Travis Valentine Memorial Brain Aneurysm Research Fund

Research Update, Dr. Juan Cebral – July 30th, 2018

The funds provided by the Valentine Memorial Fund are very valuable and greatly appreciated. Support for the Travis fund allows 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.

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:

1) Analysis of aneurysm stability and rupture: in this study we identified aneurysm hemodynamic and geometric parameters associated with aneurysm instability and rupture. Briefly, we found that high flow activity within the aneurysm, characterized by strong inflow jets, complex and unstable flow patterns, and non-uniform wall shear stress distributions are associated with both aneurysm instability and rupture. These results have will appear in the American Journal of Neuroradiology (AJNR).
2) Probabilistic models of aneurysm rupture at the PCOM artery: in this study we consider aneurysms at a single (but dangerous) location, the posterior communicating artery or PCOM. Using all aneurysms of our database at this location, we built a statistical model of aneurysm rupture, i.e. the model provides a probability that a given aneurysm belongs to the ruptured or unruptured groups. We showed that these models can discriminate between these types of aneurysms with an accuracy of approximately 85%. These results will appear in Acta Neurochirurgica.
3) Probabilistic models of aneurysm rupture at multiple locations: in this study we constructed a statistical model based on hemodynamic, geometric, anatomical and patient characteristics to compute the probability that an aneurysm belongs to the ruptured or unruptured group using our entire database of more than 2000 aneurysms. We showed that these models can discriminate ruptured (high risk) from untuptured (low risk) aneurysms with approximately 86% accuracy. These models can be the basis for improved evaluation of cerebral aneurysm rupture risk. These results will appear in the International Journal of the Computed Assisted Radiology Society (IJCARS).
4) MATCH challenge: we participated in a challenge study in which different research groups were asked to identify in a patient with 5 cerebral aneurysms, the aneurysm that was most likely the ruptured one. We applied our statistical models to assess the relative risk of rupture of each aneurysm and selected the one with the highest probability, which happened to be the correct choice and coincided with the actual ruptured aneurysm. This result was presented at the International Cerebrovascular Symposium in Magdeburg, Germany.
5) Analysis of hemodynamic changes during aneurysm evolution: in this study, we analyzed how blood flow characteristics, which presumably are connected to mechanisms of wall degeneration and weakening, change as the aneurysms enlarge. The main finding was that the hemodynamic evolution is different if the aneurysm orifice enlarges as the aneurysm grows or not. Aneurysms with enlarging orifices or necks progress more rapidly towards adverse hemodynamic environments and may result in destabilization and rupture. Preliminary results at a single location were presented at the World Congress of Biomechanics in Dublin Ireland, and will be submitted for publication to a journal once we complete the analysis at other locations.

6) Analysis of aneurysm shape irregularity: aneurysm irregularity has been proposed as an aneurysm characteristic associated with rupture, but assessment of irregularity has been done visually and subjectively. In this study we developed a statistical model of aneurysm shape irregularity based on shape indices that are calculated automatically and objectively. Using this approach we tested whether irregularity was able to discriminate between ruptured and unruptured aneurysms, and found that it can do so but with moderate accuracy (approximately 75% of cases are correctly classified). This implies that other characteristics such as aneurysm location and hemodynamics should be included in rupture risk models. These results will be submitted for journal publication.

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.

Future Plans

Our research plans for the next year include:

a) External validation of rupture models: we will evaluate and validate predictive models constructed with our database of 2000 aneurysms (training set) using data from other external databases (testing sets) such as the Aneurisk database and the AneuX database that contain approximately 100 cases each. We will also test the models on a Finnish database provided by one of our clinical collaborators in Finland. The objective of this study is to evaluate the predictive power of our statistical models on aneurysm data that was not used to construct these models (i.e. external validation).
b) Incorporate 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 are robust and incorporate this variability into the risk assessment process. We plan to work with our collaborators at the Barcelona Supercomputing Center in Spain to run all our aneurysm models under different flow conditions (i.e. 10's of thousands of simulations) and add the flow variability information into our predictive models.
c) Build a web-based aneurysm risk assessment tool: in order to facilitate the use of our statistical models and the data stored in our database, we plan to develop a web-based system for the assessment of aneurysm rupture risk based on aneurysm location, geometry, hemodynamics and patient demographics. The ultimate objective of this effort is to translate the findings and information to the clinical practice to identify high risk aneurysms that need immediate intervention and low risk aneurysms that could be safely be conservatively followed.
d) Analysis of hemodynamic evolution from aneurysm inception to rupture: we will continue 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.

Support from the Valentine Memorial Fund

During the last year funds from the Valentine Memorial Fund were used to:

1) Support two Graduate Research Assistants (GRAs) during the summer, which allowed these PhD students (Ms. Felicitas Detmer and Ms. Setareh Salimia) to focus on some of the research activities described above (specifically statistical model construction and analysis of aneurysm evolution).
2) Travel to international conferences to present results from our research. This included:
    a. International Cerebrovascular Symposium (ICS2018), Magdeburg, Germany: Ms. Detmer presented results of the MATCH challenge and Dr. Cebral presented results related to rupture risk assessment based on statistical models.
    b. Computer Assisted Radiology Society (CARS), annual meeting, Berlin, Germany: Ms. Detmer presented the development and internal validation of rupture probability models for aneurysms at multiple locations.
    c. World Congress of Biomechanics (WCB2018), Dublin, Ireland: Dr. Cebral gave a keynote lecture presenting statistical rupture prediction models as well as relationships between local hemodynamic conditions and aneurysm wall characteristics. Ms. Salimia presented a poster describing the findings related to hemodynamic evolution of aneurysms at a single location.
3) Cover publication costs of a paper in AJNR describing a study of the hemodynamic characteristics in stable, unstable and ruptured aneurysms.

In the near future, we plan to continue using these funds to support PhD students and faculty, travel to international conferences to present research findings, as well as research visits to collaborating institutions, and publication costs (including journal papers and conference posters) to disseminate research results of activities supported by the Valentine memorial research fund.