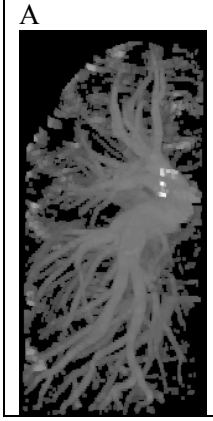
Introduction: Pulmonary arterial hypertension (PAH) is a devastating yet understudied disease. Several pediatric populations commonly have PAH: (1) children with congenital heart disease (CHD); (2) newborns with persistent pulmonary hypertension (PPHN); and (3) infants born at < 26 gestation (i.e., "extremely premature"). Cardiac catheterization is the gold standard for direct measurement of pulmonary arterial pressure, but is not easily nor safely administered in children because of the degree of invasiveness and the technical challenge of inserting and maintaining catheters in small vessels. Therefore, treatment decisions are often made based on clinical impressions, which are highly subjective, often misleading, and can lead to tragic results. Pulmonary vasculature in children can be observed directly using modern 3-dimensional (3D) imaging technology, including computed tomography (CT), but methods of image-based assessment have not yet been successfully translated to the clinic. Unfortunately, current imaging analysis techniques are not sufficiently quantitative or sensitive to small structural changes in the pulmonary vasculature. We hypothesize that dedicated image processing tools can be used to quantify biomarkers of structurally abnormal pediatric pulmonary vasculature that will lead to improved diagnosis of disease, objective assessment of disease progression, and more effective evaluation of treatment response.

Materials and Methods: A semi-automated, multi-step procedure was implemented for efficient and unbiased extraction of vascular structures from 3D medical images. These steps included extraction of the lung volume; snake-based deliniation of the vasculature roots in the hilar regions; vessel segmentation using fast-marching with adaptive thresholding; vessel centerline extraction using 3D skeletonization; tree traversal with correction for abberant branch connections; and computation of metrics, such as branch lengths, diameters, tortuosity, bifurcation angles, and overall vascular volume. 2D and 3D virtual phantoms of increasing complexity were used to validate the approach and tools. Human CT chest datasets (without use of vascular contrast agents) were obtained retrospectively under an approved protocol from pediatric patients with varying degrees of PAH.

Results and Discussion: The right hemi-lung of a pediatric patient with (Pt_1) and a patient without (Pt_2) severe PAH were processed, each using a single seed point placed at the root of the main right pulmonary artery. PT_1's scan was comprised of 193 axial CT slices that intersected the lung volume at a reconstructed voxel size of 0.69 x 0.69 x 1.25 mm. PT_2's scan was comprised of 263 CT slices that intersected the lung volume at a reconstructed voxel size of 0.83 x 0.83 x 1.0 mm. Pt_1 had a total of 264 branches with a total vascular volume of 29,465 mm^3. Pt_2 had 264 branches, 11 distinct vascular trees, and a total vascular volume of 32,371 mm^3.



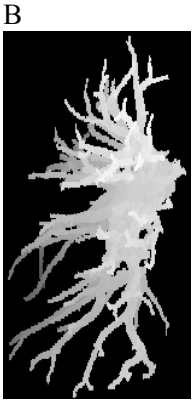


Figure 1. Depiction of segmentation results for a patient with chronic PAH (Pt_1). [A] The maximum intensity projection (MIP) from an anterior view of the chest CT of the right hemi-lung shows both arterial and venous trees. [B] The extracted vessel tree emminating from a seed point in the root of the main pulmonary artery includes many arterial vessels, down to the smallest size visible in the CT MIP image. [C] We smoothed each branch centerlines and applied the initial estimates of branch radii to construct a 3D geometric model of the vessel trees. Each is given a unique color with white being the largest.

Conclusions: We have developed and implemented a mostly automated toolkit that extracts the pulmonary vascular tree, calculates metrics that represent tree morphology, and is applicable to pediatric patients with PAH. Novel attributes include a sophisticated traversal algorithm that repairs abberant branch connections and the ability to easily generate 3D models of the tree structure. Future work will include further validation on 3D test datasets and application to patients and animal models at varying stage of disease progression.