Individualized positive end-expiratory pressure and regional gas exchange in porcine lung injury

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**Supplemental Digital Content 2 - Single Photon Emission Computed Tomography scans**

Single Photon Emission Computed Tomography (SPECT) 1 was used to analyze the spatial ventilation and perfusion distributions during ventilation with different PEEP levels.

Ventilation distribution was assessed by inhalation of Krypton gas (81mKr) 2, being produced by a Rubidium generator on site (Mallinckrodt; Netherlands). Regional pulmonary blood flow was assessed by intravenous injection of 99mTc-labeled macroaggregated albumin (99mTc-MAA) (Pulmocis; CISbiointernational, Gif sur Yvette, France) 2. The animals were put in supine position with their front legs stretched cranially. Since changes in PEEP caused a caudal/cranial shift of the diaphragm and a change of the lung shape, a background SPECT was done directly before the next isotope injection, measuring the radioactivity from the previous isotope injection. This enabled a subtraction of the background radioactivity when the second injection was done during the second SPECT measurement period. In order to obtain high pulmonary emission activity in relation to the contribution of activity from proceeding measurements, the injected activity was increased from about 25 MBq 99mTc-MAA for the first SPECT scan to 40 MBq 99mTc-MAA for the next SPECT, respectively 3–5.

Low-resolution computer tomography (transmission scan) was obtained together with the radiation measurement to evaluate lung borders and to enable attenuation correction 3–5.

Images were acquired on a dual-head gamma camera (Millenium; General Electric Systems, Milwaukee, WI) equipped with all-purpose, medium-energy collimators. Acquisition was performed in two separate energy windows, one at 140±10keV for 99mTc and on at 190±10keV for 81mKr. SPECT acquisition was made in 60 projections (30 per head) and stored in a 128 by 128 matrix. The acquisition time was 30 seconds per projection. This rather long time resulted from the comparatively low activity of 81mKr. The overall scan time for SPECT and CT was approximately 42 min.

Data were reconstructed using a Xeleris workstation (Millennium; General Electric Systems, Milwaukee, WI). The reconstruction was done with an iterative model (OSEM, 4 iterations and 8 subsets) and a Hann filter (cutoff 0.85) for the post reconstruction filtering 3–5. The reconstructed volume was corrected for radiation spill-over and for baseline offset using a HERMES workstation (Hermes Medical Solution, Stockholm, Sweden). For each reconstructed slice in apex-base and anterior-posterior directions, the SPECT data was analyzed by custom-made software 3–5.

To eliminate noise, a certain number of counts had to be subtracted from every voxel signal (noise correction) 3–5. Guided by optically matching the SPECT and CT images, respectively, noise correction was increased until no voxel outside the lung (as seen on the superimposed CT scan) showed a ventilation or perfusion signal. The CT investigator was blinded to the animal number and ventilation mode. The absolute number of cutoff counts depends on the total activity applied during the respective measurement phase. Cutoff counts amounted to 31.1% (±5.8%) and 16.5% (±5.7%) of the maximum counts/voxel for the ventilation and the perfusion signal, respectively, and were comparable between all ventilatory modes.

Based on the relative distribution of the total activity (counts) and the global pulmonary gas (minute ventilation) and blood flow (cardiac output), regional gas and blood flows were calculated for any single voxel using a custom-made software (MATLAB ®, The MathWorks Inc., Ismaning, Germany).

For every single voxel were calculated:

* regional ventilation/voxel ($\dot{V}$, gas flow per voxel), and
* regional perfusion /voxel ($\dot{Q}$, blood flow per voxel)

$\dot{V}\dot{/Q}$-ratio was calculated according to the voxels $\dot{V}$ and $\dot{Q}$ and voxels were assigned to one of the following SPECT-compartments (figure S2):

* shuntSPECT ($\dot{V}$/$\dot{Q}$<0.005),
* low-$\dot{V}$/$\dot{Q}$SPECT (0.005$\leq \dot{V}$/$\dot{Q}$<0.1),
* normal-$\dot{V}$/$\dot{Q}$S-PECT 0.1$\leq \dot{V}$/$\dot{Q}$<10),
* high-$\dot{V}$/$\dot{Q}$SPECT (10$\leq \dot{V}$/$\dot{Q}$<100), and
* dead spaceSPECT ($\dot{V}$/$\dot{Q}$≥100).

## *Figure S2*



Processing of SPECT-derived data to analyze regional blood- and gas flow distribution.

For any compartment blood and gas flows were calculated by adding up the specific perfusion ($\dot{Q}$) and ventilation ($\dot{V}) $values of all assigned voxels, respectively, to divide total gas flow into low-$\dot{V}$/$\dot{Q}$-, normal-$\dot{V}$/$\dot{Q}$-, high-$\dot{V}$/$\dot{Q}$-, and dead-space-ventilation, and total blood flow into shunt-, low-$\dot{V}$/$\dot{Q}$-, normal-$\dot{V}$/$\dot{Q}$-, and high-$\dot{V}$/$\dot{Q}$-perfusion, respectively.

Accordingly, proportions of the respective lung compartments were calculated by counting all assigned voxels. Finally, proportions of perfused lung tissue and ventilated lung tissue were calculated by summarizing the amounts of the perfused and ventilated compartments, respectively. Total lung tissue was the sum of all voxels.

Side note: lung voxels that were neither perfused nor ventilated could not be included into these analyses.

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