Normal Pulmonary Hypertension

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

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INTRODUCTION
- Pulmonary Hypertension (PH) is a complex disorder associated with elevated mean pulmonary arterial pressure (>25 mmHg at rest) and progressive pathologies in pulmonary arteries.
- Increased resistance and stiffness in vessels, stiffened Pulmonary Artery (PA).
- Right ventricle increased after-load
- Left untreated, the median survival: 2.8 years

Objectives
- Develop a model to account for the micro-structural stiffness in PA and represents the overall stiffness in macro scale for each constituent

METHODS
Clinical Data
- Clinical data was prospectively acquired in four PH subjects (UM1-2 and UM5-6) and a control subject (CT1) with cardiac transplant with pulmonary normotensive response.
- 3D data on vascular anatomy were acquired using cine MRI. PC-MRI to obtain dynamic data for luminal area changes and blood flow velocity.

Finite Element Analysis
- 3D anatomy is meshed and the finite element is performed.
- Constrained-mixture theory for three constituent of elastin, collagen and smooth muscle cells is adopted.

\[
\begin{align*}
\omega_c &= \frac{c}{2} (C: I - 3) \\
\omega_k &= \sum_k \frac{k}{4k_0} \left[ \exp \left( \frac{k_0^2 (\lambda - 1)^2}{2} \right) - 1 \right] \\
\omega_m &= \frac{m_1}{4m_2} \left[ \exp \left( \frac{m_2 (\lambda - 1)^2}{2} \right) - 1 \right] + \omega_0 \\
F_o &= G_o F
\end{align*}
\]

Optimization
- The adjoint-based method is employed for optimizing the vascular constituent parameters.

\[
\min_{\mathcal{F}} J_p = \frac{1}{2} \| D - D_c \|^2 \quad \frac{dJ}{d\mathcal{F}} = -\left[ \frac{\partial F}{\partial \mathcal{U}} \right]^T \left[ \frac{\partial F}{\partial \mathcal{U}} \right]^{-1} \left( \frac{\partial J}{\partial \mathcal{U}} \right) + \frac{\partial J}{\partial \mathcal{F}}
\]

RESULTS
- The optimized parameters are collected for the smallest functionals for three sets of low, middle and high pre-stretch G.
- The optimized stiffness parameters (c, k₁, m₁) and circumferential stresses for the patients are significantly higher than the normotensive subject.

Stress and Stiffness Analysis
- For all the subjects, elastin carry more load compared to the other two constituent.
- Stiffness as the change in the nominal stress with respect to the fiber stretch is calculated. For all patients the stiffness has been higher for PH subjects.
- Over a cardiac cycle toward the systole the stiffness of elastin drops as the other two stiffens.

DISCUSSION
- The elevated stiffness could be attributed to fiber growth, removal and remodeling of different constituents with varying intrinsic stiffness.
- The dominance of the load-carrying capacity of elastin over the other two constituents could be due to the fact that the PA operates in low range of pressure and collagen and smooth muscle stiffening behavior is activated when the pressure is high.
- The younger age of the patients even though hypertensive could be a factor to be looked at. The constituent production and removal vary by age.

REFERENCES

Project Title: (U01 HL135842) Image-based Multi-scale Modeling Framework of the Cardiopulmonary System: Longitudinal Calibration and Assessment of Therapies in Pediatric Pulmonary Hypertension