2020-2021 Grand Challenge Award Final Report

Awardee: **Manuel Rausch, Assistant Professor**
Aerospace Engineering & Engineering Mechanics

Research Award Title: **A Machine-Learning Based Training Tool for Tricuspid Valve Repair: A Prototype**

Introduction

The tricuspid valve, as one of our four heart valves, has the vital role of directing blood flow through the heart. Its basic function is that of a check valve. However, in contrast to a check valve, the tricuspid valve's leaflets (tissue flaps) are suspended by fibrous strings, so called chordae tendineae. Only an optimally orchestrated interaction between the leaflets and chordae allows for proper valve closure and prevention of leakage. In an astounding 86% of us the tricuspid valve shows some degree of leakage and in another 1.6 million of us it is severely compromised[1]. Unfortunately, the valve most commonly dysfunctional is also the most complex valve and therefore the hardest to repair. In contrast to the other three valves, the tricuspid valve has an inconsistent anatomy that makes predicting the effects of changes (during disease or repair) difficult. Illustratively, to date, the literature is still divided on how many leaflets the tricuspid valve actually has[2]. Similarly, there is no consistent chordae structure with chordae inserting into the right ventricular endocardium seemingly without a discernable pattern. Every day surgeons and cardiologists make life-or-death decisions trying to predict how changes to the valve may affect function. To date, they learn the effect of their actions through years of hands-on experience and proctored training. **Our goal** was to develop a prototype learning tool that may accelerate surgical training by incorporating all complexities of a human tricuspid valve and providing in-depth didactic insight into the effects of repair and device implantation on valve function.

Accomplishment

Task 1: Anatomic Study. Our original goal had three subtasks. First, we set out to use an organ preservation system for detailed anatomic studies of a healthy and diseased beating human heart. We worked with our collaborators at Spectrum Health, MI who conducted all beating heart experiments to collect a rich set of data on in-situ valve dynamics combining echocardiography with sonomicrometry. Upon conclusion of their study portion, they sent the tissues to University of Texas at Austin, where we diligently digitized the geometry and mechanical properties of all valve components. Based on these combined data, we build the first, subject-specific, high-fidelity model of the human tricuspid valve. Thus, we accomplished our first task, see Figure 1.

Task 2: High-Fidelity Finite Element Model. Our second task was to transform our high-fidelity anatomic model of the human tricuspid valve into a finite element model. To this end, we discretized all valve geometries such as valve leaflets and chordae using structural finite elements. Next, we applied Dirichlet and Neumann boundary conditions to the valve that were based on in-situ measurements, such as transvalvular pressure and annular motion. Finally, we simulated the dynamic valve closure problem using the explicit finite element method where we accounted for leaflet self-contact. We also accomplished this second task, see Figure 1.

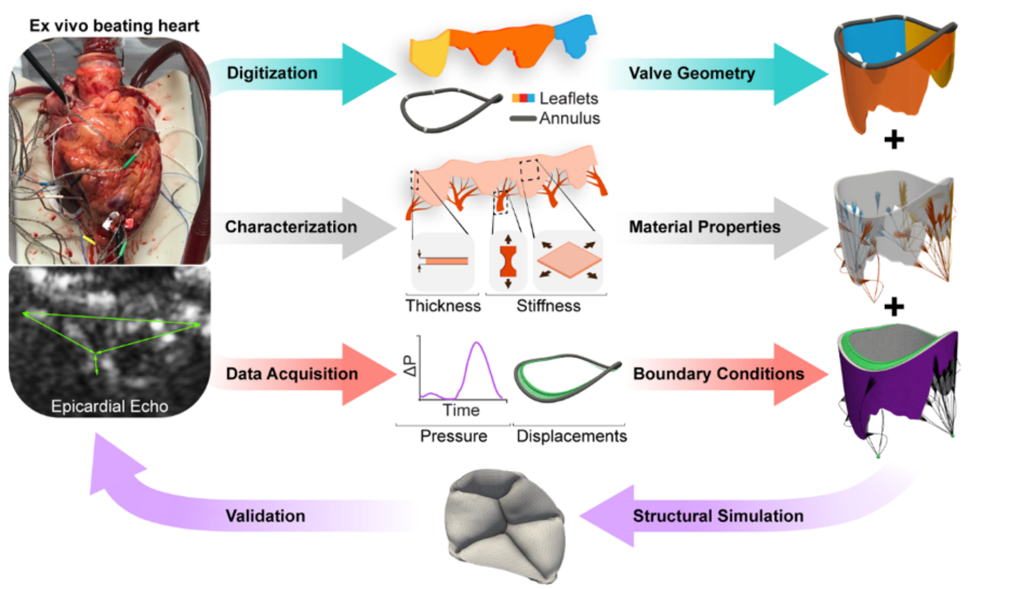

Figure 1: Overview over the results of Tasks 1 and 2. The successful creation of a high-fidelity finite element model based on beating heart anatomic studies of the human tricuspid valve.

Task 3: Surrogate Modeling. Our last task was to use our validated finite element model to train a machine-learning based surrogate model that would accelerate our valve simulations. Unfortunately, we have not achieved our third task because of delays in Tasks 1 and 2. However, we were able to use our data and accomplishments from Tasks 1 and 2 to attract funding from the National Institutes of Health to hire a post-doctoral fellow (starting date July 1st) to continue this work and accomplish our Task 3. We anticipate that we will conclude the proposed work during Year 2022.

Presentations made

1. Iwasieczko A, Jazwiec T, Malinowksi M, Rausch MK, Timek TA. Impact of reductive tricuspid ring annuloplasty on right ventricular size, geometry, and strain in a chronic ovine model of functional tricuspid regurgitation. *Proc. of the 35th Annual Meeting of the European Association for Cardiothoracic Surgery 2021*, Barcelona, Spain.

2. Rausch MK, Sugerman GP, Toaquiza J, Kakaletsis S, Tepole AB, Dortdivanlioglu B, Parekh SH. Blood clot as the body's own hydrogel. *Proceedings of the IUTAM Symposium on Smart and Though Hydrogels*, 2021, Virtual.

3. Kakaletsis S, Sugerman GP, Jazwiec T, Malinowski M, Timek TA, Rausch MK. Mechanics and microstructurally based modeling of the passive right ventricular myocardium. *Proceedings of the US National Congress on Computational Mechanics, 2021*, Virtual.

4. Mathur M, Meador WD, Malinowski M, Timek TA, Rausch MK. Engineering a structural twin of the human tricuspid valve. *Carnegie Mellon Biomedical Engineering Forum, 2021*, Virtual.

5. Rausch MK, Sugerman GP, Kakaletsis S, Dortivanlioglu B. Modeling the viscoelastic-damage mechanics of blood clot. *Proceedings of the US National Congress on Computational Mechanics, 2021*, Virtual.

6. Kakaletsis S, Jazwiec T, Malinowski M, Timek TA, Rausch MK. Pulmonary hypertension and histomechanics of the right ventricle. *Carnegie Mellon Biomedical Engineering Forum, 2021*, Virtual.

7. Mathur M, Meador WD, Malinowski M, Tomasz TA, Rausch MK. True subject-specific computational models of the human tricuspid valve. *Proceedings of the Annual Meeting of the Heart Valve Society 2021*, Virtual.

8. Mathur M, Meador WD, Malinowsk M, Timek TA, Rausch MK. Using predictive simulations to uncover the effects of ring-based annuloplasty on the human tricuspid valve. Proceedings of the US National Congress on Computational Mechanics, 2021, Virtual.

9. Kakaletsis S, Lejeune E, Rausch MK. Using machine-learning to simplify fitting constitutive laws to anisotropic and heterogeneous mechanical testing data. Proceedings of the IMECE Virtual Conference, 2021, Virtual.

10. Meador WD, Iawsieczko AJ, Jazwiec T, Mathur M, Malinowski M, Timek TA, Rausch MK. The tricuspid valve (mal)adapts in two ovine models of ventricular heart disease. Proceedings of the Annual Summer Biomechanics, Bioengineering, and Biotransport Conference, 2021, Virtual.

11. Kakaletsis S, Sugerman GP, Malinowski M, Timek TA, Rausch MK. Histo-mechanics of the passive right ventricular myocardium. Proceedings of the Annual Summer Biomechanics, Bioengineering, and Biotransport Conference, 2021, Virtual.

12. Lin CY, Mathur M, Meador WD, Sugerman GP, Rausch MK. Significance of a non-invasive method to quantify heterogeneous thickness in membranous soft tissues. Carnegie Mellon Biomedical Engineering Forum, 2021, Virtual.

13. Mathur M, Malinowksi M, Jazwiec T, Timek TA, Rausch MK. Tricuspid valve mechanics after surgical repair – An in-vivo study in sheep. Proceedings of the Annual Summer Biomechanics, Bioengineering, and Biotransport Conference, 2020, Virtual.

14. Meador WD, Mathur M, Malinowski M, Jazwiec T, Timek TA, Rausch MK. The Tricuspid Valve Also Maladapts: Evidence From Sheep With Functional Tricuspid Regurgitation. Proceedings of the Annual Meeting of the AHA Basic Cardiovascular Sciences, 2020, Virtual.

15. Malinowski M, Jazwiec T, Ferguson H, Bush J, Rausch MK, Timek TA. Tricuspid Leaflet Kinematics after Annular Size Reduction in Ovine Functional Tricuspid Regurgitation. Proc. of the 100th Annual Meeting of the American Association for Thoracic Surgery 2020, New York, NY (cancelled due to COVID-19).

Invited Talks Given

1. University of Illinois – Urbana Champaign Departmental Seminar (2021), "A Truly Subject-Specific, Shared Model of the Human Tricuspid Valve."

2. Interinstitutional Seminar in Biomechanics at University of Wisconsin and University of Minnesota (2021), "Right Ventricular Histo-Mechanics: In Health and Sickness."

3. Workshop on Soft Tissue Damage – SB3C (2021), "What is Thrombus Failure?"

4. Simulia Workshop (2021), "Subject-Specific Computational Models of the Human Tricuspid Valve" (presented by Mrudang Mathur).

5. Washington University at St. Louis (2021), "Blood clot: Steps toward understanding its mechanics."

6. Ecole des Mines de Saint Etienne (France, 2021), "Quantification and modeling blood clot's nonlinear mechanics."

7. Virginia Commonwealth University BME Seminar (2020), "Subject-specific modeling of the tricuspid valve – The struggle of building a good model."

Papers published

1. Meador WD, Sugerman GP, Tepole AB, Rausch MK. The biaxial mechanics of denaturing skin – Part I: Experiments, Acta Biomaterialia, 2021.

2. Rausch MK, Meador WD, Tubon JT, Flores OM, Tepole AB. The biaxial mechanics of denaturing skin – Part II: Modeling, Acta Biomaterialia, 2021.

3. Rausch MK, Parekh SH, Dortdivanlioglu B, Ronsales AM. Synthetic hydrogels as blood mimicking wound healing materials, Progress in Biomedical Engineering, 2021.

4. Sugerman GP, Rausch MK. Teaching material testing and characterization with an open, accessible, and affordable mechanical test device. Biomedical Engineering Education, 2021.

5. Sugerman GP, Chockshi A, Rausch MK. Preparing and mounting of whole blood clot for mechanical testing. Current Protocols, 2021.

6. Rausch MK, Sugerman GP, Kakaletsis S, Dordtivanlioglu B. Hyper-viscoelastic damage modeling of blood clot under large deformation. Biomechanics and Modeling in Mechanobiology, 2021.

7. Meador WD, Zhou J, Malinowski M, Jazwiec T, Calve S, Timek TA, Rausch MK. The effects of a simple optical clearing protocol on the mechanics of collagenous soft tissue. Journal of Biomechanics, 2021.

8. Meador WD, Mathur M, Sugerman GP, Jazwiec T, Wang X, Malinowksi M, Lacerda C, Timek TA, Rausch MK. The tricuspid valve also maladapts: A multi-scale study in sheep with biventricular heart failure. eLife, 2021.

9. Wang Y, Kumar S, Nisar A, Bonn M, Rausch MK, Parekh SH. Effect of shear and tensile loading on fibrin molecular structure revealed by coherent Raman microscopy. Acta Biomaterialia, 2021.

10. Kakaletsis S, Meador WD, Mathur M, Sugerman GP, Jazwiec T, Malinowski M, Lejeune E, Timek TA, Rausch MK. Right ventricular myocardium: Multi-modal deformation, microstructure, modeling, and a comparison to the left ventricle. Acta Biomaterialia, 2021.

11. Malinowski M, Jazwiec T, Quay N, Goehler M, Wodarek J, Bush J, Parker J, Langholz D, Rausch MK, Timek TA. Tricuspid leaflet kinematics after annular size reduction in ovine functional tricuspid regurgitation. Journal of Thoracic and Cardiovascular Surgery, 2021.

12. Sugerman GP, Kakaletsis S, Thakkar P, Chockshi A, Parekh S, Rausch MK. Mechanics of an in-vitro blood clot mimic: Constitutive behavior under simple shear. Journal of the Mechanical Behavior of Biomedical Materials, 2021.

13. Rausch MK, Nguyen TC. Commentary: On the basis of stasis: Mechanistic insight into TAVR thrombosis. Journal of Thoracic and Cardiovascular Surgery, 2021.

14. Sugerman GP, Parekh SH, Rausch MK. Nonlinear, dissipative phenomena in whole blood clot mechanics. Soft Matter, 2020.

15. Jazwiec T, Malinowski M, Mathur M, Ferguson H, Parker JL, Rausch MK, Timek TA. Tricuspid valve anterior leaflet strains in ovine functional tricuspid regurgitation. Seminars in Thoracic and Cardiovascular Surgery, 2020.

16. Mathur M, Meador WD, Jazwiec T, Malinowski M, Timek TA, Rausch MK. Tricuspid valve annuloplasty alters leaflet mechanics. Annals of Biomedical Engineering, 2020.

17. Smith KJ, Mathur M, Meador WD, Phillips-Garcia B, Sugerman GP, Menta AK, Jazwiec T, Malinowksi M, Timek TA, Rausch MK. Tricuspid chordae tendineae mechanics: Insertion site, leaflet, and size-specific analysis and constitutive modelling. Journal of Experimental Mechanics, 2020.

Awards or recognition received

1. R21 (NIH, Role: PI, 12/2021-11/2023) "Human-Specific Prediction, Training, and Visualization Tools for the Tricuspid Valve from Existing Data."

2. Collaborative Standard Grant (NSF, Role: PI, 1/2022-12/2024) "Inferring the Micro-Mechanics of Embedded Fiber Networks by Leveraging Limited Imaging Data."

3. Long Range Grant (ONR, Role: PI, 1/2022-12/2022) "Casualty Safe Ride Standards: A Study of Ride-induced Blood Clot Dislodgement."

4. CAREER Award (NSF, Role: PI, 3/2021-3/2026) "Toward a Fundamental Understanding of Why Thrombus Dissolves, Persists, or Breaks Off."

5. Standard Grant (NSF, Role: PI, 6/2021-6/2024 "Understanding Mechano-Fibrinolysis: Fiber-Scale Multiphysics Experiments and Models."