PhD Thesis title: "*In Vivo* Human Right Ventricle Shape and Kinematic Analysis with and without Pulmonary Hypertension"

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Graduation Date: May 24th, 2013
Available on line: http://d-scholarship.pitt.edu/18841/

ABSTRACT: Pulmonary hypertension (PH) is a severe cardio-pulmonary illness which has been commonly observed to induce substantial and ultimately deleterious changes to the human right ventricle (RV) shape and function. As such, the functional state of the RV is thought to be a major determinant of symptoms and survival rates for PH. However, there has been little success to-date to identify clinically obtainable metrics of RV shape and deformation as a means to detect the onset and progression of PH. This difficulty is largely the result of the absence of a proven approach that is generally applicable for consistent and reliable quantitative analysis of anatomical shapes, particularly the RV, between patients and over time. Therefore, a computational framework which can quantitatively analyze RV shape and deformation could be a key to assist in clinically detecting the onset and progression of PH.

Statistical shape analysis techniques were developed, implemented, and assessed to analyze variations in human RV endocardial surface (RVES) shapes and kinematics from noninvasive clinical medical imaging data with respect to a spectrum of hemodynamic states. A computational framework for the quantitative analysis and statistical decomposition of sets of 3D genus-0 shapes that combines a modified harmonic mapping approach directly with proper orthogonal decomposition (DM-POD) is presented. The DM-POD approach is shown to be a robust technique for recovering inherent shape-related features through the analysis of sets of artificially generated shapes. The DM-POD approach is then applied to obtain kinematic features of the human RV based on the relative change in shape of the endocardial surface using cardiac computed tomography images. In addition, the kinematic features of the RVES obtained by the DM-POD approach are shown to be consistent and associated with intrinsically physiological components of the heart, and thus may potentially provide a more accurate means for classifying the progressive change in RV function caused by PH, in comparison to traditional clinical hemodynamic and volume-based metrics. Statistical shape analysis for the human RV is further evaluated through analysis of alternate components of the DM-POD approach, as well as through comparison of the DM-POD work flow with an alternate spherical harmonic function-based work flow (SPHARM), with respect to the aspects of surface representation, alignment, and decomposition. Additionally, different ways of utilizing the available imaging data with respect to the classification potential are investigated by considering analysis results when applying both the various DM-POD and SPHARM approaches with several different combinations of the

phases captured throughout a single cardiac cycle for the patient set. Lastly, a novel statistical decomposition technique known as independent component analysis (ICA) was incorporated into the statistical shape analysis framework (i.e., DM-POD) to produce an alternative work flow (DM-ICA). Both the DM-POD and DM-ICA approaches are applied to analyze sets of artificially generated data and the human RVES datasets, and the respective results are compared. The DM-POD and DM-ICA work flows are shown to produce consistent, but substantially different results due to the various principles and views of each of the two statistical decomposition algorithms (i.e., POD and ICA). Most importantly, the results from the DM-POD and DM-ICA work flows appear to relate to RV function in unique ways, with respect to both traditional clinical metrics and each other, and have the potential to provide new metrics for better understanding of the human RV and its relationship to PH.

References to author publications that relate specifically to the dissertation:

Journal Articles:

- **J. Wu**, Y. Wang, M.A. Simon, and J.C. Brigham, "A Comparison of Global Shape Analysis Methods for the Assessment of Right Ventricular Function," Submitted.
- **J. Wu**, K.G. Brigham, Y. Wang, M.A. Simon, and J.C. Brigham, "An Implementation of Independent Component Analysis for 3D Statistical Shape Analysis," Submitted.
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- **J. Wu**, Y. Wang, M.A. Simon, and J.C. Brigham (2012), "A New Approach to Kinematic Feature Extraction from the Human Right Ventricle for Classification of Hypertension: a Feasibility Study," Physics in Medicine and Biology, 57, 23, December, 7905-7922.

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- **J. Wu** and J.C. Brigham (2012), "Computational Techniques for Analysis of Organ-Level Shape and Kinematics," in Image-based Geometric Modeling and Mesh Generation, Editor: Yongjie (Jessica) Zhang, Springer.

Conference Proceedings:

- **J. Wu**, Y. Wang, M.A. Simon, and J.C. Brigham (2012), "Analysis of In Vivo Human Right Ventricle Shape Change with and without Pulmonary Hypertension," 10th International Symposium on Computer Methods in Biomechanics and Biomedical Engineering, Berlin, Germany, April.

- **J. Wu** and J.C. Brigham (2011), "Geometric Analysis and Decomposition of 3-D Closed Surfaces for Applications in Diagnostic Medical Imaging," 2nd International Conference on Mathematical and Computational Biomedical Engineering, Washington, DC, March.

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- **J. Wu,** Y. Wang, M.A. Simon, and J.C. Brigham (2012), "A Novel Approach for Anatomically Consistent Analysis of Organ-Level Shape and Kinematics," 10th International Symposium on Computer Methods in Biomechanics and Biomedical Engineering, Berlin, Germany, April.
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- **J. Wu,** J.C. Brigham, M.A. Simon, K. Kim, and M.S. Sacks (2011), "Geometric Analysis and Decomposition of Normal and Hypertensive Human Right Ventricle from Diagnostic Medical Imaging," ASME 2011 Summer Bioengineering Conference, Farmington, PA, June.
- **J. Wu,** J.C. Brigham, M.A. Simon, S. Tripathy, K. Kim, and M.S. Sacks (2010), "Computational Geometric Analysis of the Normal and Hypertensive Human Right Ventricle," BMES 2010 Annual Meeting, Austin, TX, October.
- **J. Wu** and J.C. Brigham (2010), "Computational Analysis and Comparison of Geometric Features of the Human Right Ventricle, with and without Pulmonary Hypertension," 4th European Conference on Computational Mechanics, Paris, France, May.