DISTINGUISHING MARKERS OF LUNG VASCULATURE DEVELOPMENT IN PRE-TERM VS. FULL-TERM PATIENTS

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I. INTRODUCTION

- Improved understanding of lung vascular development in prematurely born babies (preemies) may improve patient care.[1]
- Prolonged use of mechanical ventilators is associated with increase risk of infection and altered development of breathing muscles.
- Of particular interest: "Is there an objective, quantitative means to determine when it is safe to take a preemie off a respirator?"

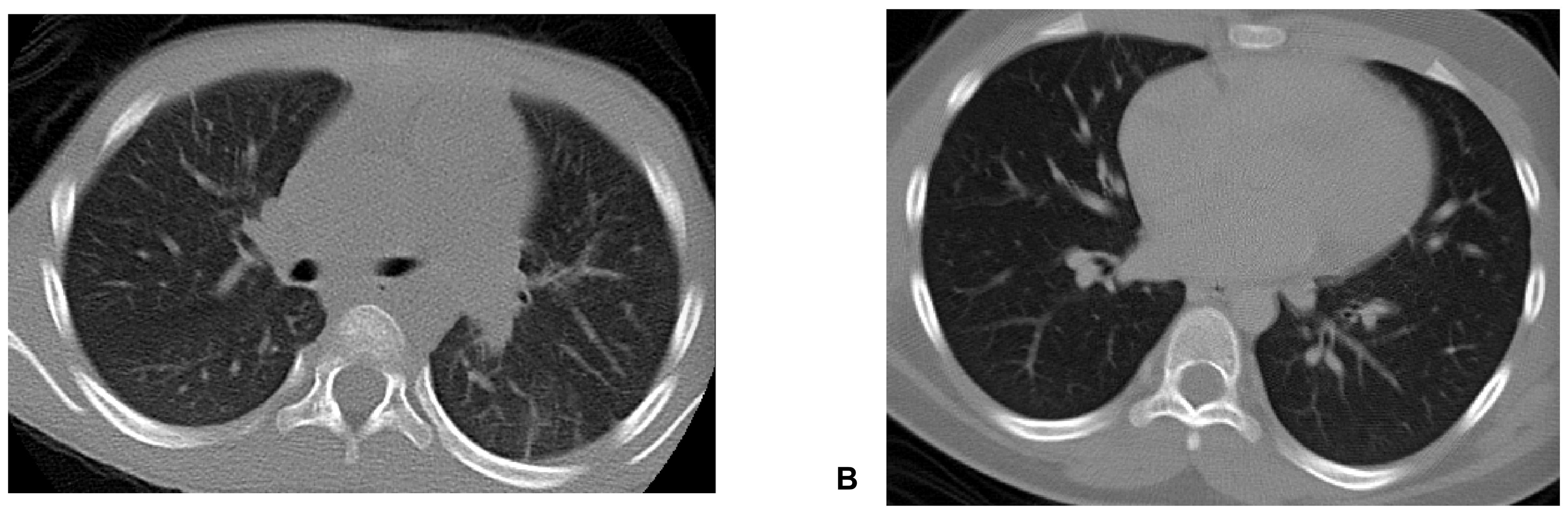

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Figure 1: Representative changes in pediatric lung CT appearance with age. [Left] shows a CT chest image of a 5-year old prematurely-born child. [Right] The same child's lung CT scan at 9 years of age, displaying lung and body growth over time.

__Objective__: To identify quantifiable markers of lung vascular development in preemies relative to full-term children to provided clinical guidance. As an initial step, we sought to document the changes with age of branch size distribution and total branch number.

II. METHODOLOGY: IMAGING AND SKELETONIZATION

__CHEST CT IMAGE ACQUISITION and LUNG VOLUME SEGMENTATION[3]__

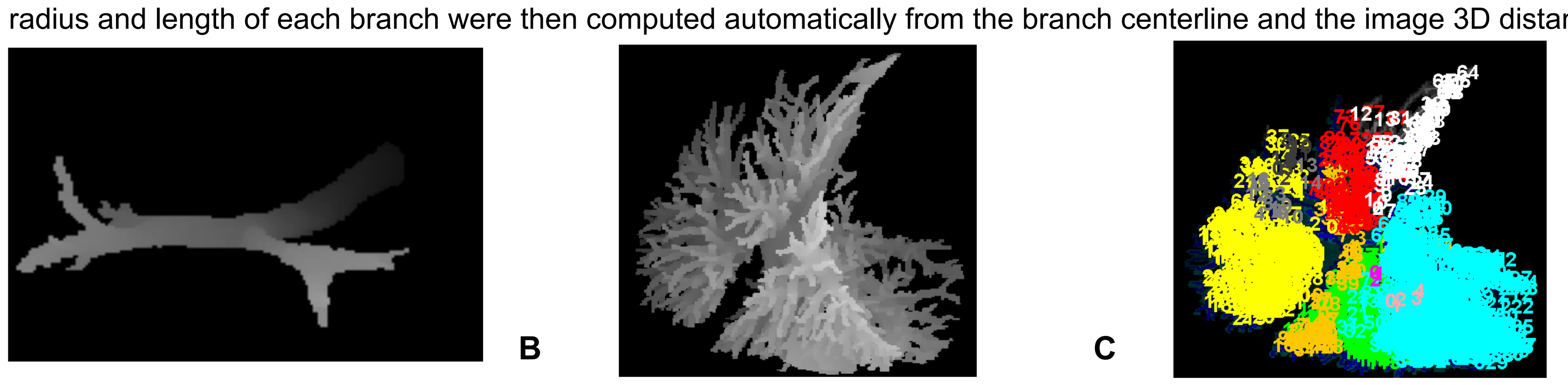
- Lung CT scans at 1 week to 20 years of age were retrospectively gathered within an IRB-approved protocol for 30 preemie and 30 full-term patients up to 18 years of age that were seen at the UF Health Shands Pediatric Pulmonary Care Center from 2014-2019.
- In-house software built upon the NIH ImageJ platform was used to automatically segment the lung volume (Fig 2A) and extract the pulmonary vessel trees and characterize the radius and length of each vessel branch.
- To-date, this approach was applied to the right-hemi-lung of 11 adolescents from 2 to 19 years of age of which four were born prematurely. Each subject provided 3-7 follow-up scans.
- For each subject we recorded gestational age, sex, and presence of infection/disease in a spreadsheet so that similarities or differences between subject factors can be analyzed later in the study.

A B C

Figure 2: 3D CT datasets and lung volume segmentation. The image in [A] shows a pediatric patient's representative chest CT scan with a snake (blue contour with red node points) used to segment the right hemi-lung volume. [B] displays the lung mask on this same slice obtained after contouring all the segmented slices across both hemi-lungs. [C] displays the 3D maximum-intensity projection (MIP) of the lung volume after stacking all segmented slices (each acquired with a 3 mm slice thickness) across both hemi-lungs.

__LUNG VESSEL TREE SEGMENTATION[3]__

- The major airways were segmented using a seeded region-growing method (Fig 3A) and subtracted from the lung volume images.
- The pulmonary vessels were extracted similarly using a manually-selected seed point placed in the pulmonary trunk (Fig 3B).
- Skeletonization of the tree structure was applied to facilitate traversing and labeling each branch in the tree structure (Fig 3C).
- The radius and length of each branch were then computed automatically from the branch centerline and the image 3D distance map.



A B C

Figure 3. Airway and vessel tree segmentation, and branch labeling. [A] shows a maximal intensity projection (MIP) or the extracted airway tree [B] shows the MIP of segmented vessel tree in the same patient. Extraction of the branch centerlines (skeletonization) enables tree traversal and the identification of individual branches within each tree structure. [C] shows the number-labeled branches where each tree structure uses a unique color.

ACKNOWLEDGEMENTS

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III. RESULTS AND DISCUSSION

- The number of branches per radii size in each subject's CT data set was automatically computed.
- The number of branches versus subject age was tabulated.

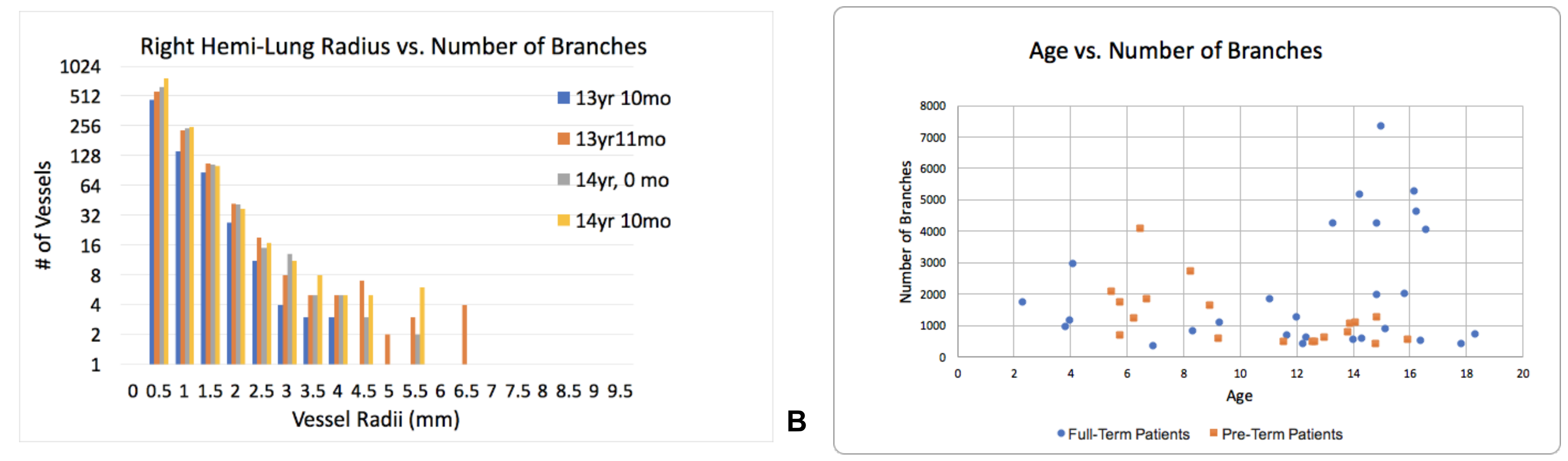

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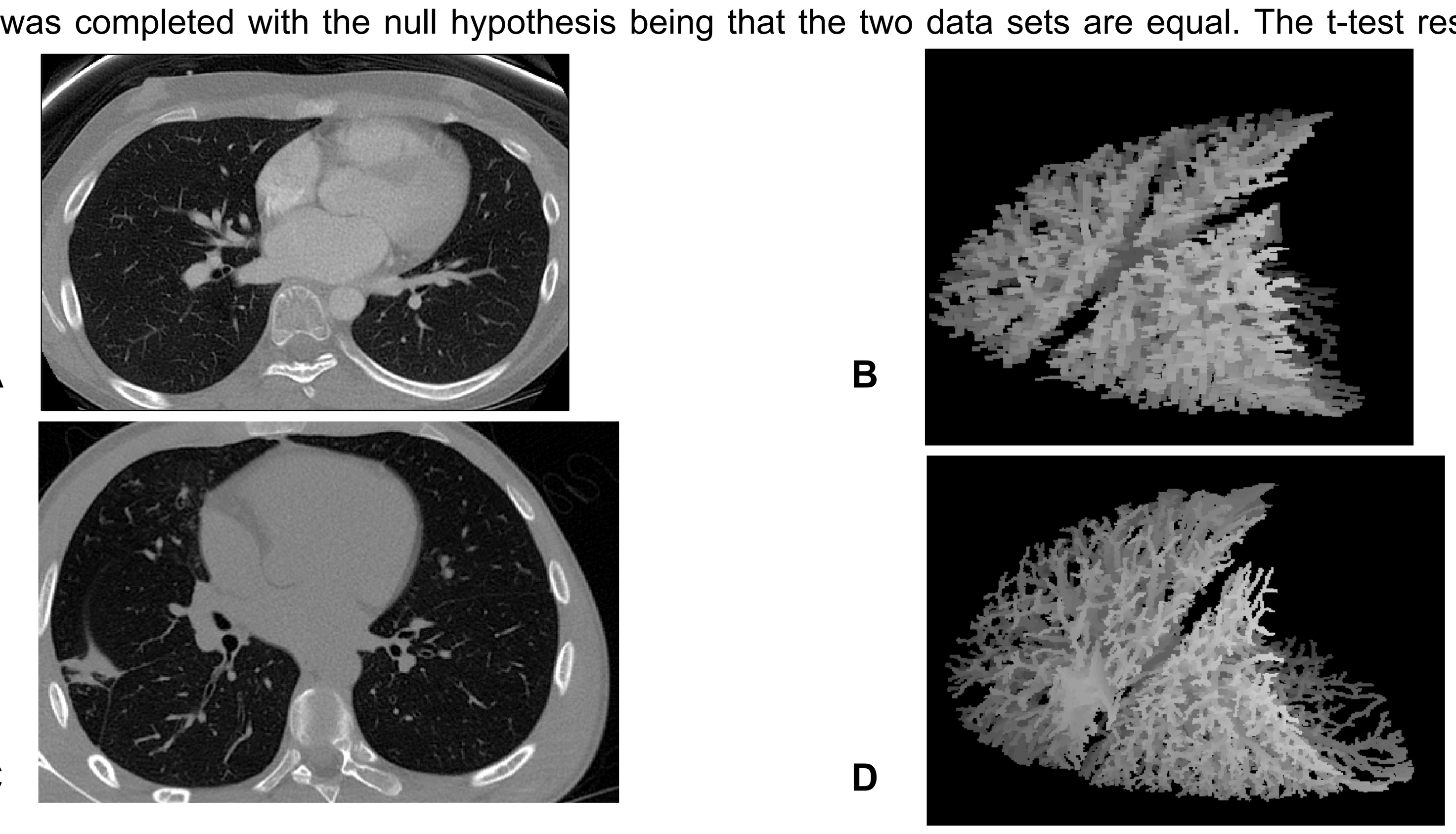
Figure 4: Number of branches versus age for pediatric subjects. [A] shows branch radius histograms for a representative preemie subject for 4 times points between 13 and 14 years of age. The slice thickness was 1 mm for all the scans. [B] shows total number of branches versus age (range 2 – 19 years) compiled over 11 subjects and 48 time points (each subject was evaluated at 3-7 time points)..

In the representative subject (Fig. 4A), there was a 36% increase in number of observable branches between the 1st and 2nd time points, but an average 20.7% increase over the subsequent 11-month span. Fig. 4B portrays how the number of branches in preterm patients aged 5-7, increased. However, between the ages 6-12, the number of vessels decreased, and slowly increased and stabilized between the ages of 12-16.

A two-sample t-test was completed with the null hypothesis being that the two data sets are equal. The t-test resulted in a p-value of 0.057.



A B C D

Figure 5: Confounding effects of growth and imaging parameters. [A] shows a single slice of a chest CT scan for a pre-term subject at 13 years of age with a 3 mm slice thickness. [B] shows a full-term subject at 16 years of age with a 1 mm slice thickness. [C] and [D] show the extracted vessel trees for the respected subjects. The number of extracted vessels is impacted both by subject age and slice thicknesses.

IV. CONCLUSIONS AND FUTURE DIRECTIONS

- Software tools have been developed to objectively quantify the number and size distribution of pulmonary vessels from repeat chest CT scans and these tools can be applied to pediatric subjects.
- The number of branches tended to increase with age in the 2-19-year range
- Once a child reaches his or her mid-teens, the number of branches is expected to level off.
- Our initial limited dataset does not show a consistent difference in branch number vs. age between preemie and full-term subjects.

Several factors that impact our ability to consistently extract vessel branches from pediatric CT scans were:

- Image pixel size and slice thickness greatly impacts the ability to detect and characterize smaller vessels.
- In these subjects, many scans exhibited acute lung infection and/or edema, which can obscure vessels in the CT image.
- The scans of younger subjects often suffer from motion artifact and variable use of vascular contrast agents.

Plans for Future Work

- Calibration curves are being developed to correct for differences in imaging parameters and use of vascular contrast agents.
- Analysis of additional pediatric datasets is on-going to increase the statistical power for detecting trends and group differences
- Future analyses will include subjects in the 1-week to 5-year age group where larger group differences are expected.
- With the larger dataset, vascular development will be correlated with gestational age, sex, body weight, and presence of secondary infection/disease (e.g. cystic fibrosis).

IV. REFERENCES

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