

ABSTRACT FACE PAGE

1. Presenting Author's name: Reza Pourmodheji
2. Presenting Author's affiliation: Department of Mechanical Engineering, Michigan State University
3. Presenting Author's title: Postdoctoral Research Associate
4. Presenting Author's email: pourmodh@egr.msu.edu
5. Presenting Author's gender (optional): _____
6. Presenting Author's race (optional): _____
7. Presenting Author's ethnicity (optional): _____
8. Presenting Author's affiliation sector: (check one or more)
 - Academia
 - Industry
 - Federal Employee/Contractor
 - Private Foundation
 - Other: _____
9. Presenting Author's Career stage: (check one)
 - K-12 student
 - Undergraduate student
 - Graduate Student
 - Post-doctoral Trainee
 - Young employee (within first 3 year of post-training position)
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10. Website / twitter handle / other public links (optional): <https://researchgroups.msu.edu/compbimech/>
11. Is this the research presented in this abstract supported by IMAG MSM-related U01 funding? Yes
12. If the Presenting Author is a trainee, who is the trainee's primary research advisor? Dr. Lik-Chuan Lee
13. If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Poster Competition*? Yes
14. If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Oral Presentation Competition**? Yes

Patient-specific in-vivo Arterial Characterization in Pediatric Pulmonary Hypertension

¹Reza Pourmodheji*, ¹Zhenxiang Jiang, ²Christopher Tossas-Betancourt, ²Alberto Figueroa, ¹Seungik Baek, ¹Lik-Chuan Lee

¹Department of Mechanical Engineering, Michigan State University, East Lansing, MI

²Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI

email: pourmodh@egr.msu.edu, website: <https://researchgroups.msu.edu/com biomech/>

BACKGROUND: Pulmonary arterial hypertension (PAH) is a complex disease that can affect the pediatric population and leads to functional and structural changes in the pulmonary arteries (PA) and right ventricle (RV). Clinical studies of PAH, on the other hand, seldom consider microstructural changes during disease progression. Arterial stiffening, which can occur in both the proximal and distal PAs, is an important biomarker for disease progression and contributes substantially to the increased RV afterload in PAH [1]. Accordingly, the contribution of micro-constituents to arterial stiffening in PAH is of great interest. In this study, clinical data are assimilated into novel computational models to characterize micro-structural properties of the PA in pediatric PAH patients.

METHODS: Clinical data was acquired in 4 pediatric PAH patients (UM1, UM2, UM5, and UM6) and a control subject (CT1), who received a heart transplant. Patient-specific cardiac and vascular geometries were reconstructed using cine magnetic resonance imaging (MRI) data while dynamic changes of the lumen area of the main PA was obtained from phase-contrast MRI. Pressure waveforms of the PA were measured with invasive right heart catheterization. The patient-specific pressure-diameter (PD) relationship and reconstructed vascular geometry are then applied in an adjoint-based data assimilation framework to obtain the contribution of each vascular constituent - elastin, collagen, and smooth muscle cells (SMC) - to the mechanical behavior of the PA based on a constitutive model [2, 3].

RESULTS: PAs are significantly affected by the deposition stretch of its constituent at production. Thus, we prescribed a range of pre-stretches in the data assimilation framework to assess the artery material stiffness. A representative geometry of the PA is shown in Figure 1(a). The contribution of each vascular constituent's stiffness (C) of all the subjects is shown in Figure 1(b). We find that the stiffnesses of all vascular constituent are larger in the PAH patients than the control subject (CT1). The PAH patients, however, have varying values of stiffness associated with the different constituents e.g., UM1 shows more elastin-dominated pattern in its PD behavior as C is the highest among all other patients.

CONCLUSIONS: PAH is associated with an increase in the material stiffness of the PA. The elevated stiffness could be attributed to fiber growth, removal and remodeling of different constituents with varying intrinsic stiffness. Since the vascular constituents are inherently nonlinear, we define the stiffness for different PA constituents and the mixture to be nonlinear. The adjoint-based data assimilation framework yielded varying constituent-wise stiffness patterns for each subject. The results of patient-specific analysis speculate that a high stiffness of elastin plays a dominant role except for CT1 (who is the oldest) and UM5 (who has the most severe PAH and may have undergone a significant remodeling). This indeed agrees with the fact that the load-carrying capacity of elastin dominates over the other two constituents when the pressure operating range is small [4], which is still the case in PAH when compared to the systemic pressure ranges.

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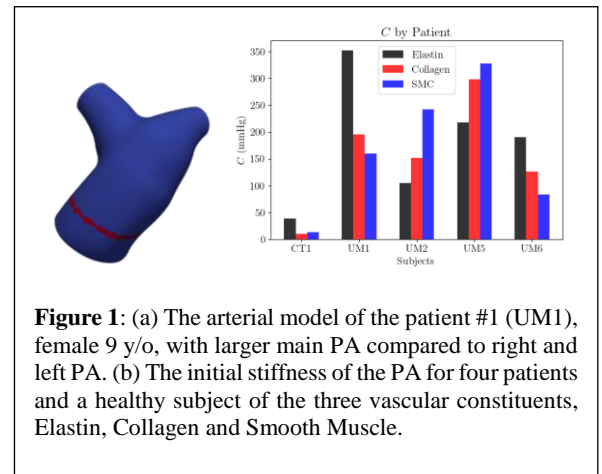


Figure 1: (a) The arterial model of the patient #1 (UM1), female 9 y/o, with larger main PA compared to right and left PA. (b) The initial stiffness of the PA for four patients and a healthy subject of the three vascular constituents, Elastin, Collagen and Smooth Muscle.