Travis C. Valentine Memorial Aneurysm Research Fund

George Mason University

2019 Annual Research Report

During the past year, we have made significant progress towards better assessment of cerebral aneurysm rupture risk. In particular, we have completed the following studies:

a) External validation of probabilistic rupture models: we evaluated and validated predictive models constructed with our database of 2000 aneurysms from the US population (training set) using data of about 260 aneurysms from two other databases from Europe (external testing set). The results showed good performance of the model with approximately 82% accuracy in discriminating between ruptured and unruptured aneurysms. This study was published in Acta Neurochirurgica.

b) Extension of rupture models to other populations: we also tested the rupture probability model on a database from Finland and another from Japan. The objective of this study was to evaluate the predictive power of our statistical models on data from these populations that are known to have higher risk of aneurysm rupture. The results indicated that it is necessary to incorporate data from these populations to extend the models and achieve similar performance as with the US and European populations. This study was published in Neurosurgical Focus.

c) Evaluation of Machine Learning for aneurysm assessment: we investigated whether more sophisticated Machine Learning approaches could improve the discriminatory power and overall accuracy of the statistical rupture probability models. We found that our statistical approach was among the best predictors of aneurysm rupture and that some more sophisticated Machine Learning approaches only gave a slightly higher accuracy. We published this study in International Journal of Computer Assisted Radiology.

d) Incorporation of flow variability into the rupture models: since flow conditions change during the day according to the patient's activity, it is important to develop models that incorporate this variability into the risk assessment process, making them more robust. For this purpose, we performed over 10,000 simulations (5 flow conditions for each of the 2,000 aneurysms in our database) to characterize the variability of hemodynamic parameters and incorporate them into the rupture probability models. We showed that using this information it is possible to construct statistical models that are robust against flow variability and that can therefore be used when patient-specific flow conditions are not known. We published these results in Acta Neurochirurgica.

e) Analysis of hemodynamic evolution from aneurysm inception to rupture: we continued investigating how flow conditions change from the time of aneurysm formation to the final stages of aneurysm rupture or stabilization. This information is important for improving our understanding of mechanisms responsible for aneurysm wall degeneration and weakening and for enabling new therapeutic strategies targeting specific pathways involved in aneurysm wall degradation. We found that flow conditions evolve differently if the aneurysm neck grows as the aneurysm enlarges instead of staying unchanged. In particular, we believe the aneurysm progresses towards a more adverse environment if the neck enlarges as the aneurysm grows. This work is under revision in the International Journal for Numerical Methods in Biomedical Engineering.

In addition, we have made progress with our two NIH projects, one focusing on combining data from multiple sources to identify different aneurysm wall characteristics and relate them to the local hemodynamic environment (in collaboration with University of Pittsburgh, Allegheny General Hospital, University of Illinois at Chicago Medical Center, and Helsinki University Hospital, Finland); the other focusing on developing computational models to understand the effects of intra-aneurysmal flow diverting devices (such as the Woven Endo Bridge or WEB device) being under development for the treatment of wide-necked aneurysms located at arterial bifurcations. These studies resulted in four additional journal papers over the last year.

Future Plans

Our research plans for the next year include:

a) Analysis of aneurysm blebs: presence of blebs or secondary lobulations are considered a risk factor for aneurysm rupture. However, preliminary data based on surgical videos and ex-vivo imaging of aneurysm tissue samples suggest that blebs can have different wall structures and thickness. This could indicate that blebs form under different biomechanical stimuli and can have different associated risks. Thus, we will identify aneurysms with blebs in our database and compare their geometrical, hemodynamic and patient characteristics. We intend to develop a grant proposal (to the NIH) based on these ideas.

b) Analysis of local aneurysm wall characteristics and hemodynamics: intra-operative surgical videos show that different aneurysms can have very different walls, some with thin translucent walls that appear red in the videos, and others with thick yellow or white walls which have undergone atherosclerotic remodeling. Thus, we will investigate the association between different wall structures and the local flow conditions in order to better understand the mechanisms associated with these changes in the aneurysm wall and ultimately their associated rupture risk.

c) Analysis of local hemodynamics and aneurysm wall enhancement: recently it has been proposed that changes in the aneurysm wall permeability and inflammation can be observed in so called aneurysm wall enhancement sequences in magnetic resonance images. We are collaborating with a group at the University of Iowa that has obtained such images at 7T in patients with cerebral aneurysms. We will analyze the possible association between local flow conditions and aneurysm wall enhancement to understand the effects of these flow conditions, as well as to better interpret the significance of these imaging techniques.

Use of Funds

During the last year funds from the Travis C. Valentine Memorial Aneurysm Research Fund were used to:

1) Support two Graduate Research Assistants (GRAs) during the summer, which allowed these PhD students to focus on some of the research activities described above (specifically statistical model construction and analysis of aneurysm evolution). One of the GRAs successfully defended her PhD thesis, and is now currently a postdoc at Harvard Medical School.

2) Travel to international conferences to present results from our research. This included:
    a. International Cerebrovascular Symposium (ICS2019), Iowa City, Iowa: Dr. Cebral gave an invited talk focusing on aneurysm rupture risk assessment.
    b. Computational and Mathematical Biomedical Engineering (CMBE2019), Sendai, Japan: Dr. Cebral delivered two talks, one on aneurysm rupture assessment, and another on modeling endovascular procedures for cerebral aneurysm treatment.
    c. Summer Bioengineering, Biomechanics and Biotransport Conference (SB3C), Seven Springs, Pennsylvania: Graduate Research Assistant and Dr. Cebral presented 5 studies, 2 oral presentations and 3 poster presentations.
    d. Computer Assisted Radiology Society (CARS), annual meeting, Rennes, France: Graduate Research Assistant presented the external validation of rupture probability models and the evaluation of machine learning algorithms.

3) Cover publication costs of a paper in American Journal of Neuroradiology.

In the near future, we plan to continue using these funds to cover travel to international conferences, as well as research visits to collaborating institutions, publication costs (including journal papers and conference posters), as well as summer support for PhD students and faculty.

The funds provided by the Travis C. Valentine Memorial Aneurysm Research Fund are very valuable and are greatly appreciated because they allow us to focus immediately on research issues that are not currently supported by other grants or projects, which have a high potential impact and could also lead to future funding from NIH.