualized wall strength assessment. Nevertheless, they represent statistical models and the predicted wall strength values are calculated using not only patient specific variables as intraluminal thrombus thickness and normalized diameter but also universal ones such as gender and family history. Therefore there is a medium correlation between predicted and actual values of wall strength while predictability of the model may be constrained by the range of the original data the authors used by Vande Geest et al. [37].

Our hypothesis suggests the feasibility of in vivo recordings of aortic wall mechanical properties and strength as well as their spatial distribution. Techniques based on ultrasonography could not be the answer to this task because of their inability to capture motion in three Dimensions (usually only the longitudinal axis is used) and thus mechanical properties in every AAA segment, along with operator dependency of ultrasound measurements. Furthermore, recent studies using ECG-gated multi-detector CT, as these mentioned by Ganten et al. [25] and Molacek et al. [26] avoid to take into consideration the entire AAA surface while Trugets et al. and Van De Veer et al. [27,38] do not record the regional variations in the mechanical properties that exist in vivo. Our hypothesis supports the feasibility of objective wall motion display along the entire AAA-wall and the use of this information to estimate actual regional properties of aortic wall throughout the AAA surface. In accordance with previous ex-vivo mechanical studies that correlate the aforementioned properties with wall strength, the latter could also be estimated using such methods and a determination of the distribution of strength throughout the AAA wall may become possible. This could represent the next step towards a more accurate, individualized AAA rupture risk estimation.
Conclusions

Peak Wall stress represents one of two factors determining the risk of rupture with the other being material properties and strength of aortic wall. In-vivo estimation of such parameters may become possible with the use of ECG-gated multi-detector CT through the documentation of aortic wall motion during the cardiac cycle. Moreover FEA can be validated comparing in vivo recorded AAA deformation to that numerically calculated and such data could be used to advance stress analysis. Such methods and models could lead to new, improved, individualized therapeutic strategies in AAs’ evaluation.

Conflict of interests

None.

References