Computational Biomechanics-Based Rupture Predictions of AAAs

INVITED COMMENTARY

Computational Biomechanics-Based Rupture Prediction of AAAs

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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 others[4]; 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 others[9] 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 ILT[12-14] 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 work[13] 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-flurodexoyglucose (FDG) PET/CT[20] 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 increasing 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-applicable[19] 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.

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Conflicts of Interest

None.

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