THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Computational Biomechanics-Based Rupture Predictions of AAAs

Citation for published version:

Doyle, B, Miller, K, Newby, D & Hoskins, P 2016, 'Computational Biomechanics-Based Rupture Predictions of AAAs', *Journal of Endovascular Therapy*, vol. 23. <https://doi.org/10.1177/1526602815615821>

Digital Object Identifier (DOI):

[10.1177/1526602815615821](https://doi.org/10.1177/1526602815615821)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Journal of Endovascular Therapy

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

INVITED COMMENTARY

Computational Biomechanics-Based Rupture Prediction of AAAs

Barry Doyle, PhD,^{1,2} Karol Miller, DSc,^{1,3} David Newby, PhD^{2,4} Peter Hoskins, DSc²

1. Vascular Engineering, Intelligent Systems for Medicine Laboratory, School of Mechanical and Chemical Engineering, The University of Western Australia, Perth, Australia.
2. BHF Centre for Cardiovascular Science, The University of Edinburgh, Edinburgh, UK.
3. Institute of Mechanics and Advanced Materials, Cardiff University, UK.
4. Clinical Research Imaging Centre, The University of Edinburgh, Edinburgh, UK.

In this latest edition of *JEVT*, the biomechanical evaluation of AAA again receives attention. This time Erhart et al.¹ show that pre-rupture AAAs (n=13) had significantly higher peak wall rupture risk (PWRR) and rupture risk equivalent diameter (RRED) compared to diameter-matched controls (n=23), and that their biomechanical analyses predicted the location of future rupture in 7/13 cases. What is important about this article is that, despite certain limitations, it demonstrates the ability of computational biomechanics to predict the location of rupture in advance, albeit in approximately 50% of their cases, and thus, helps to generate useful pilot data towards larger scale investigations in the area. Although vascular surgeons would rather know which cases *will* rupture rather than *where* they might rupture; by providing evidence that rupture locations can be predicted helps the credibility of such modeling in the clinical community. The authors have had similar experiences in rupture prediction studies to those reported here. The exact location of rupture was predicted in some cases^{2,3} and the same transverse location but on the opposite wall, was predicted in others⁴; similar to some cases in Erhart et al.¹ Furthermore, Xenos et al.⁵ used a sophisticated fluid-structure interaction computational approach with an orthotropic material model and embedded calcifications and also showed that they could predict the locations of rupture in the two cases examined.

What is still unclear, however, is how complicated does the model need to be in order to predict rupture risk? Gasser et al.⁶ showed the impact of model complexity on the predictability of rupture risk and concluded that the inclusion of the ILT and a non-homogenous wall thickness are the most important parameters. So, is the most sophisticated material model needed? Does mechanobiology need to be included into the framework? In order to better understand the growth and remodeling of AAAs, mechanobiological information is certainly required, but perhaps not for the purpose of generating a rupture risk index based on wall stress and an estimate of wall strength. Reports such as those from Erhart et al.^{1,7} and others^{6,8} are making important steps towards defining a risk threshold, akin to the

diameter threshold. However, any new criterion will of course require validation and major interrogation before it can be used clinically. The use of the rupture risk equivalent diameter (RRED) by Erhart et al. and others⁹ represents an excellent example of ‘translating’ the results of computational biomechanics into a language familiar in the clinic, that is, presenting the risk profile as a simple diameter equivalency. Perhaps the use of the RRED will make it easier for clinicians to appreciate the biomechanical risk of different aneurysms in a format they are well accustomed to.

It is now about four years since the authors commented on an article published in *JEVT* that reviewed the current state of the art in computational AAA rupture prediction.^{10,11} This area of research is commonly known as patient-specific modeling (PSM) of AAA. However it is becoming apparent that many aspects are not as ‘patient-specific’ as one would like. A typical PSM framework assumes values of wall thickness and models the thrombus as the same homogenous mass across all patients. In our 2011 commentary,¹⁰ we proposed four key areas, or challenges, that require both further research and standardization: (1) modeling intraluminal thrombus (ILT); (2) capturing AAA wall thickness; (3) determining appropriate material properties; and (4) effectively incorporating calcifications. Only by addressing these issues will robust protocols be created, enabling large scale efficacy testing to inform clinical practice.

Challenge 1: Intraluminal Thrombus

Over recent years there has been substantial research aimed at understanding the ILT¹²⁻¹⁴ and classification of the thrombus is now possible based on its morphology.¹³ It is generally understood that ILT must be included into computational models, however, the way it is included is currently not patient-specific and ILT is assumed to buffer the wall stress to the same extent for all patients. Based on our work¹³ and others^{12,14} this cannot be the case, as there is simply too much inter-patient variation in the structure. A strategy needs to be devised whereby patient-specific information on the ILT can be included, and this may be possible through additional magnetic resonance (MR) imaging. It is common for ILT to develop into distinct layers from fresh luminal thrombus, to older abluminal thrombus.¹⁵ Importantly, the excellent soft tissue discrimination possible with MR means that ILT can be better visualized, compared to routine CT. Therefore MR can be used to guide CT-reconstructions of the ILT and create a layered ILT geometry true to the *in vivo* situation of the patient. Whether or not this enhances the biomechanical assessment is yet to be seen.

Challenge 2: Wall Thickness

Accurate measurement of wall thickness remains one of the most elusive components of the entire PSM workflow. Whereas some groups have developed methods to measure the wall thickness from CT,^{16,17} the methods are yet to be widely adopted. MRI, on the other hand, is better suited to measure aortic wall thickness.¹⁸ Therefore, the authors have begun to use a combination of MRI and CT to generate our AAA reconstructions.¹⁹ In this approach, the two image datasets are registered and the best information from both sources is combined, i.e. the wall is defined using calcifications visible on CT in conjunction with the soft tissue visibility

of MRI. We believe that this represents the most accurate reconstruction of the AAA wall currently available and enables a better prediction of wall tension.

However, measuring the wall thickness is only one side to the story as, generally speaking, the thicker the wall, the weaker it is. Biochemical and remodeling processes result in increased wall thickness, often by the addition of non-load bearing constituents. So, now another problem arises; if the wall thickness can be measured, how is information on wall strength obtained? As with the thrombus, non-invasive imaging may hold the key. Both 18F-fluorodeoxyglucose (FDG) PET/CT²⁰ and ultrasmall superparamagnetic particles of iron oxide (USPIO)-MRI^{21,22} are proving to be valuable ways to visualize and quantify processes active in the AAA wall. With further work the strength of the wall may be able to be determined from such imaging.²⁰ This may better inform rupture risk models that couple wall stress and wall strength, such as the rupture potential index (RPI)²³ and the peak wall rupture risk (PWRR) used in the study by Erhart et al.¹

Challenge 3: Material Properties

This aspect of the analysis was long believed to be one of the most critical elements of the PSM framework, and major research effort has focused on experimentally measuring the behaviour of AAA tissue within the physiological range in the lab using excised tissue.²⁴⁻²⁶ The earliest reports of PSM in AAA used linear elastic models to characterize the wall. Later work used nonlinear constitutive models that have since become increasingly complex. Then the focus aimed at recovering the unloaded geometry, or stress-free configuration, of the AAA using inverse methods (as, of course, the AAA is internally loaded at the time of CT). A result which may seem surprising to some when first encountered is that if the inverse method is used correctly, the importance of material properties becomes negligible.²⁷ In fact, increasing the stiffness of the AAA wall a thousand-fold does not change the resulting wall stress.¹⁹ The internally loaded AAA (as observed with CT) is thus a statically determinate structure even though the thin-walled assumption is not introduced. Moreover, as the deformed geometry is available from CT, the stress distribution in the wall that balances the internal pressure load can be established via (geometry preserving) linear finite element analysis, which can be performed in a matter of seconds on a typical desktop computer. The segmentation of the geometry still is a semi-automatic task that takes about 40 minutes using dedicated software.²⁸

Challenge 4: Calcifications

The vast majority of AAA computational biomechanics studies omit calcifications. There is much disagreement in the literature as to how best to incorporate calcifications into the geometry.²⁹⁻³¹ It was recently shown that partially calcified tissue has a much lower strength than fibrous wall tissue (1.21 vs. 0.88 MPa).³² Interestingly, there is little difference in the mechanical behaviour of the tissues in the physiological stretch range and there is no significant difference in the stiffness parameters that mathematically characterize the two tissue types. Partially calcified tissue predominantly fails at the boundary of the micro-calcifications and the fibrous tissue, which implies that calcifications are likely ‘stress-

raisers' and these junctions are potential AAA rupture locations. This was observed in the work of Xenos et al.⁵ where they observed high wall stress and location of rupture at sites of calcification. It is important to note that micro-calcifications are not typically visible on CT, unlike established macro-calcifications, and as such, other imaging modalities such as 18F-sodium fluoride (NaF) PET/CT may be needed to effectively visualize these micro-structures.³³

The authors of this commentary believe they have developed methods for stress estimation in AAA that are easy to implement, significantly faster and more clinically-applicable¹⁹ than the current state of the art. Furthermore, Erhart et al.¹ mention that “*no study has been performed to investigate the validity of biomechanical parameters to predict the future rupture sites of asymptomatic AAA.*” This is difficult for many reasons however, we are currently testing our own methods on a large prospective cohort of patients and hope to soon demonstrate the added value that PSM brings to the clinical management of AAA patients.

Acknowledgements

The authors gratefully acknowledge the National Health and Medical Research Council (Grants APP1063986 and APP1083572), the Medical Research Council Institute for Health Research Efficacy and Mechanism Evaluation (NIHR EME) program, the British Heart Foundation (CH/09/002) and the Wellcome Trust (WT103782AIA).

Conflicts of Interest

None.

References

1. Erhart P, Roy J, de Vries J-P, et al. Prediction of rupture sites in abdominal aortic aneurysms after finite element analysis. *J Endovasc Ther.* 2015, in press.
2. Doyle BJ, McGloughlin TM. Computer aided diagnosis of abdominal aortic aneurysm. In: McGloughlin TM, Biomechanics and mechanobiology of aneurysms. Springer, Berlin.
3. Doyle BJ, McGloughlin TM, Miller K, et al. Regions of high wall stress can predict the future location of abdominal aortic aneurysm rupture. *Cardiovasc Intervent Radiol*, 2014;37:815-818.
4. Doyle BJ, Callanan A, Grace PA, et al. On the influence of patient-specific material properties on computational simulations: a case study of a large ruptured abdominal aortic aneurysm. *Int J Numer Meth Biomed Engng*, 2013;29:150-164.

5. Xenos M, SH Rambhia, Y Alemu, et al. Patient-based abdominal aortic aneurysm rupture risk prediction with fluid structure interaction modeling. *Ann Biomed Eng.* 2010;38:3323-3337.
6. Gasser TC, Auer M, Labruto F, et al. Biomechanical rupture risk assessment of abdominal aortic aneurysms: model complexity versus predictability of finite element simulations. *Eur J Vasc Endovasc Surg.* 2010;40:176-185.
7. Erhart P, Hyhlik-Durr A, Geisbusch P, et al. Finite Element Analysis in asymptomatic, symptomatic, and ruptured abdominal aortic aneurysms: in search of new rupture risk predictors. *Eur J Vasc Endovasc Surg.* 2015; 49:239-245.
8. Maier A, Gee MW, Reeps C, et al. A comparison of diameter, wall stress and rupture potential index for abdominal aortic aneurysm rupture risk prediction. *Ann Biomed Eng.* 2010;38:3124-3134.
9. Gasser TC, Nchimi A, Swedenborg J, et al. A novel strategy to translate the biomechanical rupture risk of abdominal aortic aneurysm to their equivalent diameter risk: method and retrospective validation. *Eur J Vasc Endovasc Surg.* 2015;47:288-295.
10. Doyle BJ, Hoskins PR, McGloughlin TM. Computational rupture prediction of AAA: what needs to be done next? *J Endovasc Ther.* 2011;18:226-229.
11. Georgakarakos E, CV Ionnou, Y Papaharilaou, et al. Computational evaluation of aortic aneurysm rupture risk: What have we learned so far? *J Endovasc Ther.* 2011;18:214-225.
12. Vande Geest JP, Sacks MS, Vorp DA. A planar biaxial constitutive relation for the intraluminal thrombus in abdominal aortic aneurysms. *J Biomech.* 2006;39:2347-2354.
13. O'Leary S, Kavanagh EG, Grace PA, et al. The biaxial mechanical behaviour of abdominal aortic aneurysm intraluminal thrombus: classification of morphology and the determination of layer and region specific properties. *J Biomech.* 2014;47:1430-1437.
14. Tong J, Holzapfel GA. Structure, mechanics, and histology of intraluminal thrombi in abdominal aortic aneurysms. *Ann Biomed Eng.* 2015;43:1488-1501.
15. Wang DHJ, Makaroun M, Webster MW, et al. Mechanical properties and microstructure of intraluminal thrombus from abdominal aortic aneurysm. *J Biomech Eng.* 2001;123:536-539.
16. Martufi G, DiMartino ES, Amon CH, et al. Three-dimensional geometrical characterization of abdominal aortic aneurysms: Image-based wall thickness distribution. *J Biomech Eng.* 2009;131:061015.
17. Shum J, Di Martino ES, Goldhammer A, et al. Semi-automatic vessel wall detection and quantification of wall thickness in CT images of human abdominal aortic aneurysm. *Med Phys.* 2010;37:638-648.
18. Mensal B, Quadrat A, Schneider T, et al. MRI-based determination of reference values of thoracic aortic wall thickness in a generation population. *Eur Radiol.* 2014;24:2038-2044.

19. Joldes GR, Miller K, Wittek A, et al. A simple, effective and clinically-applicable method to compute abdominal aortic aneurysm wall stress. *J Mech Behav Biomed Mat.* 2015. DOI:10.1016/j.jmbbm.2015.07.029.
20. Reeps C, Maier A, Pelisek J, et al. Measuring and modelling patient-specific distributions of material properties in abdominal aortic aneurysm wall. *Biomech Model Mechanobiol.* 2013;12:717-733.
21. Richards JM, Semple S, MacGillivray TJ, et al. Abdominal aortic aneurysm growth predicted by ultrasmall superparamagnetic particles of iron oxide: a pilot study. *Circ Cardiovasc Imag.* 2011;4:274-281.
22. McBride OMJ, Berry C, Burns P, et al. MRI using ultrasmall superparamagnetic particles of iron oxide in patients under surveillance for abdominal aortic aneurysms to predict rupture or surgical repair: MRI for abdominal aortic aneurysms to predict rupture or surgery—the MA³RS study. *OpenHeart.* 2015;2: DOI:10.1136/openhrt-2014-000190.
23. Vande Geest JP, Di Martino ES, Bohra A, et al. A biomechanics-based rupture potential index for abdominal aortic aneurysm risk assessment: demonstrative application. *Ann NY Acad Sci.* 2006;1085:11-21.
24. Vande Geest JP, Sacks MS, Vorp DA. The effects of aneurysm on the biaxial mechanical behavior of human abdominal aorta. *J Biomech.* 2006;39:1324-1334.
25. O'Leary S, Healey DA, Kavanagh EG, et al. The biaxial biomechanical behaviour of abdominal aortic aneurysm tissue. *Ann Biomed Eng.* 2014;42:2440-2450.
26. Tong J, Cohnert T, Holzapfel GA. Diameter-related changes variations of geometrical, mechanical, and mass fraction data in the anterior portion of abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg.* 2015;49:262-270.
27. Miller K, Lu J. On the prospect of patient-specific biomechanics without patient-specific properties of tissues. *J Mech Behav Biomed Mat.* 2013;27:154-166.
28. Hyhlik-Dürr A, Krieger T, Geisbüsch P, et al. Reproducibility of deriving parameters of AAA rupture risk from patient-specific 3D finite element models. *J Endovasc Ther.* 2011;18:298-298.
29. Speelman L, Bohra A, Bosboom EMH, et al. Effects of wall calcifications in patient-specific wall stress analyses of abdominal aortic aneurysms. *J Biomech Eng.* 2007;129:1-5.
30. Li ZY, U-King-Im J, Tang TY, et al. Impact of calcification and intraluminal thrombus on the computed wall stresses of abdominal aortic aneurysm. *J Vasc Surg.* 2008;47:928-935.
31. Maier A, MW Gee, C Reeps, et al. Impact of calcifications on patient-specific wall stress analysis of abdominal aortic aneurysms. *Biomech Model Mechanobiol.* 2010;9:511-521.
32. O'Leary S, Mulvihill J, Barrett H, et al. Determining the influence of calcification on the failure properties of abdominal aortic aneurysm (AAA) tissue. *J Mech Behav Biomed Mat.* 2015;42:154-167.
33. Joshi NV, Vesey AT, Williams MC, et al. 18F-fluoride positron emission tomography for identification of ruptured and high-risk coronary atherosclerotic plaques: a prospective clinical trial. *Lancet.* 2014;383:705-713.