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MULTI-FACETED STUDY OF THORACIC AORTIC DISEASE

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MINI-SYMPOSIUM PROPOSAL

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1 MINI-SYMPOSIUM PROPOSAL

1.1 Background of the clinical problem addressed.

Ascending thoracic aortic disease is an important clinical problem that is incompletely defined at the cellular, molecular, genetic, and biomechanical levels. Aneurysm can arise in patients due to a number of etiologies that are genetically-triggered, degenerative (age-related), and idiopathic and can render the aorta vulnerable to dissection and/or rupture. While rupture often results in sudden death, Type A aortic dissection carries an alarmingly high mortality rate in the absence of emergent surgical aortic replacement. [1] Ascending thoracic aortic disease has an exceedingly broad presentation and can be asymptomatic, making patient-specific risk assessment and mitigation challenging. A multi-faceted approach is warranted to better understand the factors driving aortic disease. Speakers of this session each contribute different talents with the unifying collective goal of understanding mechanisms of aortic disease. The session will serve as a culmination of all facets, that when integrated, will accelerate the field's understanding of what factors mediate onset, progression and predict risk of dissection and to identify therapeutic targets that can be addressed non-invasively. A short (maximum of 5 minutes) Q&A period will follow each speaker. At the conclusion of all presentations, all speakers will be invited to field questions from the audience in a panel discussion format moderated by the session Chair.

1.2 Session speakers

Speakers in this session are sourced from various institutions and represent individuals with a history of active and productive interdisciplinary collaboration. There will be wide-spread appeal for this session due to participation of physician-scientists, bioengineers and mechanical engineers with interests in the biological, genetic, and biomechanical basis of thoracic aortic disease and due to the panel discussion format for Q&A. Presentations are curated in six different facets of study each with computational biology approaches: 1) state-of-the art clinical management of patients with aortic disease, 2) clinical imaging modalities, 3) genetics of thoracic aortic disease, 4) vessel biomechanics, 5) matrix stress mapping, and 6) single-cell force measurement approaches.

Speaker 1: Clinical and Surgical Management of Thoracic Aortic Disease
Thomas G. Gleason, MD, Ronald V. Pellegrini Endowed Chair, Chief-Division of Cardiac Surgery, Professor- Department of Cardiothoracic Surgery, University of Pittsburgh. Dr. Gleason's clinical and basic science career has focused on disease of the aortic valve and associated aortopathies. In this session, Dr. Gleason will discuss the clinical and surgical management of thoracic aortic disease with a focus on the aortopathy associated with the congenital heart malformation of bicuspid aortic valve. He will also provide a comprehensive overview of the biological, microstructural, and biomechanical alternations associated with BAV-related aortopathy and the need for multi-faceted study, which will successfully segue to subsequent presentations of the session representing other technical approaches.

Speaker 2: Hemodynamic Flow and Wall Stress using 4D Magnetic Resonance Imaging
Alex Barker, PhD, Assistant Professor of Radiology, Northwestern University

Dr. Barker will provide an overview on cardiovascular magnetic resonance imaging and biomedical engineering techniques that investigate the relationship between aortic and aortic valve morphologic anomalies and their impact on blood flow. Using a mathematical framework, multiple parameters such as pressure, resistance, impedance, drag forces, and energy loss can be extracted and evaluated in the context of human aortic disease.

Speaker 3: Genetics of Thoracic Aortic Disease
Mark Lindsay, MD, PhD Massachusetts General Hospital. A major focus of Dr. Lindsay's laboratory is to characterize novel genetic alterations in individual patients and families affected by aortic disease. His laboratory currently reports enrollment of over 400 people as part of this effort. Dr. Lindsay will present his body of work studying human and murine genetics and incorporating animal models of aortic disease to uncover genetically-based mechanisms of human aortic disease.

Speaker 4: Vessel Biomechanics of Human Aorta
David Vorp, PhD, Vice Dean for Research, Swanson School of Engineering, William Kepler Whiteford Professor-Department of Bioengineering, University of Pittsburgh. Dr. Vorp has an extensive history of defining large vessel biomechanics and vascular tissue engineering. Dr. Vorp will present on the ascending aortic biomechanics and implications of using finite element modeling to estimate wall stress and fluid structure interaction analysis for shear stress as predictive metrics of risk for aortic rupture.

Speaker 5: Matrix Stress Mapping in Human Ascending Aorta

Spandan Maiti, PhD, Assistant Professor-Department of Bioengineering, University of Pittsburgh. Dr. Maiti will share his work in computational biomechanics related to dissection of human ascending aorta. In particular, Dr. Maiti incorporates experimentally-obtained biomechanical and microarchitectural data from human aortic tissue to derive computational multi-parameter models that identify focal areas of matrix stress that may indicate risk of tissue rupture.

Speaker 6: An Engineered Tunable Platform for Single Cell Force Measurements
Amrinder Nain, PhD, Associate Professor, Department of Mechanical Engineering, Virginia Polytechnic University. Dr. Nain pioneered a novel spinneret-based tunable engineered platform to create nanofiber polymer scaffolds on which a computational approach to make single cell force measurements and to determine the impact of extracellular forces on cell phenotype, viability, focal adhesions, and morphology is employed. Force measurements in single primary human aortic smooth muscle cells from the ascending aorta are obtained in two modes: step strain and cyclic to extract the viscoelastic constants for direct comparison between cell phenotypes.

REFERENCES

[1] Y. Masuda, Z. Yamada, N. Morooka, S. Watanabe and Y. Inagaki. Prognosis of patients with medically treated aortic dissections. Circulation, 84, III7-13, 1991.