

**PhD Thesis Title:** Quantification of Respiratory Induced Pulmonary Blood Flow from 4DCT

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## **ABSTRACT:**

This work evaluates a measurable variation in the pulmonary blood mass (PBM) during respiration, from four-dimensional computed tomography (4DCT). This phenomenon was comprehensively evaluated at the scale of the entire lung in an 89-patient retrospective analysis. The spatially heterogeneous behaviour of this signal was further quantified by breaking the lungs into smaller geometrically distinct subregions. To evaluate the potential use for this signal as a surrogate for local perfusion, a prospective clinical trial was conducted. The trial included 15 patients entering the emergency department, who were suspected of pulmonary embolism (PE). Patients with confirmed PE received additional (*sequential cine*) 4DCT and single photon emission computed tomography (SPECT) perfusion imaging. The 4DCT images were sorted into full inhale and exhale phases, which were then used to generate pulmonary perfusion images, representing the local change in pulmonary blood mass ( $\Delta$ PBM). The 4DCT imaging technique was tested for reproducibility, while the  $\Delta$ PBM images were evaluated against the SPECT images to determine the efficacy of  $\Delta$ PBM imaging as a perfusion surrogate.

In the retrospective patient cohort, the mean change in pulmonary mass was  $50.9 \pm 3.9$  g, with the (average) maximum and minimum occurring at respiratory phases 9 and 6, respectively. We observed a positive change pulmonary mass during inspiration (exhale to inhale) and a negative change during expiration (inhale to exhale) was observed for 86 (96.0%) patients. In each case, a linear regression line was fit from phase 5 to 9, representing inhalation, and phase 0 to 5 for exhalation. The Spearman correlation of this relationship was found to be 0.61. A greater  $\Delta$ PBM is expected in patients with a larger radiographic volume. In the prospective study, the average variation in radiographic tidal volume ( $\Delta$ RTV), and parenchymal lung mass ( $\Delta$ PBM) between consecutive 4DCT imaging events was  $14.84 \pm 10.58$  % and  $18.23 \pm 10.4$  %, respectively. Four patients (27%) exhibited inter-scan variations in radiographic tidal volume larger than 20%.

The reproducibility of the 4DCT imaging algorithm was examined between consecutive time points for corresponding respiratory phase images using a suite of image analysis tools written with MATLAB software to compute the mean squared error (MSE), structural similarity index matrix (SSIM), and normalized joint entropy ( $\Delta$ JE). The intra-scan variation in MSE was negligible. The mean SSIM was  $0.896 \pm 0.050$  and  $0.897 \pm 0.043$ , while the  $\Delta$ JE was  $24.7 \pm 10.6$  % and  $7.50 \pm 11.1$  % for corresponding inhale and exhale image volumes, respectively. A 3D gamma analysis between SPECT and PBM images was used to quantitatively assess the performance of  $\Delta$ PBM imaging as a perfusion surrogate. Image sets were normalized and standardized prior to gamma analysis with a 12.5%, 10mm search criteria. Average gamma pass rate was  $48.9 \pm 7.25$  %.  $\Delta$ PBM images from the prospective study were qualitatively reviewed by a board-certified radiologist and scored on

an ascending scale of 1-5, ranking their similarity to SPECT images acquired for the same patients. The average ranking was  $3.55 \pm 0.78$ .

This work presents a thorough evaluation of respiratory induced changes in pulmonary mass, observable from 4DCT ( $\Delta$ PBM) and qualifies these observations as a surrogate for pulmonary perfusion through comparison with contemporary findings in the literature. A numerical method is also presented to create spatially resolved images of the local  $\Delta$ PBM signal, which are also tested as a potential surrogate against existing perfusion measurement techniques. These results indicate that 4DCT derived perfusion imaging may serve as a viable surrogate for perfusion imaging in future medical applications.

#### **References to author publications that relate specifically to the dissertation:**

1. **Myziuk NK**, Guerrero TM, Sakthivel G, et al., "Pulmonary blood mass dynamics on 4DCT during tidal breathing." *Physics in Medicine & Biology*, Volume 64, Number 4 (2019). doi:10.1088/1361-6560/aaff7b
2. Castillo E, Nair G, Turner-Lawrence D, **Myziuk, N**, et al., "Quantifying pulmonary perfusion from noncontrast computed tomography." *Medical Physics*, Volume 48, Issue 4, pp 1804-1814 (2021). doi:<https://doi.org/10.1002/mp.14792>