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Quantitative lung perfusion blood volume (PBV) using dual energy CT (DECT)-based effective atomic number ($Z_{eff}$) imaging

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[Running title]: DECT perfusion blood volume imaging
Abstract

Background: Iodine material images (aka iodine basis images) generated from dual energy CT (DECT) have been used to assess potential perfusion defects in the pulmonary parenchyma. However, iodine material images do not provide the needed absolute quantification of the pulmonary blood pool, as materials with effective atomic numbers ($Z_{\text{eff}}$) different from those of basis materials may also contribute to iodine material images, thus confounding the quantification of perfusion defects.

Purpose: The purposes of this work were to (i) demonstrate the limitations of iodine material images in pulmonary perfusion defect quantification and (ii) develop and validate a new quantitative biomarker using effective atomic numbers derived from DECT images.

Methods: The quantitative relationship between the perfusion blood volume (PBV) in pulmonary parenchyma and the effective atomic number ($Z_{\text{eff}}$) spatial distribution was studied to show that the desired quantitative PBV maps are determined by the spatial maps of $Z_{\text{eff}}$ as $\text{PBV}_{Z_{\text{eff}}}(x) = a \, Z_{\text{eff}}(x) + b$, where $a$, $b$, and $\beta$ are three constants. Namely, quantitative $\text{PBV}_{Z_{\text{eff}}}$ is determined by $Z_{\text{eff}}$ images instead of the iodine basis images. Perfusion maps were generated for four human subjects to demonstrate the differences between conventional iodine material image-based PBV ($\text{PBV}_{\text{iodine}}$) derived from two-material decompositions and the proposed $\text{PBV}_{Z_{\text{eff}}}$ method.

Results: Among patients with pulmonary emboli, the proposed $\text{PBV}_{Z_{\text{eff}}}$ maps clearly show the perfusion defects while the $\text{PBV}_{\text{iodine}}$ maps do not. Additionally, when there are no perfusion defects present in the derived PBV maps, no pulmonary emboli were diagnosed by an experienced thoracic radiologist.

Conclusion: Effective atomic number based quantitative PBV maps provide the needed sensitive and specific biomarker to quantify pulmonary perfusion defects.
Keywords: Dual energy CT, multi-energy CT, pulmonary embolism, functional lung imaging, pulmonary perfusion imaging, effective atomic number map, material decomposition, quantitative imaging

1. Introduction

Venous thromboembolism is a major global health concern and an economic burden with approximately 10 million cases occurring each year and a high lifetime risk of 8% after 45 years of age.\(^5\) Pulmonary embolism (PE) is a venous thromboembolic event associated with high morbidity and mortality.\(^5\) Currently, pulmonary CT angiography (CTA) is the preferred imaging modality for evaluating patients with clinically suspected acute PE.\(^6\)–\(^17\) Pulmonary CTA can also be used for the evaluation of other pulmonary thromboembolic diseases such as chronic PE and chronic thromboembolic pulmonary hypertension (CTEPH). Pulmonary emboli often manifest as partial or complete intraluminal pulmonary vessel filling defects on pulmonary CTA images and each defect usually presents a sharp interface with the iodinated contrast. However, these radiological features are not specific to pulmonary emboli and can also result from a number of other pathological factors (e.g., the presence of a mucus plug or perivascular edema) and anatomical factors (e.g., vascular bifurcations, misidentification of pulmonary veins, etc.), all of which can generate PE-mimicking filling defects on pulmonary CTA images.\(^8\) In addition, the success rate and diagnostic accuracy of anatomic imaging with pulmonary CTA drop as the vessel size decreases to the subsegmental level.\(^17\) Furthermore, pulmonary CTA only provides anatomic imaging of pulmonary vessels and does not provide a direct assessment of the impact of PE on lung parenchymal perfusion. Pulmonary CTA also cannot directly provide prognostic biomarkers of hemodynamic compromise nor identify patients at risk for fatal or other adverse events. The incapability to demonstrate parenchymal perfusion abnormalities remains an important limitation of CTA-based evaluation of pulmonary thromboembolic diseases.
As an alternative to pulmonary CTA, lung ventilation/perfusion (V/Q) scintigraphy and single photon emission computed tomography (SPECT) are used to evaluate pulmonary thromboembolic diseases. For patients with suspected CTEPH or chronic PE, the selection between CTA and nuclear medicine imaging often creates a diagnostic dilemma: CTA provides direct imaging of the embolus itself without parenchymal perfusion information while nuclear medicine imaging provides functional information without direct proof of emboli. To extricate physicians from this dilemma, patients with suspected CTEPH may need to receive both CTA and nuclear medicine lung imaging, which increases both the overall healthcare cost and the ionizing radiation dose to patients. As a result, there is a compelling unmet clinical need to develop a method for simultaneous pulmonary vessel morphological assessment and parenchymal perfusion assessment without applying separate CT and nuclear medicine scans to the same patient.

Towards providing a “one-stop-shop” solution to morphological and functional lung imaging, prior studies have investigated the use of dynamic CT imaging to extract pulmonary perfusion information. However, this approach has not been clinically accepted resulting from concerns regarding radiation dose.\textsuperscript{18-20} the effective dose of dynamic chest CT is approximately 7 mSv, compared to 2 mSv for a typical static pulmonary CTA scan.\textsuperscript{21} Another strategy employed is to use static dual energy CT (DECT) or multi-energy CT (MECT) which do not require a prolonged breath-hold or a significant increase in radiation dose.\textsuperscript{22-29} A DECT scan generates the so-called iodine material images (from iodine-water or iodine-soft tissue-air material decompositions) that can be used as a corollary for pulmonary perfusion blood volume (PBV) maps to depict the location and pattern of pulmonary perfusion defects. For a given pulmonary embolus identified on CTA images, the addition of those iodine material image-based PBV (PBV\textsubscript{iodine}) maps can assist physicians in estimating the probability and severity of tissue damage while providing a prognosis and risk stratification in
patients presenting with pulmonary thromboembolic diseases, including typical presentations and those associated with alternate diagnoses, such as COVID-19 pneumonia.\textsuperscript{7,30-35}

However, as shown by a recent survey conducted by the Society of Thoracic Radiology,\textsuperscript{36} iodine material image-based pulmonary perfusion imaging remains underutilized in clinical practice due to several important limitations. The first important limitation of the iodine material image is that its signal does not necessarily reflect the magnitude of the pulmonary blood pool, as non-iodine materials with $Z_{\text{eff}}$ different from that of the counterpart basis material (e.g., water) can also contribute to the iodine image signal. This is particularly a problem for pulmonary consolidation and ground glass opacity that may not only have different $Z_{\text{eff}}$ (relative to water), but also much higher densities than the normal lung tissue: as shown by the analysis in Section 2.2 and published literature,\textsuperscript{37-39} those tissues can generate a relatively high signal in $\text{PBV}_{\text{iodine}}$ images which can mislead the evaluation of regional perfusion conditions. The second limitation lies in the fact that DECT-based iodine material images can only provide a relative measurement of PBV. In fact, physicians heavily rely on comparing the iodine intensity across different lung lobes to identify regional perfusion defects. Due to this relative assessment nature, literature on DECT pulmonary perfusion imaging rarely reports the physical units of the pulmonary perfusion maps. This limitation poses a challenge in diagnosing systematic pulmonary defects.

The purpose of this work was to develop a new framework to derive quantitative pulmonary PBV maps from the available DECT data to overcome the current limitations of iodine image-based perfusion assessment and also achieve simultaneous functional and anatomical lung imaging using DECT acquisitions. The method was developed based on the physiological meaning of PBV and the imaging physics of DECT. The main contribution of this work is to show that the quantitative and absolute PBV measurements are determined by the local effective atomic number ($Z_{\text{eff}}$) distribution and can become an intrinsic absolute quantification of the perfused blood pool.
2. Material and Methods

2.1 Pulmonary perfusion blood volume (PBV) from dual energy CT imaging

By definition, as shown in the model presented in Figure 1, PBV is the blood volume perfused into a unit mass of lung tissue in a volume-of-interest (VOI) located at x:

$$\text{PBV}(x) = \frac{V_{\text{cap}}(x)}{m_{\text{lung}}(x)},$$  \(\#(1)\)

where \(V_{\text{cap}}(x)\) denotes the volume of the capillary bed within the VOI; \(m_{\text{lung}}(x)\) denotes the mass of the lung tissue in the VOI (Figure 1).

In practice, it is difficult to directly measure the volume of the capillary bed within a VOI due to the limited spatial resolution of CT relative to the capillary size. Therefore, PBV must be determined from other quantities measurable in CT images. Using the mass conservation principle, as shown by the derivations presented in Appendix I, Eq. (1) can be recast into the following form:

$$\text{PBV}(x) = \frac{1}{\rho_{\text{lung}}(x)} \frac{\rho_l(x)}{\rho_{l_0}},$$  \(\#(2)\)

where \(\rho_{\text{lung}}(x)\) denotes the mass density of the lung tissue in the VOI at \(x\), \(\rho_{l_0}\) is the concentration of the injected iodine at the feeding pulmonary artery and \(\rho_l(x)\) is the iodine concentration in the VOI. The key difference between Eq. (1) and Eq. (2) is that the three quantities in Eq. (2) are, in principle, measurable using DECT imaging technology. For example, \(\rho_l(x)\) and \(\rho_{l_0}\) can be measured based on the signal values of the iodine material image, and \(\rho_{\text{lung}}(x)\) can be measured using the water material image. These measurements do not require the CT to have capillary-level spatial resolution. In reality, however, the signals of the iodine and water material images do not always provide quantitatively accurate iodine concentrations and lung tissue densities. To explain this reason, let’s review the so-
called “material decomposition”, in which the linear attenuation coefficient of the VOI at \( x \) is decomposed into two material bases as

\[
\mu(x, E) = a_i(x) \left( \frac{\mu}{\rho} \right)_i (E) + a_w(x) \left( \frac{\mu}{\rho} \right)_w (E), \quad \#(3)
\]

or three material bases as

\[
\mu(x, E) = a_i(x) \left( \frac{\mu}{\rho} \right)_i (E) + a_w(x) \left( \frac{\mu}{\rho} \right)_w (E) + a_{air}(x) \left( \frac{\mu}{\rho} \right)_{air} (E). \quad \#(4)
\]

Here \( E \) denotes the x-ray energy, and \( \left( \frac{\mu}{\rho} \right)_i \), \( \left( \frac{\mu}{\rho} \right)_w \), and \( \left( \frac{\mu}{\rho} \right)_{air} \) denote the mass attenuation coefficients of pure iodine, water, and air, respectively. The material “water” can also be replaced by a “standard soft tissue material” defined by the CT vendor or the end-user, but the overall working principle remains the same.

### 2.2 Conventional “relative PBV” measurements using iodine basis images

The iodine material image, \( a_i(x) \), which describes the concentration of "iodine like" materials, was used in literature\(^{24,33,34}\) as a surrogate for the PBV since it is assumed to be equivalent to \( \rho_i(x) \), the true iodine concentration in the VOI, namely

\[
PBV_{\text{iodine}}(x) = \kappa a_i(x) \quad \#(5)
\]

where \( \kappa \) is a numerical constant. In other words, the iodine material image is assumed to be linearly proportional to the PBV, and \( \rho_{\text{lung}}(x) \) in Eq. (2) is assumed to constant throughout the lungs. However, these assumptions are not well supported by imaging physics as discussed below:

First, the iodine material image, \( a_i(x) \), does not necessarily provide the accurate iodine concentration distribution, \( \rho_i(x) \), despite the fact that the physical units of \( a_i(x) \) and \( \rho_i(x) \) are the same (i.e., mg/ml). The actual physical meaning of \( a_i(x) \) and \( a_w(x) \) from water-iodine material decompositions are given by the following formulae:\(^{40,41}\)
where $\beta$ is an energy- and material-independent numerical constant, $N_a$ is the Avogadro constant, $\rho_e$ denotes electron density, $A$ denotes the atomic mass number, and $Z$ denotes the atomic number. For example, $Z_i (=5.3)$ and $Z_w (=7.4)$ are the atomic numbers of pure iodine and water, respectively. As shown in Appendix II, $a_i(x)$ is equal to $\rho_i(x)$ only under the condition that the VOI is entirely composed of the basis materials. When a voxel contains a foreign material with a $Z_{\text{eff}}$ different from those of the basis materials, its contribution to the x-ray attenuation will be assigned to both material basis images. In that case, the assumption that $a_i(x)$ is same as $\rho_i(x)$ inevitably leads to either over- or under-estimation of the PBV.

Second, compared with the PBV formula in Eq. (2), using $a_i$ as a surrogate for the PBV ignores the dependence of the PBV on the lung tissue density $\rho_{\text{lung}}(x)$, a quantity that varies spatially in the lung. Therefore, the lack of consideration of the spatially varying $\rho_{\text{lung}}(x)$ in $\text{PBV}_{\text{iodine}}$ is problematic.

To experimentally demonstrate the possible contribution of consolidation to the iodine material image signal, the $Z_{\text{eff}}$ of pulmonary consolidation was experimentally measured using the DECT images (Gemstone Spectral Imaging (GSI), GE Healthcare) of a human subject. Information about the patient and the scan protocol is provided in Table II (Subject 1). Ideally, the measurement of the $Z_{\text{eff}}$ of pulmonary consolidation should use non-contrast DECT data to avoid the impact of iodine to the $Z_{\text{eff}}$ result. Since no non-contrast chest DECT exam is performed at the authors’ institutions, we had to use contrast-enhanced chest DECT: we carefully chose a subject that had both pulmonary consolidation and known acute
PE and impaired blood perfusion to the consolidated regions to minimize the influence of the iodine. Measurement of consolidation $Z_{\text{eff}}$ was performed in a carefully chosen VOI without perceivable contrast-enhanced vessels as corroborated by the pulmonary CTA images. As shown by Figure 2 and Table I, $Z_{\text{eff}}$ of the consolidated tissue (8.11 [7.91, 8.29]) is indeed higher than that of water (7.42). Therefore, even without any iodine uptake, the consolidation can contribute to the signal of iodine material images. Further, the electron density ($\rho_e$) of the consolidated tissue measured by DECT is approximately 3 times that of the normal lung tissue’s $\rho_e$. According to Eq. (6), a larger $\rho_e$ further increases the signal of consolidated tissue in the iodine material image.

As another demonstration, Figure 3 plots low-kV $\mu$ values against high-kV $\mu$ values for consolidated and normal lung tissues of a human subject. A line connecting the consolidation and normal lung tissue data points has a slope of 1.19 (99% CI [1.17, 1.21]), which is larger than the slope of water (1.14). Because the slope is positively correlated to the effective atomic number, this figure implies that compared with normal lung tissues, consolidations contain additional materials with $Z_{\text{eff}}$ larger than that of water. All these experimental data support the premise that consolidated lung tissue contributes to the iodine material image and thus PBV$_{\text{iodine}}$ is not a robust and accurate metric of pulmonary perfusion, as a higher PBV$_{\text{iodine}}$ value does not necessarily mean a higher blood volume, and a “normal” PBV$_{\text{iodine}}$ value does not necessarily rule out perfusion defects.

### 2.3 Absolute quantification of pulmonary PBV from DECT-based $Z_{\text{eff}}$ imaging

Instead of using the iodine material image-based PBV$_{\text{iodine}}$, a new metric was developed in this work to quantitatively measure PBV. As shown in Appendix II, the PBV defined in Eq. (2) is quantitatively related to the effective atomic number $Z_{\text{eff}}$ as follows:

$$\text{PBV}_{Z_{\text{eff}}}(x) = k Z_{\text{eff}}^\beta(x) + b, \#(8)$$

where constants $a$ and $b$ are determined as follows:
A value of 2.94 is widely used in literature for the exponent $\beta$.\textsuperscript{43,44} For the term $\rho_i$ (iodine concentration in a feeding pulmonary artery), it can be reliably measured from the iodine material image due to the absence of consolidations within the large artery. Eq. (8) provides an absolute (rather than relative) measurement of PBV with a physical unit of [ml/g] or [ml/100 g] depending on the user’s preference.

\section*{2.4 Proof-of-concept human subject evaluation studies}

As an initial proof-of-concept evaluation of the proposed quantitative $\text{PBV}_{z_{\text{eff}}}$ measurement method, pulmonary DECT angiography data of 4 human subjects were retrospectively collected and processed under IRB approval. Among these subjects, three received DECT on a 256-slice MDCT scanner (Revolution CT, GE Healthcare) equipped with the GSI DECT technology; one subject received DECT on a 64-slice MDCT scanner (Discovery CT750 HD, GE Healthcare) equipped with GSI. The age, gender, BMI and other relevant information about the DECT exams are listed in Table 2.

\subsection*{2.4.1 DECT scan protocol}

For scans performed on the 256-slice CT system, the intravenous contrast injection used 100 ml of iohexol 300 mgI/ml (Omnipaque 300, GE Healthcare) with a 10 ml saline flush, both at a rate of 5 ml/s. A bolus tracking scan (SmartPrep, GE Healthcare) was used to determine the scan timing: once the enhancement in the left atrium exceeded 60 HU, the actual DECT angiography scan was triggered and performed under the helical mode with a helical pitch of 0.992. The scan range extended from the apices of the lung to just below the diaphragm. The x-ray tube potential rapidly switched between 80 kV and 140 kV while the gantry rotated at a speed of 0.5 s per revolution. The tube current (mA) was adjusted for each subject based on their body size under the guidance of the GSI-Assist technology. The

\begin{equation}
\begin{align*}
 k &= \frac{1}{\rho_i(Z_i^{\beta} - Z_w^{\beta})}, \\
 b &= -\frac{Z_w^{\beta}}{\rho_i(Z_i^{\beta} - Z_w^{\beta})}.
\end{align*}
\end{equation}
beam collimation was 80 mm and the reconstruction slice thickness was 1.25 mm. For the subject who received the DECT on the 64-slice scanner, the beam collimation was 40 mm and the reconstruction slice thickness was 2.5 mm. The contrast injection was 100 ml of iopamidol 370 mg/ml (Iovue 370, Bracco Diagnostics Inc.) at a rate of 4 ml/s, followed by 45 ml of saline at 2 ml/s. The bolus tracking scan used a region-of-interest (ROI) placed on the pulmonary artery at the level of carina, and the trigger threshold was 110 HU. Other scan parameters are listed in Table 2.

2.4.2 Image processing and data analysis

For the DECT acquisition of each subject, iodine(water) and water(iodine) material images were directly generated by the CT scanner. According to the CT manufacturer, these material images were generated via a two-material (water-iodine) decomposition process without requiring any knowledge of each material's volume fraction or the volume-conservation assumption. GE DECT systems also provide \( Z_{\text{eff}} \) maps. If \( Z_{\text{eff}} \) is not directly available, it can be computed from the water and iodine material images as follows:

\[
Z_{\text{eff}}(x) = \left( \frac{a_w(x) \left( \frac{Z}{A} \right)_w \int \frac{Z_w}{\frac{Z}{A}_w} - a_i(x) \left( \frac{Z}{A} \right)_I \int \frac{Z_i}{\frac{Z}{A}_I} }{a_w(x) \left( \frac{Z}{A} \right)_w \int - a_i(x) \left( \frac{Z}{A} \right)_I \int} \right) \beta
\]

where \( Z_w = 7.42, Z_I = 53, \left( \frac{Z}{A} \right)_w = 0.555, \left( \frac{Z}{A} \right)_I = 0.418 \), and \( \beta = 2.94 \).

The iodine concentration of the feeding artery, \( \rho_{l_0} \), was measured by placing an ROI on the pulmonary trunk in the iodine material image. Since the ROI is completely within the iodinated blood, its \( a_i \) signal can be safely used to estimate the input iodine concentration, \( \rho_{l_0} \). Next, Eq. (8) and the measured \( Z_{\text{eff}} \) and \( \rho_{l_0} \) were used to calculate \( \text{PBV}_{Z_{\text{eff}}} \) of each pixel within the lungs. The measured \( \rho_{l_0} \) was applied to the whole lung regions of a given patient. The calculation of \( \text{PBV}_{Z_{\text{eff}}} \) was performed off the CT console on a computer using the Matlab software (version R2020b, Mathworks, Inc.) and the results were saved as RGB DICOM.
images for radiologist review. For comparison purposes, conventional PBV\textsubscript{iodine} maps were also generated from iodine material images. The lung region of each PBV map was color-coded using the “hot” color map and overlaid on the corresponding grayscale 140 kV-equivalent CT image.

A radiologist with 35 years of clinical experience evaluated both PBV\textsubscript{Z\textsubscript{eff}} and PBV\textsubscript{iodine} maps. For each patient and each type of PBV map, the reader evaluated whether the images demonstrated evidence of perfusion defects, ground-glass opacities (GGO), consolidations, atelectasis, lung tumors, or other pulmonary abnormalities; the gold-standard diagnosis was established based on clinical and laboratory records, CT and nuclear medicine images (if available), and other relevant imaging results. The diagnostic performance of PBV\textsubscript{Z\textsubscript{eff}} and PBV\textsubscript{iodine} were compared qualitatively by the experienced radiologist.

3. Results

Figures 4-7 show color-coded PBV\textsubscript{Z\textsubscript{eff}} and PBV\textsubscript{iodine} maps of the patients’ lung regions overlaid on top of the corresponding grayscale CT images. Quantitative measurement results of PBV, material image signals, Z\textsubscript{eff}, and electron density (\rho\textsubscript{e}) values are summarized in Table 3. In addition, the online Supplemental Material provides the original water and iodine material images, Z\textsubscript{eff} maps, and \rho\textsubscript{e} maps without using the color overlay display method.

Figure 4 shows images of Subject 1 with clinically confirmed acute PE and pneumonia. Extensive GGO and consolidation were found in the posterior regions of both lungs. As shown by this subject’s pulmonary CTA source images in the first row of Figure 4, multiple emboli exist in the pulmonary vessels supplying the posterior lung regions. PBV\textsubscript{Z\textsubscript{eff}} maps demonstrate regional perfusion defects in the lungs. In comparison, PBV\textsubscript{iodine} maps do not clearly show the perfusion defects. This is because the consolidation and GGO contributed to the iodine material images and counteracted the reduction of iodine uptake in those areas.
Figure 5 shows images of Subject 2 with clinically confirmed PE. The subject has a history of lung infection and consolidations and GGOs within the bilateral upper and right middle lobes. The bilateral lobar, segmental and subsegmental pulmonary emboli can be seen on the pulmonary CTA images in the first row in Figure 5. The PBV maps show a global reduction in blood volume; some regions such as the bilateral upper lobes show severe perfusion defects. Although the PBV$_{iodine}$ maps also show regional defects in the upper lobes, they failed to show the systematic reduction in blood perfusion because their values do not provide the quantitative blood volume level and are dependent on extrinsic factors such as the injected iodinated contrast level. The GGOs contributed to the iodine material image signal and reduced the sensitivity of PBV$_{iodine}$ maps to perfusion defects.

Figure 6 shows images of Subject 3 who has large left and medium right pleural effusions, loculations in the right oblique fissure, compressive collapse of the left lower lobe, and lung edema with atelectasis in the left lung. However, no PE or pulmonary hypertension was found in this patient. The PBV$_{Z_{eff}}$ maps show normal perfusion with an average PBV value of 33 [27, 37] ml/100g in the left lung and 32 [19, 46] ml/100g in the right lung. In comparison, the iodine material images of this subject show a much higher signal in the left lung (6.7 [5.8, 7.6] mg/ml) than the right lung (3.0 [1.8, 4.2] mg/ml, p<0.001). Instead of a greater blood perfusion, the high iodine material image signal of the left lung was actually caused by the lung fluid that has a $Z_{eff}$ different from that of water. If a sub-optimal display range is used for the iodine basis image (4th column in Figure 6), the right lung may appear hypoperfused compared with the left lung. This example shows a limitation of the iodine image-based relative perfusion measurement and an advantage of the proposed quantitative PBV measurement.

Finally, Figure 7 shows images of a “control” case (Subject 4) whose gold-standard clinical diagnosis has ruled out PE, CTEPH, or other lung diseases. For this subject without any consolidation and GGO, both PBV$_{Z_{eff}}$ and PBV$_{iodine}$ maps show normal pulmonary perfusion.
signals without any false positives or false negatives. Meanwhile, blood vessels in PBV\textsubscript{iodine} show higher PBV\textsubscript{iodine} signals than the normally aerated lung parenchyma because of the higher electron density of the vessels (see the Supplemental Material for the electron density maps). In clinical practice, the much brighter vessels can be distracting for the evaluation of parenchymal perfusions and they are segmented and hidden on PBV\textsubscript{iodine} maps in some products\textsuperscript{47,48}. In comparison, the proposed PBV\textsubscript{Z\textsubscript{eff}} map is more homogenous since the definition of PBV in Eq. (2) requires a normalization of the local tissue density.

4. Discussion

In the current DECT PBV\textsubscript{iodine} method, pulmonary perfusion conditions are estimated using iodine material images generated by applying a two-material or three-material decomposition to the acquired DECT data. There are two fundamental pitfalls of this approach: First, as shown in Eq. (5), a material with an effective atomic number different from those of the basis materials can be partially assigned to the iodine basis images. Therefore, the iodine material images, a\textsubscript{i}(x), do not necessarily provide quantitatively accurate iodine density distribution, \(\rho_i(x)\). The difference between a\textsubscript{i}(x) and \(\rho_i(x)\) can be significant for consolidations and GGOs that have not only a higher \(Z_{\text{eff}}\) relative to water but also a higher density relative to the normal lung tissue. Second, by definition, PBV is the volume of blood perfused per unit mass of lung tissue [Eq. (1)]. The iodine material images do not reflect the mass of the lung tissue. One can argue that the signal of a\textsubscript{i}(x) with a unit of [mg/ml] has a positive correlation with \(\rho_i(x)\) and thus has a positive correlation with PBV according to Eq. (2). However, the existence of a positive correlation is not equivalent to quantitatively accurate PBV due to the fact that an important quantity, \(\rho_{\text{tung}}(x)\), in the PBV formula in Eq. (2) is not characterized by a\textsubscript{i}(x).

Due to the two pitfalls of PBV\textsubscript{iodine}, the identification of perfusion defects in PBV\textsubscript{iodine} maps would have to rely heavily on the choice of display window/level, the choice of display color...
map, the relative difference in color between different lung regions, and the reader’s experience. In addition, as shown by the human subject results in this work, lung regions with consolidations and GGOs can generate a higher PBV\text{\textsubscript{iodine}} signal relative to the normally aerated lung regions. In fact, data published in multiple prior studies support the existence of this effect.\textsuperscript{37-39} For example, in a fast kV switching DECT study of patients with COVID-19 pneumonia and suspected PE, two of the three showcases demonstrated higher iodine material image signal in the consolidation regions than the normally aerated parenchyma regions: one case shows a $a_i$ value of 6.053 mg/ml in the consolidation, compared to 0.723 mg/ml in the normally aerated region.\textsuperscript{37} In another dual-source DECT-based study of patients with GGOs, two of the three showcases demonstrated higher $a_i$ signals in the GGO regions than normally aerated regions.\textsuperscript{38} The increased signal of consolidations and GGOs in PBV\text{\textsubscript{iodine}} maps can be misleading, as both the reflex pulmonary artery vasoconstriction theory and nuclear medicine perfusion imaging can indicate a decreased (instead of increased) perfusion for consolidations and GGOs.\textsuperscript{45,46} Due to this limitation of PBV\text{\textsubscript{iodine}}, some DECT postprocessing tools exclude consolidation or GGO regions in the final PBV\text{\textsubscript{iodine}} maps, despite the strong clinical needs to assess perfusion conditions of these regions, particularly for patients with COVID-19 pneumonia.\textsuperscript{47,48}

In contrast to PBV\text{\textsubscript{iodine}}, this work shows that PBV\text{\textsubscript{z\textsubscript{\textit{eff}}}} derived from DECT data is a quantitative biomarker of pulmonary perfused blood volume. As shown by the preliminary human subject results presented in Section 4, for patients with acute PE and pneumonia, the quantitative PBV maps clearly demonstrate regional perfusion defects in the area supplied by the embolized vessels, while the iodine material images failed to demonstrate the defects since pneumonia-induced consolidations add a positive signal to the iodine material image to counteract the reduced perfusion in the area. More interestingly, for a patient without PE, but with pleural effusion and atelectasis, the quantitative PBV\text{\textsubscript{z\textsubscript{\textit{eff}}}} maps correctly demonstrate normal perfusion and are more specific than iodine image-based relative perfusion maps.
Although Eq. (8) provides a formula to calculate $\text{PBV}_{Z_{\text{eff}}}$ from the $\beta^{\text{th}}$ power of $Z_{\text{eff}}$, it is not the only approach to calculate $\text{PBV}_{Z_{\text{eff}}}$: as shown by Eq. (S18) in Appendix II, $\text{PBV}_{Z_{\text{eff}}}$ can also be obtained via a pixel-wise division of the iodine material image by the electron density image, albeit some commercial DECT systems do not directly provide electron density images. Fundamentally speaking, both of the two calculation methods are derived from the definition of PBV and are equivalent. In practice, one can choose either one based on the types of DECT images provided by a given clinical system.

This work has the following limitations. First, only four representative human subject cases were studied to demonstrate the pitfalls of the conventional $\text{PBV}_{\text{iodine}}$ evaluation method and to show the effectiveness of the proposed quantitative $\text{PBV}_{Z_{\text{eff}}}$ metric based on the effective atomic number maps. To fully demonstrate the clinical value of $\text{PBV}_{Z_{\text{eff}}}$, a large cohort of human subject studies needs to be studied in the future. Second, it is worth emphasizing that $\text{PBV}_{Z_{\text{eff}}}$ derived from DECT data only represents a steady-state perfusion measurement. It does not provide other important hemodynamic information such as pulmonary blood flow. If one desires to obtain a complete set of perfusion measurements including pulmonary flow information, time-resolved CT scans are required for measuring the contrast dynamics of pulmonary vasculature and tissues. Third, the iodine material images and $\text{PBV}_{\text{iodine}}$ maps in this work were generated by commercial CT scanners from a single vendor that uses two-material (water and iodine) decomposition. It is possible that by using three- or multi-material decompositions (especially with one basis material similar to consolidations and GGOs in terms of $Z_{\text{eff}}$), the issues of the iodine material image and $\text{PBV}_{\text{iodine}}$ in quantifying the perfusion of consolidated and GGO regions can be mitigated. However, the selection of the proper basis material can be challenging, considering the $Z_{\text{eff}}$ of consolidations and GGOs may vary across patients. How to further improve DECT material decomposition for more accurate pulmonary embolism detection and how $\text{PBV}_{\text{iodine}}$ from improved multi-material decomposition compares to $\text{PBV}_{Z_{\text{eff}}}$ deserves further investigation in the future.
5. Conclusion

In conclusion, a new quantitative biomarker, $\text{PBV}_{\text{z\text{eff}}}$, from DECT imaging was developed to quantitatively assess pulmonary perfusion blood volume (PBV). Compared with the relative pulmonary perfusion measurements using iodine images derived from two-material decomposition, the proposed $\text{PBV}_{\text{z\text{eff}}}$ provides a more accurate and robust imaging biomarker of potential pulmonary perfusion defects.

Appendix I: Pulmonary perfused blood volume (PBV)

Using the relationship between mass, mass density, and volume, the PBV formula in Equation (1) can be recast to

$$\text{PBV}(x) = \frac{1}{\rho_{\text{lung}}(x) V_{\text{lung}}(x)} V_{\text{cap}}(x), \quad \text{#(S1)}$$

where $\frac{V_{\text{cap}}(x)}{V_{\text{lung}}(x)}$ denotes the volume fraction of the capillary bed in the VOI at $x$. When the iodinated contrast medium is injected into the blood stream and the pulmonary capillary bed is perfused with the iodinated blood, the mass of iodine that flows into the VOI in the lung is the same mass of iodine in the capillary bed, namely,

$$m_{l,\text{cap}} = m_{l,\text{VOI}}, \quad \text{#(S2)}$$

However, the mass of iodine in the capillary bed is given by the product of iodine concentration in the input artery, $\rho_{l_0}$, and the volume of the capillary bed in the VOI, $V_{\text{cap}}(x)$, i.e.,

$$m_{l,\text{cap}} = \rho_{l_0} V_{\text{cap}}(x) = m_{l,\text{VOI}}, \quad \text{#(S3)}$$

Therefore, the averaged concentration of iodinated blood in the lung tissue VOI is given by
This formula can be re-arranged to obtain the ratio of the capillary bed in the lung tissue VOI as the ratio between the iodine concentration in the VOI and the iodine concentration in the input artery as follows:

\[
\frac{V_{\text{cap}}(x)}{V_{\text{lung}}(x)} = \frac{\rho_l(x)}{\rho_{l_0}}. \tag{S5}
\]

By combining Equations (S1) and (S5), the following equation is obtained for PBV:

\[
\text{PBV}(x) = \frac{1}{\rho_{\text{l}_0}} \frac{\rho_l(x)}{\rho_{\text{l}_0}}. \tag{S6}
\]

This is the primary result presented in Eq. (2) in the main text.

Appendix II: PBV Measurement using DECT Imaging

In DECT-based lung perfusion assessment, the iodine basis image, \(a_l(x)\), is used as a surrogate for iodine concentration \(\rho_l(x)\). The problem with this approach is that the physical meaning of \(a_l(x)\) is not the same as \(\rho_l(x)\). Instead, its formula is given by\(^{40,41}\)

\[
a_l(x) = \frac{\rho_e(x)}{N_\alpha \left(\frac{Z}{A}\right)} \frac{Z_{\text{eff}}^\beta(x) - Z_{\text{w}}^\beta}{Z_{\text{i}}^\beta - Z_{\text{w}}^\beta}. \tag{S7}
\]

in which \(Z_{\text{eff}}\) is defined as

\[
Z_{\text{eff}} = \left[ \sum_{j=1}^{n} f_i Z_i^\beta \right]^{1/\beta}. \tag{S8}
\]

Here \(Z_i\) is the atomic number of the \(i^{th}\) constituent material in the VOI at \(x\), and \(f_i\) is the fraction of electrons associated with the \(i^{th}\) material. As shown by Eq. (S7), \(a_l(x)\) is not necessarily the same as \(\rho_l(x)\). They are equal only in the following special case:
**Special Case:** The VOI is entirely composed of iodine and water. Under this special condition,

\[
Z_{\text{eff}}^{\beta}(x) = f_i(x)Z_i^{\beta} + [1 - f_i(x)]Z_w^{\beta} = f_i(x)\left(Z_i^{\beta} - Z_w^{\beta}\right) + Z_w^{\beta}, \tag{S9}
\]

where \( f_i \) denotes the fraction of electrons coming from the iodine atoms. Under the condition in (S9), the formula of \( a_i(x) \) in (S7) can be written as

\[
a_i(x) = \frac{\rho_e(x)}{N_a} \frac{f_i(x)}{A} \left(\frac{Z_i^{\beta} - Z_w^{\beta}}{Z_i^{\beta} - Z_w^{\beta}}\right) + \frac{Z_w^{\beta}}{Z_i^{\beta} - Z_w^{\beta}} = \frac{\rho_e(x) f_i(x)}{N_a} = \frac{\rho_e(x)}{N_a} = \rho_i(x). \tag{S10}
\]

Aside from the above special case, \( a_i(x) \) is not the same as \( \rho_i(x) \). To find an alternative way to estimate PBV, the \( Z_{\text{eff}} \) formula in Eq. (S8) can be recast into the following form:

\[
Z_{\text{eff}}^{\beta} = f_i Z_i^{\beta} + \sum_{j=2}^{n} f_j Z_j^{\beta}, \tag{S11}
\]

where \( f_j \) (\( j = 2, \ldots, n \)) denotes the electron fraction for non-iodine materials in the VOI. As shown in Table 1, the atomic numbers of non-iodine materials in the lung are relatively similar to \( Z_w \) and are much smaller than \( Z_i \). As a result, the following approximation can be justified:

\[
Z_{\text{eff}}^{\beta} \approx f_i Z_i^{\beta} + Z_w^{\beta} \sum_{j=2}^{n} f_i = f_i Z_i^{\beta} + Z_w^{\beta}(1 - f_i), \tag{S12}
\]

Therefore,

\[
\frac{f_i(x)}{Z_i^{\beta} - Z_w^{\beta}} \approx \frac{Z_{\text{eff}}^{\beta}(x) - Z_w^{\beta}}{Z_i^{\beta} - Z_w^{\beta}}. \tag{S13}
\]

Per the definition of electron fraction, \( f_i(x) \) can be written as
\[ f_i = \left( \frac{Z}{A} \right)_i f_{m_i} \approx \frac{1}{2} \sum_j \left( \frac{Z}{A} \right)_j f_{m_j} \approx \frac{m_i}{m_{\text{lung}}} = \frac{m_i}{\rho_{\text{lung}} V_{\text{lung}}}, \tag{S14} \]

where we used the fact that for the majority of tissue materials, \( \frac{Z}{A} \approx \frac{1}{2} \). Based on both (S13) and (S14):

\[ \frac{m_i(x)}{\rho_{\text{lung}}(x)V_{\text{lung}}(x)} \approx \frac{Z_{\text{eff}}^\beta(x) - Z_{w}^\beta}{Z_{I}^\beta - Z_{w}^\beta}. \tag{S15} \]

The mass of iodine in the VOI, \( m_i(x) \), is related to \( V_{\text{cap}}(x) \) and \( \rho_{I_0} \) by

\[ V_{\text{cap}}(x) = \frac{m_i(x)}{\rho_{I_0}}. \tag{S16} \]

According to (S15)-(S16) and the PBV formula in (S1),

\[ \text{PBV}_{Z_{\text{eff}}}(x) = \frac{m_i(x)/\rho_{I_0}}{\rho_{\text{lung}} V_{\text{lung}}} \approx \frac{1}{\rho_{I_0}} \frac{Z_{\text{eff}}^\beta(x) - Z_{w}^\beta}{Z_{I}^\beta - Z_{w}^\beta}. \tag{S17} \]

This is the desired result presented in Eq. (8) and Eq. (9) in the main text.

By comparing the formula of \( \text{PBV}_{Z_{\text{eff}}}(x) \) in Eq. (S17) with the formula of \( a_i(x) \) in Eq. (S7), one can observe that \( \text{PBV}_{Z_{\text{eff}}}(x) \) and \( a_i(x) \) are related by

\[ \text{PBV}_{Z_{\text{eff}}}(x) = \frac{N_{a} \left( \frac{Z}{A} \right)_i a_i(x)}{\rho_{I_0} \rho_e(x)}. \tag{S18} \]

Therefore, an alternative method to calculate \( \text{PBV}_{Z_{\text{eff}}}(x) \) is to normalize the iodine material image \( a_i(x) \) by the electron density image \( \rho_e(x) \) and then scale the result by \( N_{a} \left( \frac{Z}{A} \right)_i /\rho_{I_0} \).

**Acknowledgements**
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Conflicts of Interest

The authors have no conflicts to disclose.

Data Availability Statement

The data supporting the results of this study are available upon reasonable request to the corresponding author.

Supplementary Material

The Supplemental Material document (Supplemental_Figures_S1-S4.docx) provides water and iodine material images, $Z_{\text{eff}}$ maps, and $\rho_e$ maps of the four human subjects.
Figure Captions

Figure 1. An illustration of the concept of pulmonary perfusion blood volume (PBV). For a given volume-of-interest (VOI) in the lung parenchyma, its PBV is given by the ratio between the volume occupied by the capillaries ($V_{cap}$) and the mass of the lung tissue in the VOI ($m_{lung}$). $m_{lung} = V_{lung} \rho_{lung}$, where $V_{lung}$ and $\rho_{lung}$ are the VOI volume and the lung tissue density, respectively. By definition, PBV is independent of the injected iodine concentration.
Figure 2. Experimental measurement of $Z_{\text{eff}}$ and $\rho_e$ using DECT data of an acute PE patient with extensive bilateral consolidations and clinically-proven pulmonary perfusion deficits. The dotted circles indicate VOIs where measurements were performed: These VOIs are located within the consolidations without perceivable iodine uptake as shown by the CTA maximum intensity projection (MIP) image. The results confirmed that $Z_{\text{eff}}$ of the consolidation (8.11 [7.91, 8.29]) is higher than that of water (7.42) and its $\rho_e$ (0.55 [0.54, 0.56] mol/ml) is more than 3 times that of the $\rho_e$ of the normally aerated lung tissue (0.16 [0.10, 0.23] mol/ml).
Figure 3. (a) 140 kV contrast-enhanced CT image of a patient showing consolidation in the right lung. Two ROIs were drawn on the consolidation and the contralateral normal lung tissue. (b) For each ROI, its mean attenuation coefficient measured in the 80 kV image ($\mu_{low}$) was plotted against the attenuation coefficient measured in the 140 kV image ($\mu_{high}$). In (b), the “+” markers indicate individual data points in each ROI while each solid disk marker represents the ROI mean. The black line connecting the data of ROI 1 and ROI 2 has a slope of 1.19 (99% CI [1.17, 1.21]), which is larger than the slope of water (1.14). This implies that compared with the normal lung tissue, the consolidation contains materials with $Z_{eff}$ slightly higher than that of water.
**Figure 4:** Images of Subject 1 with clinically proven pneumonia and acute pulmonary embolism. The CT angiography source images in Row 1 show multiple segmental and subsegmental pulmonary emboli (pointed by the arrows) in the vessels that supply the posterior regions of the left and right lungs. The CT images in Row 2 with a wider display range show extensive ground glass opacity and consolidation in both lungs. PBV$_{z_{\text{eff}}}$ maps (color overlay on the grayscale CT image) in Row 3 demonstrated regional perfusion defects in the posterior area of both lungs. In contrast, PBV$_{\text{iodine}}$ maps (color overlay on the grayscale CT image) in Row 4 do not clearly show the perfusion abnormalities because the consolidated tissue contributed to the iodine material image signal such that the reduction of iodine concentration in the consolidated area was counteracted in PBV$_{\text{iodine}}$. 
Figure 5. Images of Subject 2 with clinically confirmed pulmonary embolism. The CTA source images in Row 1 show bilateral lobar, segmental and subsegmental pulmonary emboli (arrows). The lung-window CT images in Row 2 show bilateral ground glass opacities. The bilateral perfusion defects can be visualized more clearly in the PBV$_{z_{eff}}$ maps (color overlay on the grayscale CT image) in Row 3 than the PBV$_{iodine}$ maps (color overlay on the grayscale CT image) in Row 4.
Figure 6: Images of Subject 3 without any pulmonary embolism or pulmonary hypertension. The patient has large pleural effusions and compressive collapse in the left lung. The atelectasis in the left lung significantly elevated the local signal in the iodine material images. Consequently, when an adaptive display range is selected for PBV$_{\text{iodine}}$ maps, the right lung appears to be hypoperfused compared with the left lung. In contrast, the PBV$_{\text{z eff}}$ maps are robust against local density variation and shows a uniform pulmonary perfusion. The lung regions of PBV$_{\text{iodine}}$ and PBV$_{\text{z eff}}$ maps are color-coded and overlaid on the grayscale CT images.
Figure 7: Images of a “control case” (Subject 4) without pulmonary embolism and without pulmonary hypertension. The lung regions of PBV$_{\text{iodine}}$ and PBV$_{\text{Z,eff}}$ maps are color-coded and overlaid on the grayscale CT images.
References


Table 1: Values of effective atomic number ($Z_{\text{eff}}$), mass density ($\rho$), and electron density ($\rho_e$) of typical materials in the chest. Except for pulmonary consolidation, the values are taken from the NIST Standard Reference Database No. 126 and other published papers. The values for the pulmonary consolidation were experimentally measured from the human subject image data shown in Figure 2.

<table>
<thead>
<tr>
<th>Material</th>
<th>Air (dry) $Z_{\text{eff}}$</th>
<th>Normal lung tissue $Z_{\text{eff}}$</th>
<th>Adipose tissue $Z_{\text{eff}}$</th>
<th>Water $Z_{\text{eff}}$</th>
<th>Muscle $Z_{\text{eff}}$</th>
<th>Iodine $Z_{\text{eff}}$</th>
<th>Pulmonary consolidation $Z_{\text{eff}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\rho$ (g/ml)</td>
<td>$1.2 \times 10^{-3}$</td>
<td>0.29 [0.17, 0.41]</td>
<td>0.95 [0.17, 0.41]</td>
<td>1.0 [0.17, 0.41]</td>
<td>1.05 [0.17, 0.41]</td>
<td>4.9 [0.17, 0.41]</td>
<td>0.98 [0.17, 0.41]</td>
</tr>
<tr>
<td>$\rho_e$ (mol/ml)</td>
<td>$6.0 \times 10^{-4}$</td>
<td>0.16 [0.10, 0.23]</td>
<td>0.53 [0.10, 0.23]</td>
<td>0.56 [0.10, 0.23]</td>
<td>0.58 [0.10, 0.23]</td>
<td>2.05 [0.10, 0.23]</td>
<td>0.55 [0.10, 0.23]</td>
</tr>
</tbody>
</table>

Table 2: Subject demographics and scan parameters.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>BMI</th>
<th>Gender</th>
<th>Scanner</th>
<th>Contrast volume</th>
<th>Contrast type</th>
<th>Helical pitch</th>
<th>Beam Collimation</th>
<th>Rotation time</th>
<th>mA</th>
<th>Slice thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>26.9</td>
<td>male</td>
<td>750HD</td>
<td>100 ml</td>
<td>Isovue370</td>
<td>1.375</td>
<td>40 mm</td>
<td>0.5</td>
<td>600</td>
<td>2.5 mm</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>36.9</td>
<td>female</td>
<td>Revolution</td>
<td>100 ml</td>
<td>Omnopaque300</td>
<td>0.992</td>
<td>80 mm</td>
<td>0.5</td>
<td>240</td>
<td>1.25 mm</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>27.4</td>
<td>male</td>
<td>Revolution</td>
<td>100 ml</td>
<td>Omnopaque300</td>
<td>0.992</td>
<td>80 mm</td>
<td>0.5</td>
<td>200</td>
<td>1.25 mm</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>20.4</td>
<td>female</td>
<td>Revolution</td>
<td>100 ml</td>
<td>Omnopaque300</td>
<td>0.992</td>
<td>80 mm</td>
<td>0.5</td>
<td>200</td>
<td>1.25 mm</td>
</tr>
</tbody>
</table>
Table 3: Results of quantitative measurements (mean value [first quantile, third quantile]) of the four subjects’ DECT image data. The p values were given by two-sample t-tests with the unequal variance assumption.

<table>
<thead>
<tr>
<th>Subject 1</th>
<th>Normally aerated</th>
<th>Consolidation</th>
<th>p &lt; 0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>HU</td>
<td>-769 [-856, -760]</td>
<td>37 [15, 69]</td>
<td></td>
</tr>
<tr>
<td>aI (mg/ml)</td>
<td>1.2 [0.2, 1.5]</td>
<td>1.2 [1.0, 1.6]</td>
<td>p=0.626</td>
</tr>
<tr>
<td>aW (g/ml)</td>
<td>0.183 [0.122, 0.202]</td>
<td>1.015 [0.998, 1.035]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>ρe (mol/ml)</td>
<td>0.108 [0.072, 0.114]</td>
<td>0.552 [0.544, 0.561]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Zeff</td>
<td>9.25 [8.63, 9.85]</td>
<td>8.11 [7.91, 8.29]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PBVZeff (mg/100g)</td>
<td>29.29 [17.10, 40.22]</td>
<td>9.42 [6.37, 11.98]</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subject 2</th>
<th>Normally aerated</th>
<th>GGO</th>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>HU</td>
<td>-885 [-926, -8.76]</td>
<td>-610 [-640, -658]</td>
<td></td>
</tr>
<tr>
<td>aI (mg/ml)</td>
<td>0.9 [0.4, 1.1]</td>
<td>1.6 [1.1, 2.2]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>aW (g/ml)</td>
<td>0.091 [0.065, 0.091]</td>
<td>0.349 [0.334, 0.377]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>ρe (mol/ml)</td>
<td>0.050 [0.036, 0.051]</td>
<td>0.194 [0.186, 0.210]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Zeff</td>
<td>10.46 [9.93, 11.11]</td>
<td>8.83 [7.89, 9.74]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PBVZeff (mg/100g)</td>
<td>32.70 [24.37, 41.46]</td>
<td>8.78 [7.66, 14.56]</td>
<td>p&lt;0.001</td>
</tr>
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<table>
<thead>
<tr>
<th>Subject 3</th>
<th>Right lung</th>
<th>Left lung with atelectasis</th>
<th>p &lt; 0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>HU</td>
<td>-517 [-652, -428]</td>
<td>197 [164, 227]</td>
<td></td>
</tr>
<tr>
<td>aI (mg/ml)</td>
<td>3.0 [1.8, 4.2]</td>
<td>6.7 [5.8, 7.6]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>aW (g/ml)</td>
<td>0.405 [0.302, 0.457]</td>
<td>1.022 [1.013, 1.030]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>ρe (mol/ml)</td>
<td>0.226 [0.168, 0.256]</td>
<td>0.570 [0.565, 0.575]</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Zeff</td>
<td>10.09 [9.71, 10.34]</td>
<td>10.10 [9.71, 10.34]</td>
<td>p=0.096</td>
</tr>
<tr>
<td>PBVZeff (mg/100g)</td>
<td>32.24 [19.40, 45.73]</td>
<td>32.82 [26.66, 36.51]</td>
<td>p=0.566</td>
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<table>
<thead>
<tr>
<th>Subject 4</th>
<th>Right lung</th>
<th>Left lung</th>
<th>p = 0.840</th>
</tr>
</thead>
<tbody>
<tr>
<td>HU</td>
<td>-725 [-778, -713]</td>
<td>-723 [-767, -699]</td>
<td></td>
</tr>
<tr>
<td>aI (mg/ml)</td>
<td>2.7 [1.9, 3.0]</td>
<td>2.6 [1.8, 3.0]</td>
<td>p=0.437</td>
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<tr>
<td>aW (g/ml)</td>
<td>0.206 [0.174, 0.206]</td>
<td>0.209 [0.186, 0.218]</td>
<td>p=0.407</td>
</tr>
<tr>
<td>ρe (mol/ml)</td>
<td>0.115 [0.098, 0.116]</td>
<td>0.117 [0.104, 0.122]</td>
<td>p=0.389</td>
</tr>
<tr>
<td>Zeff</td>
<td>11.21 [10.09, 11.67]</td>
<td>11.13 [10.04, 11.86]</td>
<td>p=0.220</td>
</tr>
<tr>
<td>PBVZeff (mg/100g)</td>
<td>44.47 [26.70, 51.02]</td>
<td>43.13 [26.00, 54.25]</td>
<td>p=0.212</td>
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