Research Highlights – 2025

Summary

During the past year (2024) we studied the hemodynamic conditions that are associated with aneurysm wall vulnerability which result in aneurysm growth and rupture. The primary objective is enhancing aneurysm management decisions by improving our understanding of the underlying processes driving aneurysm weakening and rupture. In parallel, we studied the effects of endovascular interventions using flow diverting stents to better understand the healing process and potential complications, with the goal of improving outcomes by optimizing devices and interventions.

These efforts resulted, in the period Jan 2024-Aug 2025, in 9 published journal papers, and 4 papers related to ischemic stroke studies conducted in parallel, 14 conference presentations, 9 invited talks, as well as an article in Forbes Argentina magazine.

In addition, we hosted the Computational and Mathematical Bioengineering Conference (CMBE 2024) at the Mason Arlington Campus June 24-26, 2024, and organized a mini-symposium on Cerebral Aneurysms. In collaboration with our colleagues from the Departments of Mathematics and Physics of the College of Science at Mason, we co-organized a conference on Digital Twins and delivered a talk on digital twins in the biomedical field. We also participated in the Scientific Committee of the Intracerebral Cerebrovascular Symposium which was held in Buffalo, New York July 31-Aug 2, 2025, and delivered 2 invited talks. Prof. Cebral was awarded a 2025 Faculty Excellence Award in Research by the College of Engineering and Computing, George Mason University, April 2025 and one of his collaborators from Pittsburgh won the 2025 Best Poster Award at the Interdisciplinary Cerebrovascular Symposium: Abdurakhmonov M, Robertson AM, Tobe Y, Cebral JR, et al. P, "Effect of regional hemodynamics to wall thickness heterogeneity in human intracranial aneurysms".

Understanding Aneurysm Wall Remodeling

We conducted several studies that relate local flow conditions and aneurysm wall properties. For this purpose, we constructed patient-specific computational models of aneurysms from pre-surgical 3D images, conducted blood flow simulations, and quantified several hemodynamic parameters at the aneurysm wall. In parallel, we analyzed videos obtained during open surgery interventions where aneurysm wall characteristics could be assessed by their appearance in the videos. For instance, thin fragile walls appear as red translucent regions, while thick walls appear as white regions, and atherosclerotic walls containing lipids appear as yellow regions. Using this information, we found that thin regions tend to occur in locations of high flow conditions and flow impingement zones, while thick or atherosclerotic regions tend to occur in locations with slow recirculating flow and vortical swirling. These results provide valuable information to help identify flow conditions that favor either thinning or thickening of the wall, and thus to assess the likelihood of further wall weakening, aneurysm progression or rupture. These studies have been reported in a series of 5 journal papers.

Understanding the Role of Vasa Vasorum

Using advanced ex-vivo imaging techniques in collaboration with our colleagues from the University of Pittsburgh aneurysm tissue samples resected during surgery were imaged with high-resolution multi-photon microscopy where small vessels irrigating the aneurysm wall (so called vasa vasorum or vessels of

vessels) were detected. Furthermore, it was found that the density of vasa vasorum vessels was denser in regions of thickened aneurysm walls. To explain this correlation, we developed a computational model that demonstrated that the vasa vasorum in these cases may develop to supply adequate levels of oxygen to the aneurysm wall which otherwise would exhibit hypoxia (lack of oxygen) due to its locally increased thickness. These findings suggest a positive role of the vasa vasorum during aneurysm growth, but it can also act as a conduit for infiltration of inflammatory cells which can result in wall damage. These results were reported in two journal papers. Further studies are needed to fully understand these processes, their relative importance, and their effect on the vulnerability of the aneurysm wall.

These studies have been conducted in collaboration with Bioengineers from University of Pittsburgh, and Neurosurgeons from University of California Los Angeles (UCLA), Allegheny General Hospital (AGH, Pittsburgh), University of Illinois at Chicago (UIC), Northwell Hospital (New York), and University Hospitals Cleveland (UHC).

Understanding Complications Associated with Endovascular Interventions of Cerebral Aneurysms

Using our recently developed model of fibrin accumulation and clot formation after deployment of flow diverting stents used to treat cerebral aneurysms, we investigated the potential adverse effects associated with jailing or partial occlusion of side branches. We found that even though jailed side branches are observed to remain open in angiography images acquired after stent deployment, there is consistently a substantial fibrin accumulation on the device wires at the origin of these branches which can potentially result in a branch occlusion and stroke. This finding is consistent with experimental results obtained in rabbits by implantation of flow diverting devices in the rabbit superior mesenteric artery jailing several smaller side branches. These experiments were performed at the Mayo Clinic by our collaborators and demonstrated significant tissue coverage of the side branch origin while remaining angiographically open except in one case that the branch was fully occluded. These results suggest further studies to improve flow diverting devices to prevent these negative effects and not to fully rely on angiographic images alone to evaluate the technical success of interventions. These findings have been reported in one paper under review and another in preparation.

Future Plans

Our future research plans include: a) investigation of the effects of flow stagnation on aneurysm stability and rupture, b) study effects of heterogeneous walls with thin and thick regions on the distribution of intramural stresses that ultimately result in wall failure, c) further investigating the association of flow structures including vortices, jet impingement, and flow stagnation with changes in the wall structure and strength, d) understanding the mechanisms of magnetic resonance wall enhancement which could be potentially used to assess the status of the aneurysm wall, and e) developing models of endothelial cell coverage of devices, which is an important process involved in the healing response to the implantation of endovascular devices.

Journal papers

1. Abdurakhmonov M, Tobe Y, Cebral JR, Asadbeygi A, Ramenzanpour M, Zamani M, Watkins SC, Phillippi JA, Yu A, Amin-Hanjani S, Charbel F, Kaneko N, Cheng B, Dehdashti A, White T, Robertson AM, “Vasa vasorum plexus formation in intracranial aneurysm associates with microcalcification and wall thickening”, Science Advances, 2025 – accepted.

2. Karnam Y, Mut F, Yu A, Cheng B, Amin-Hanjani S, van Keulen M, Charbel F, White T, Niemelä M, Tulamo R, Rezai Jahromi B, Frösen J, Tobe Y, Robertson AM, Cebral JR, “Intracranial Aneurysm Wall Phenotypes: Clinical, Morphological, and Hemodynamic Influences”, Stroke: Vascular and Interventional Neurology, 2025 – accepted.
3. Cebral JR, Mut F, Lohner R, Mukhayyirkhuja A, Ramezanpour M, Tobe Y, Robertson AM, “Analysis of the Role of Vasa vasorum in the Oxygen Transport to the Aneurysm Wall“, IJNMBE, 41(6): e70051, 2025 (DOI: 10.1002/cnm.70051).
4. Ramezanpour M, Robertson AM, Tobe Y, Jia X, Cebral JR. “Phenotyping calcification in vascular tissues using artificial intelligence”. ArXiv [Preprint]. 2024 Jan 17:arXiv:2401.07825v2.
5. Cebral JR, Mut F, Lohner R., Marsh L, Chitsaz A, Bilgin C, Bayraktar E, Kallmes D, Kadirvel R, “Influence of Vessel Geometry, Flow Conditions, and Thrombin Concentration on Fibrin Accumulation and Cerebral Aneurysm Occlusion after Flow Diversion”, IJNMBE 41(1): e3904, 2025 (DOI: 10.1002/cnm.3904).
6. Cebral JR, Mut F, Lohner R., Marsh L, Chitsaz A, Bilgin C, Bayraktar E, Kallmes D, Kadirvel R, “Modeling Fibrin Accumulation on Flow Diverting Devices for Intracranial Aneurysms”, IJNMBE, 40(12): e3883, 2024 (DOI: http://doi.org/10.1002/cnm.3883).
7. Karnam Y, Mut F, Robertson AM, Cebral JR, "Competing Pathways of Intracranial Aneurysm Growth: Linking Regional Growth Distribution and Hemodynamics," Journal of Neurosurgery, 142(6):1741-1750, 2025 (DOI: 10.3171/2024.9.JNS241208).
8. Karnam Y, Mut F, Yu AK, Cheng B, Amin-Hanjani S, Charbel FT, Woo H, Niemela M, Tulamo R, Rezai Jahromi B, Frosen J, Tobe Y, Robertson AM, Cebral JR, "Description of the local hemodynamic environment in intracranial aneurysm wall subdivisions", IJNMBE, 40(8):e3844, 2024 (DOI: 10.1002/cnm.3844).
9. Karnam Y, Mut F, Yu AK, Cheng B, Amin-Hanjani S, Charbel FT, Woo H, Niemela M, Tulamo R, Rezai Jahromi B, Frosen J, Tobe Y, Robertson AM, Cebral JR, “Distribution of Rupture Sites and Blebs on Intracranial Aneurysm Walls Suggests Distinct Rupture Patterns in ACom and MCA Aneurysms”, IJNMBE, 40(8): e3837, 2024 (DOI: 10.1002/cnm.3837).

Journal papers related to stroke

10. Pradhan AM, Mut F, Sosale M, Cebral JR, “Flow Reduction Due To Arterial Catheterization During Stroke Treatment – A Computational Study Using a Distributed Compartment Model”, IJNMBE, 40(10): e3853, 2024 (DOI: 10.1002/cnm.3853).
11. Jreij G, Canton G, Hippe DS, Balu N, Crone C, Sikdar S, Cebral JR, Hatsukami T, Gray V, Desikan S, Beach K, Lal BK, “Biomechanical forces associated with carotid plaque disruption and stroke: a systematic review”, J Vas Surg, S0741-5214(25) 01043-2, 2025 (DOI: 10.1016/j.jvs.2025.05.014).
12. Marsh L, Lohner R, Abou-Mrad T, Stone McGuire L, Charbel FT, Cebral JR, “Modeling Hemodynamic Effects of the Closure Procedure of Carotid Artery Endarterectomy”, IJNMBE 41(5): e70048, 2025 (DOI: doi.org/10.1002/cnm.70048).
13. Abou-Mrad T, Stone McGuire L, Marsh L, Cebral JR, Charbel F, “A Pilot Study on the Hemodynamic Changes and Restenosis Risk in Carotid Endarterectomy: To Patch or Not to Patch, Is that the Real Question?”, Journal of Neurosurgery: Case Lessons, 9(14): CASE24824, 2025 (DOI: doi.org/10.3171/CASE24840).

Conference Presentations

1. Abdurakhmonov M, Robertson AM, Tobe Y, Cebral JR, Marsh L, Kaneko N, Amin-Hanjani S, Asadbeygi A, Zamani M, Angrawal Y, Morel S, Vouilamoz A, Sandralegar A, Juchler N, Bochaton-Piallat, ML, Kwak B, Bijlenga P, “Effect of regional hemodynamics to wall thickness heterogeneity in human intracranial

aneurysms", Interdisciplinary Cerebrovascular Symposium, Buffalo, NY, July 31-Aug 1, 2025 [Best poster award].

2. Karnam Y, Mut F, Robertson AM, Cebral JR, "Characterizing Local Hemodynamics and Wall Features in Intracranial Aneurysms Walls", BMES, Baltimore, MD, Oct 23-26, 2024.
3. Aryan, Marsh L, Cebral JR, Kaneko N, "The Role of Contrast Stagnation in Identifying Ruptured Cerebral Aneurysms through Digital Subtraction Angiography", WFITN, New York, Oct 6-10, 2024.
4. Abou-Mrad T, McGuire L, Marsh L, Cebral JR, Charbel F, "Hemodynamic changes and restenosis risk in carotid endarterectomy: the patching dilemma", SNIS, 2024-A-28-SNIS, Colorado Springs, CO, July 22-26, 2024.
5. Kaneko N, Selim O, Cebral JR, Komuro Y, Tateshima S, Guo L, Villablanca JP, Tobe Y, Robertson AM, Duckwiler G, Hinman J, "Endothelial Inflammation Induced By Vortex Flow In Patient-derived 3d Intracranial Aneurysm Models" SNIS, 2024-A-434-SNIS, Colorado Springs, CO, July 22-26, 2024.
6. Bilgin C, Cebral JR, Kallmes D, Kadirvel R, "In Vitro Evaluation of Flow Diverter Performance Using a Fibrinogen Based Flow Model", SNIS, Colorado Springs, CO, July 22-26, 2024.
7. Antil H, Lohner R, Mut F, Cebral JR, "Role of PDE Constrained Optimization in Evaluating Sensitivity of Clinical Measures in Arteries", CMBE, Arlington, VA, June 24-26, 2024.
8. Cebral JC, Marsh L, Chitzas A, Mut F, Bilgin C, Kadirvel R, Kallmes D, "modeling fibrin deposition in flow diverting devices for cerebral aneurysm treatment", CMBE, Arlington, VA, June 24-26, 2024.
9. Cebral JR, Marsh L, Karnam Y, Mut F, Kaneko N, "Understanding aneurysm flow features and their influence on what happens to the wall", CMBE, Arlington, VA, June 24-26, 2024.
10. Karnam Y, Mut F, Robertson AM, Cebral JR, "What flow conditions predispose ACOM & MCA intracranial aneurysms to grow & rupture?", CMBE, Arlington, VA, June 24-26, 2024.
11. Marsh L, Abou-Mrad T, Charbel, Cebral JR, "Hemodynamics of the carotid bulb: CEA with patch versus primary closure", CMBE, Arlington, VA, June 24-26, 2024.
12. Pradhan A, Mut F, Sosale M, Cebral JR, "A Computational Study of Flow Alteration in Realistic Arterial Networks During Stroke Treatment", CMBE, Arlington, VA, June 24-26, 2024.
13. Ramezanpour M, Robertson AM, Cebral JR, "The role of adventitial collagen fibers in modulating the mechanical environment of cerebral bifurcations", CMBE, Arlington, VA, June 24-26, 2024.
14. Kaneko N, Samarage M, Kawaguchi R, Selim O, Guo L, Villablanca JP, Marsh L, Komuro Y,Tobe Y,Robertson AM, Cebral JR, Hinman J, "Impact of vortex flow on endothelial cells in Cerebral aneurysms", CMBE, Arlington, VA, June 24-26, 2024.

Invited talks

1. Cebral JR, Kaneko N, Abdurakhmonov M, Tobe Y, Robertson AM, "Role of flow stagnation and vasa vasorum in aneurysm growth", Interdisciplinary Cerebrovascular Symposium (ICS), Buffalo, NY July 31-Aug 1, 2025.
2. Cebral JR, Marsh L, Bilgin C, Bayraktar E, Kallmes D, Kadirvel R, "Fibrin accumulation after flow diversion: aneurysm and jailed branches", Interdisciplinary Cerebrovascular Symposium (ICS), Buffalo, NY July 31-Aug 1, 2025.
3. Cebral JR, "Flow-driven remodeling of aneurysms", Interdisciplinary Cerebrovascular Symposium (ICS), Tampere, Finland, Dec 12-14, 2024.
4. Cebral JR, "Use of Machine Learning to identify at risk aneurysms", Interdisciplinary Cerebrovascular Symposium (ICS), Tampere, Finland, Dec 12-14, 2024.
5. Cebral JR, "Introduction: Organ-on-Chip", Interdisciplinary Cerebrovascular Symposium (ICS), Tampere, Finland, Dec 12-14, 2024.
6. Cebral JR, "Where do aneurysms grow and rupture? (and what are the prevalent flow conditions)", Semana de Intervencionismo Minimamente Invasivo (SIMI2024), Buenos Aires, Argentina, Sep. 10-12, 2024.

7. Cebral JR, “Study of fibrin accumulation on Flow diverters”, Semana de Intervencionismo Minimamente Invasivo (SIMI2024), Buenos Aires, Argentina, Sep. 10-12, 2024.
8. Cebral JR, “Flow conditions that affect the aneurysm wall”, Semana de Intervencionismo Minimamente Invasivo (SIMI2024), Buenos Aires, Argentina, Sep. 10-12, 2024.
9. Cebral JR, “Cerebral aneurysm research using image-based computational modeling”, Grand Rounds, Neurosurgery Department, University of Louisville, Louisville, Kentucky, May 16, 2024.

Press Releases

“Un físico Argentino se instaló en Washington y logro desarrollar un modelo personalizado pare predecir la rotura de aneurismas cerebrales”, Forbes Argentina, Jul 30, 2024 (in Spanish) (https://www.forbesargentina.com/innovacion/un-fisico-argentino-instalo-washington-logro-desarrollar-modelo-personalizado-predecir-rotura-aneurismas-cerebrales-n56888)

Use of Valentine Memorial Funds:

During the last year, funds were used to:

a) Support Graduate Research Assistants (GRAs) during the summer:
   Alireza Chitzas: research on intramural stress modeling
   Yogesh Kranam: research on flow and wall structure
b) Support faculty research over the summer:
   Prof. Juan R. Cebral: research on flow stagnation, fibrin accumulation modeling
c) Cover publication costs (paper by GRA Yogesh Karnam)
d) Cover conference costs for GRAs (Yogesh Karnam, Aseem Pradhan, Alireza Chitzas), postdoctoral fellow (Dr. Laurel Marsh), and faculty (Prof. Juan R. Cebral)
e) Cover costs to repair/upgrade hardware, including hard drives, graphic cards, network cards, and monitors.

Support from the Valentine Memorial Fund is extremely valuable (and highly appreciated) because of its flexibility which allows us to focus on otherwise unfunded efforts that we believe will have an important impact on the clinical practice and management of aneurysms and to continue to maintain a highly productive research team.