PROFESSOR DANIEL RÜFENACHT ON THE SWISSNEUROFOUNDATION-ANEURYSMDATABASE – WHICH OFFERS SHAPE-BASED CATEGORISATION LIBRARY SERVICES, AND CABMM EFFORTS TOWARDS ANEURYSM DISEASE UNDERSTANDING

The shape of things to come

Numerical assessment and simulation, as a 'virtual reality' method for better disease understanding, risk prediction, and planning endovascular treatment of aneurysm disease has, in recent years, received increasing attention by engineering and medical, as well as by basic and clinical scientists. Mathematically describing the shape of a diseased vascular segment, including an aneurysmal out-pouching, may become an image biomarker of such destructive arterial degeneration. These concepts, developed in the FP6 and FP7 VPH IT-project, are well received and have become implemented by translational efforts such as those produced by the CABMM and the SwissNeuroFoundation-AneurysmDataBase activities.

Intracranial aneurysm disease presents with a low but risky incidence of haemorrhage (10/100,000/y) due to rupture, while there is a high prevalence of silent lesions (approx. 3,000/100,000), that are increasingly found incidentally during regular brain imaging evaluations. Once diagnosed, the incidental finding of an aneurysm leads to the difficult question of whether or not to treat a patient to prevent them from experiencing a risky aneurysm bleeding.

With diagnosis based on imaging information alone, use of an image disease surrogate (i.e. a computational phantom or indices), would be welcome and efficient in many ways. The wall of an aneurysm being too thin to be directly visualised by current imaging methods, and the characterisation of its biomechanical strength, is a matter of indirect assessment. While in normal arteries the rules of mechanobiological transduction govern the interaction of blood flow and vessel wall strength by using shear and pressure as information, sensed and translated by cellular elements of the vessel wall, this transduction capability is lost in the largely decellularised, pathological aneurysm wall.

Fig.1 Professor Daniel Rüfenacht (right)

Pathological pathways

In the normal artery, increased flow mediated shear leads to enlarged lumen and increased blood pressure to wall thickening. In the diseased wall, however, where stepwise the cellular elements are lost, the ambassadors transducing mechanical signals in biological signals have vanished and different, pathological pathways now apply and govern the situation. These pathways have largely been unravelled by research in atherosclerosis and through observations of human intracranial aneurysms.

The process starts with flow-induced thrombus adhesion (atherothrombosis) to the wall, leading secondarily to the release of biological mediators of inflammation and ensuing destructive remodelling. Loss of mechanical wall integrity is followed by pressure-related ballooning-out, with increasing risk of rupture. Such mechanisms of destructive wall remodelling jeopardise the mechanical wall integrity, and often lead to only circumscribed softening, possibly uneven aneurysm expansion, and consequently to an irregular aneurysm shape.

These are the critical steps of the mechanobiological transduction chain in aneurysm disease as it is currently understood. Further illumination of the exact interconnection of these steps encompassing an 'aneurysm lifecycle' (see Fig. 2) is a matter of continuous research. This involves a variety of validation and computational biology studies, with the potential of further unravelling the secrets of this degenerative arterial disease, in the interest of understanding and developing predictive *in*

silico capabilities to estimate the evolution potential of an incidental aneurysm, and with the potential of simulating and designing flow-modulating corrective endovascular measures.

In summary, current concepts of mechanobiological transduction in aneurysms suggest that initial local wall quality and local blood flow conditions are inducing a complex inflammatory cascade, governing wall remodelling by multiple biological steps. These biological processes are further investigated at the CABMM in collaboration with medical centres, public and private funding and industrial support.

Actual aneurysm status

With wall inflammation yet being difficult to capture directly by current medical imaging techniques, the morphological appearance of an aneurysm is used as an indicator of wall quality. At any point, imaging of the vessel lumen, and where present, of intraluminal wall adherent thrombus, are used to assess the actual aneurysm status. In general, it is assumed that regular aneurysm surfaces mirror stability, whereas irregularities indicate areas of instability, of locally prevailing areas of destructive remodelling. Therefore, with currently used medical imaging evaluation methods for aneurysms, which are able to provide flow-based and contrast material-enhanced visualisation of the circulating blood, a precise digital 3D replica of the vascular lumen is produced for more detailed analysis.

In the FP6-ANEURIST project (by the University Pompeu Fabra), methods of aneurysm shape analysis using Zernike moments were introduced and tested positively. Being automated and reproducible, this method is time efficient and can be used to categorise all aneurysms.

Promise

A method holding the promise towards image biomarker for personalised aneurysm assessment has been found. FP7-VPH-SHARE (University of Sheffield) is supporting on-going translation of this method towards the continuation of a growing AneurysmDataBase, a library that will be open for researchers and regulation purposes. The library is now under the auspices of the SwissNeuroFoundation and endorsed by a large international community with interest in this field, and having an annual ICS meeting since 2004. ICS initially stood for

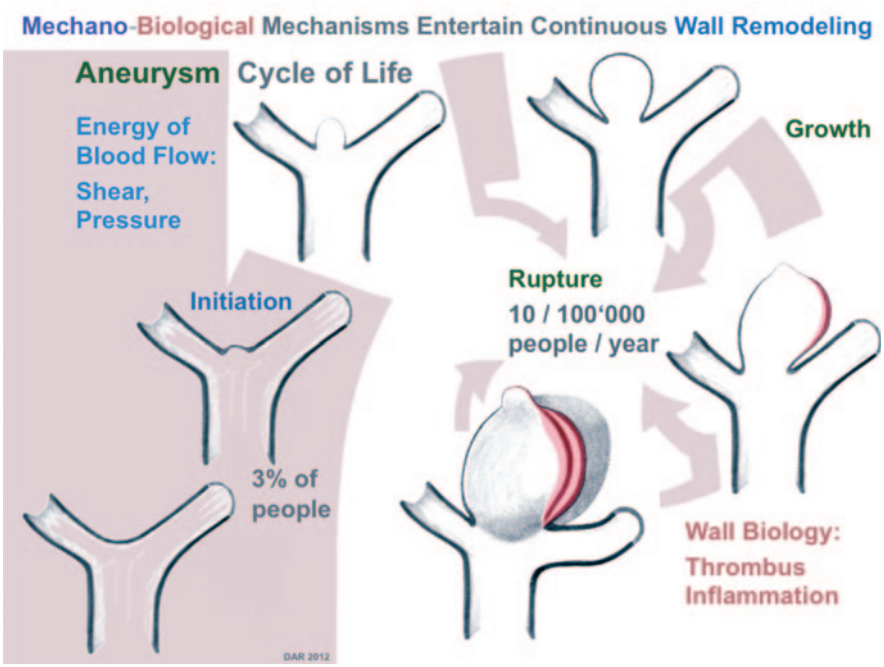

Fig. 2

ICS 2014

IntraCranialStent and later also for International Cerebrovascular Symposium, and is welcoming as many PhDs as MDs providing a balanced platform to discuss and to make progress towards translational issues. The ICS is next set to meet on 2-4 June 2014 at Technopark, Zurich.

Today, shape analysis methods have become robust and allow for personalised morphological description of any individual aneurysm. Shape analysis has become the most promising instrument for characterising reproducible intracranial aneurysms, potentially allowing for the prediction of their evolution in an individual case. Therefore, this method holds the promise of becoming an image biomarker to aid in predicting rupture risk besides providing a method of identifying comparable lesions, as may be required when it comes to assessing results in databases and registries.

The service of shape analysis is offered by the SwissNeuroFoundation-AneurysmDataBase, where a library will be accessible for research and regulation purposes. The translational effort requiring further validation efforts continues to be supported by activities at the CABMM and acknowledges generous support provided by FP6 and FP7, the Swiss National Science Foundation, the ZHAW, and clinical research support offered by centers including the University Clinics of Geneva, Sheffield, Essen, Berlin, Helsinki and Kuopio, and the Interventional Work Research group of Clinic Hirslanden.

HIRSLANDEN
KLINIK HIRSLANDEN

The University Of Sheffield.

Professor Daniel Rüfenacht
Center for Applied Biotechnology and Molecular Medicine (CABMM)
University of Zurich

browse www.cabmm.uzh.ch