Investigating the correlation between pulsatile-flow hemodynamics and aneurysm growth: a patient-specific, CFD study.

Alisa Selimovic[1], Roland Zoephel[2], Alexander Brawanski[2], Paul N. Watton[1]

[1]*Department of Engineering Science, University of Oxford, Oxford, UK*
[2]*Department of Neurosurgery, University of Regensburg Medical Centre, Regensburg, Germany*

Intracranial aneurysms (IAs) appear as sac-like out-pouchings of the arterial wall inflated by the pressure of the blood. Prevalence rates in populations without comorbidity are estimated to be 3.2%. Most remain asymptomatic; however, there is a small but inherent risk of rupture: 0.1% to 1% of detected aneurysms rupture every year. Subarrachnoid haemorrhage (SAH) due to aneurysm rupture is associated with a 50% chance of fatality and of those that survive, nearly half have long term physical and mental sequelae. Management of unruptured IAs by interventional procedures, i.e. minimally invasive endovascular approaches, or surgical clipping, is highly controversial and not without risk. Given the very low risk of IA rupture, there is both a clinical and an economic need to identify those IAs which are actually in need of intervention. Investigating the complex interplay of physical forces and their biological sequelae will aid further understanding of the formation and rupture of IAs and their management, and may lead to a cure. Computational models may yield insight into the aetiology of the disease and offer the potential to aid clinical decisions.

In particular, the focus of many recent computational fluid dynamics (CFD) studies has been the link between specific hemodynamic conditions, and aneurysm inception and growth. With regards to aneurysm growth, two main and conflicting theories have emerged: the first is that *low* wall-shear stress[1] (WSS) drives aneurysm growth, while the second is that *high* WSS[2] drives aneurysm growth. In the case of aneurysm inception, several pulsatile-flow indices –the Oscillatory Shear Index (OSI) [3], the Aneurysm Formation Indicator (AFI) [4], and the Gradient Oscillatory Number (GON) [5] –have been proposed in an attempt to identify regions susceptible to aneurysm formation.

In this study, a novel algorithmic, automated method was developed to quantify the growth of an IA that had evolved over a two year period. This entailed two challenges: the first, to align two geometries obtained at different time-points (the position of which varies according to the patient's position in the scanner), and the second to devise a displacement, or "growth scalar" (GrS) index to capture both the amount and direction of growth of the aneurysmal wall. Briefly, images of real patient vasculature (taken in 2008 and 2010) were obtained. An algorithm was devised to automatically translate and rotate the geometries so as to achieve consistent alignment with respect to a common reference coordinate system. The aneurysm domes were isolated by segmentation using @neufuse[6] segmentation software.

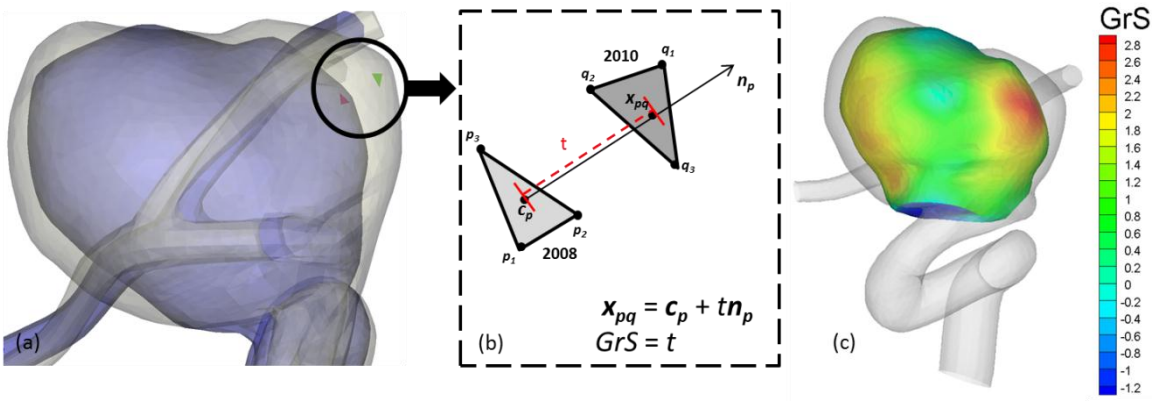

Figure 1: (a) 2008 and 2010 domes, with two corresponding elements highlighted; (b) The GrS equates to the distance, *t*, between the centrepoint of the 2008 element and the point of intersection between the 2008 element normal, $\boldsymbol{n_p}$, and the corresponding 2010 element; (c) Colour map showing the GrS, plotted on the 2008 dome, with the 2010 geometry overlaid

An algorithm was then applied to automatically calculate growth of the aneurysm dome over the two year period (see Fig 1 above). The "amount" of growth corresponds to the perpendicular distance between the centrepoint of each element on the 2008 geometry, and the intersection point of the normal of that element, with an element on the 2010 geometry. The "direction" of growth relates to whether the intersection point is located on the inner or outer side of the 2008 geometry. Hence, a positive GrS indicates outward growth, while a negative GrS indicates inward growth of the 2008 geometry surface over the 2-year period.

The method for solving the pulsatile-flow hemodynamics is as follows. Each geometry was imported into ANSYS ICEM (ANSYS Inc, Canonsburg, PA) and an unstructured, tetrahedral mesh with prism layers lining the boundaries was generated for the fluid domain. After meshing, pulsatile flow and pressure boundary conditions were taken from a 1D model of the arterial tree[7], which has been integrated into @neufuse. The flow was then solved using ANSYS CFX (ANSYS Inc, Canonsburg, PA) which solves the incompressible Navier-Stokes equations using a finite volume formulation[8]. Blood was modeled as a Newtonian fluid, and a no slip condition was applied at the arterial wall.

In this study, alongside WSS and the WSS gradient, the OSI, AFI and the GON were investigated in the context of aneurysm growth.

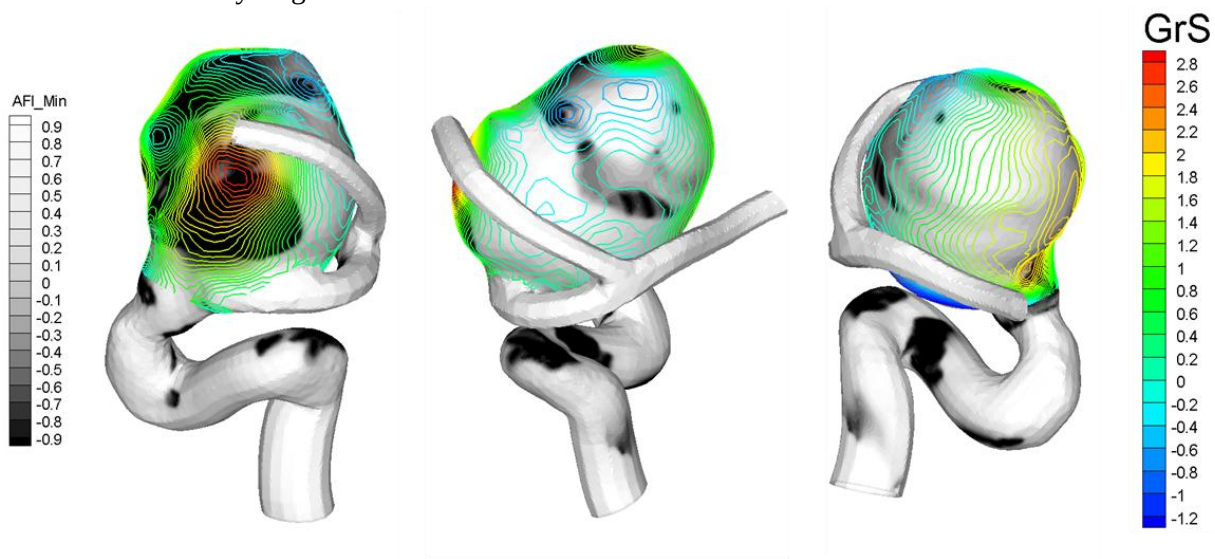

Figure 3: Plot of growth scalar (rainbow contour map, range -1.3mm to 3mm) compared with a plot of the AFI (black and white map, range -1 to 1) on the 2008 geometry, shown in three orientations

In this study, the AFI showed the best correlation with regions of aneurysm growth. Interestingly, some regions of the 2008 dome showed a negative GrS, which suggests that growth and remodeling of aneurysmal tissue may not be strictly outward.

Conclusion

Interestingly, this study did not show a clear correlation between neither low, nor high WSS. Rather, it appears that growth has occurred in regions where there is high oscillation in the direction of the WSS vector. However, while these results are interesting, the algorithm has only been applied to a single case; an examination of a larger set of geometries is needed. The adaptability and ease of implementation of the GrS algorithm will facilitate an investigation on a larger number of cases. The model is purely heuristic, and examination is focused on wall-shear stress, and shear-stress-derived indices. It is likely that the influence of blood pressure on wall tensile stress is also a key factor in the growth and remodeling of the aneurysmal wall, and thereby merits investigation. Furthermore, as with many image-based CFD-studies, the quality of the images, and the usual assumptions of rigid-walls and Newtonian flow may influence the results of hemodynamics simulations. Finally, fundamental to the usefulness of CFD studies is a greater understanding of the mechanobiological events that underlie aneurysm development. As such, improved models of endothelial cell mechanobiology –particularly in pathophysiological conditions –are needed to progress this research.

References

1. Doenitz, C., Schebesch, K.-M., Zoephel, R., & Brawanski, A., 2010, *A mechanism for the rapid development of intracranial aneurysms: a case study*, Neurosurgery, *67*(5), 1213-21
2. Meng, H., Wang, Z., Hoi, Y., Gao, L., Metaxa, E., Swartz, D. D., & Kolega, J., 2007, *Complex hemodynamics at the apex of an arterial bifurcation induces vascular remodeling resembling cerebral aneurysm initiation*, Stroke, *38*(6), 1924-31
3. Ku, D. N., Giddens, D. P., Zarins, C. K., & Glagov, S., 1985, *Pulsatile flow and atherosclerosis in the human carotid bifurcation. Positive correlation between plaque location and low oscillating shear stress, Arteriosclerosis, Throbmosis, and Vascular Biology* (Dallas, Tex.), *5*(3), 293-302
4. Mantha, A., Karmonik, C., Benndorf, G., Strother, C., & Metcalfe, A. (2006). *Hemodynamics in a Cerebral Artery before and after the Formation of an Aneurysm*, Ajnr. American Journal Of Neuroradiology, *27*, 1113-18.
5. Shimogonya, Y., Ishikawa, T., Imai, Y., Matsuki, N., & Yamaguchi, T., 2009, *Can temporal fluctuation in spatial wall shear stress gradient initiate a cerebral aneurysm? A proposed novel hemodynamic index, the gradient oscillatory number (GON)*, Journal of biomechanics, *42*(4), 550-4
6. Villa-Uriol, M.C., Berti, G., Hose, D. R., Marzo, A., Chiarini, A., Penrose, J., Pozo, J., Schmidt, J. G., Singh, P., Lucett, R., Larrabide, I., Frangi, A. F., 2011, *@neurist complex information processing toolchain for the integrated management of cerebral aneurysms*, Interface Focus 1, 308-319
7. Reymond, P., Merenda, F., Perren, F., Rüfenacht, D., Stergiopulous, N., 2009, *Validation of a one-dimensional model of the systemic arterial tree*, AJP: Heart and Circulatory Physiology 297, H208-H1182
8. Patakar, H.S., 1980, *Numerical Heat Transfer and Fluid Flow (Hemisphere Series on Computational Methods in Mechanics and Thermal Science)*, Taylor & Francis