Supplemental Digital Content

Detailed Positron Emission Tomography (PET) Methods

Following a scout-view and low-dose computed tomography (CT) (120 kVp, CareDose), a preliminary positron emission tomography (PET) scan was performed to detect residual radioactivity in the lungs (PET_{before}). Afterwards, microspheres B20 (ROTOP Pharmaka AG, Dresden, Germany) were labeled with ^{68}Ga (ITG Isotope Technologies Garching GmbH, Garching, Germany)[1] and injected intravenously as a slow bolus over approximately 1 min and the distribution of the activity was measured (PET_{after}).

Injection volumes were increased prior to each scan, consecutively raising the activity throughout the study (Baseline2: 3.3 MBq to 9.4 MBq; relative increases in injected activity compared to previous scan: Time 1: +21.7% to +162.8%; Time 2: +27.3% to +126.2%; Time 3: +56.8% to +255.1%; Time 4: +36.4% to +114.1%). Image reconstruction was carried out iteratively (ordered subset expectation maximization, 6 iterations, 4 subsets, post-filtering Gauss 5 mm) with attenuation correction. The voxel size of PET was 4.06 x 4.06 x 5 mm^3.

For lung segmentation in PET scans, the resolution of the respective PET dataset was increased by interpolation to fit the CT dataset. Then, the region of interest of the higher resolution CT was applied to respective PET images.

For each measuring point, the *net activity* (PET_{net}) of the attenuation-corrected images was calculated as shown in Eq. 1:

$$PET_{net} = PET_{after} - PET_{before} \quad \text{(Eq. 1)}$$

The activity of each voxel was normalized to the total activity inside the region of interest (PET_{total}), yielding PET_{norm}, as shown in Eq. 2:

$$PET_{norm} = PET_{net} / PET_{total} \quad \text{(Eq. 2)}$$

To account for varying numbers of blood vessels inside an imaged lung volume element, $\dot{Q}_{rel}$ was calculated per voxel as the normalized activity PET_{norm} relative to the CT density of each voxel (δ), as shown in Eq. 3:

$$\dot{Q}_{rel} = PET_{norm} / \delta = PET_{net} / (PET_{total} * \delta) \qquad \text{(Eq. 3)}$$

Values of $\dot{Q}_{rel}$ of voxels with CT density ≤ 0.05 were set to zero.

The centers of $\dot{Q}_{rel}$ along the dorsal-ventral and the caudal-cranial axes were calculated from the center of the distribution curve of $\dot{Q}_{rel}$.

Besides ^{68}Ga-labeled microspheres, the distribution of $\dot{Q}_{rel}$ was also visualized with fluorescent-labeled microspheres as described in detail elsewhere [2]. The comparison of these methods is beyond the scope of this study, but cross-interference is unlikely.

References of the Supplemental Digital Content

1. Kotzerke J, Andreeff M, Wunderlich G, Wiggermann P, Zophel K: [Ventilation-perfusion-lungscintigraphy using PET and 68Ga-labeled radiopharmaceuticals]. Nuklearmedizin 2010; 49: 203-8

2. Gama de Abreu M, Spieth P, Pelosi P, Carvalho AR, Walter C, Schreiber-Ferstl A, Aikele P, Neykova B, Hübler M, Koch T: Noisy pressure support ventilation: A pilot study on a new assisted ventilation mode in experimental lung injury. Crit Care Med 2008; 36: 818-27