Visualisation of aerosolized Perfluorcarbon in the pig lung in-vivo by 19F MRI

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Introduction

By non-invasive 19F MRI imaging the effect of aerosolized perfluorocarbon (PFC) on pulmonary gas exchange and lung mechanics was studied in a surfactant depleted piglet model. Sixty minutes after induction of lung injury by bronchoalveolar lavage, the piglets received aerosolized PFC (Aerosol-PFC, 10 ml/kg/h for 2h). After 2 h, an intermittent mandatory ventilation (IMV) was continued for another 1 h. From previous measurements it is known that sixty minutes after the onset of therapy, PaO2 was significantly higher and PaCO2 was significantly lower in the Aerosol-PFC (cf. Kandler et al., 2001). The increase of the PaO2 lasted at least for 6h. Using 19F MRI we imaged the distribution of the PFC in the lung before, during, and after the treatment. The main aim of the study was describe the spatial distribution of PFC within the lung over time. Therefore, the temporal activity changes over time per pixel were analysed and clustered.

Materials and Methods

Twelve newborn piglets weighing 3.0 to 3.5 kg were anesthetized intravenously by an injection of ketamine, midazolam, and fentanyl. An endotracheal tube was placed via tracheotomy and endotracheal pressure was recorded via a 5-Fr. catheter. After paralyzation with vecuronium,a 4-Fr. thermodilution catheter was placed in the pulmonary artery. The left femoral artery was cannulated with a 20-G arterial catheter. Arterial blood pressure, central venous pressure, pulmonary artery pressure and body temperature were continuously recorded. Cardiac output was calculated with the CMF 24 Omnicare. Arterial blood gas analysis was performed in 15-min intervals during therapy and in 30-min intervals during the post-therapy period. Breath rate was 50 breaths/min. A peak inspiratory pressure (PIP) of 32 cm H2O, a positive end-expiratory pressure (PEEP) of 8 cm H2O, and an FIO2 of 1 was used. Lung injury was induced by repeated saline lung lavage using 30 ml/kg per side. Lavage was performed in left and right lateral position, respectively. During instrumentation and for the duration of the experiment animals were in the supine position. Lung injury was considered to be stable, when the PaO2 constantly remained below 100 mm Hg for 60 min. After transferring the animals into the MRI scanner the Aerosol-PFC was applied with 10 ml/kg/h FC77 (C_8F_{18} and $C_8F_{16}O$, density 1.78 g/cm^3) by an aerosolization catheter. The catheter consists of gas and liquid capillaries, converging and terminating at the distal tip of the catheter. The close contact of gas and liquid results in efficient nebulization, with gas flow rates as low as 0.05 L/min.

MRI was performed on a 4.7 T BRUKER Biospec scanner with a free bore of 40cm, equipped with an actively shielded gradient system with inner diameter 258 mm and maximal gradient strenght 50 mT/m. A whole-body birdcage resonator with inner diameter 195 mm was used. The scanning procedure started with the acquisition of T2 weighted spin echo coronal, sagittal, and axial anatomical reference images on proton frequency (slice thickness 6mm, field of view 20x20 cm, matrix 128x128, TR 1500 ms, TEeff 22.7 ms) using a rapid acquisition relaxation enhanced sequence (RARE). Uptake and washout images were acquired using RARE sequence working on fluor frequency. Single slices coronal, sagittal, and axial (72 mm slice thickness, matrix 64x64, in plane resolution 3.125 x 3.125 mm/pixel, 6 averages, TEef 21 ms, TR 1400 ms, total measurement time 4 min 30 sec per scan) were acquired during time of 2h PFC therapy and afterwards for 1 h. The time profiles per pixel were analysed by a k-means cluster algorithm (cf. Fig. 2) and mean intensities of the different clusters plotted over time (cf. Fig. 3).

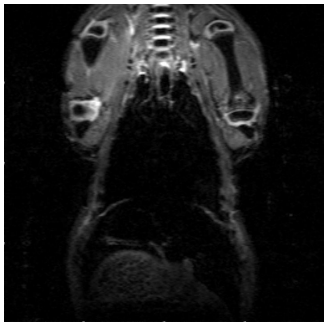

Fig. 1: 1H image of pig lung

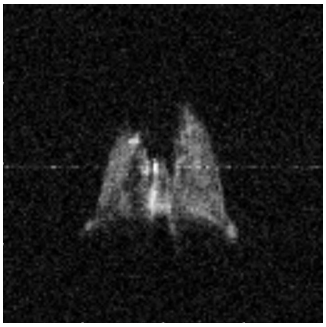

Fig. 2: 19F image of pig lung

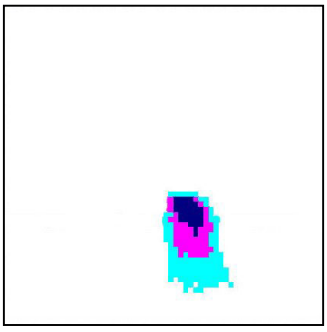

Fig. 3: Cluster analysis (3 clusters)

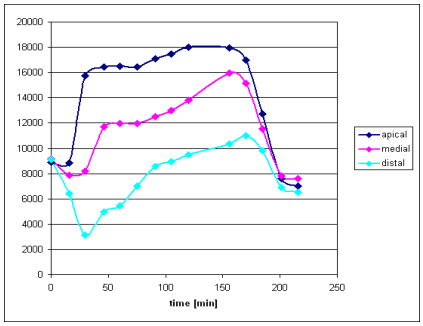

Fig. 4: Timeprofile of cluster PFC concentration

Results and Discussion

First 19F signal was measurable after 30 min onset of the therapy. Initially the signal was detectable in the apical part of the lung. At this location the concentration of the PFC increased fast to near maximal levels and remained at this high value as long as the therapy lasted. After the end of the therapy, the signal dropped within 30 min to baseline level. As could be confirmed in all cutting directions, the PFC appeared later in the medial and after that in the distal parts of the lung. The time profiles show a slower increase in the signal intensity and the more distal the less maximal end concentration was reached. After the end of the therapy the decrease of PFC concentration was very fast but nearly similar in all regions and reached baseline level after 30 min. Moreover, in all animals the right half of the lung showed much higher 19F PFC signal (data not shown in the abstract). In 4 animals only the right half of the lung showed a measurable signal. At an application amount of 7 ml/kg/h Aerosol-PFC no signal could be detected after 120 min. At 8ml/kg/h after 21 min first 19F signal was detectable. The kinetics of the lung filling by PFC, taking together the results from all cutting directions is from apical ventral to distal ventral over the whole anterior-posterior extend of the lung. Afterwards, the lungs are filled from ventral to dorsal directions. Since the pure amount of applied PFC is not sufficient to fill the lung by condens liquid PFC we have to assume, that we are not only measuring liquid, condens PFC, but also the PFC aerosol.

Conclusion

Aerosolized perfluorocarbon improved pulmonary gas exchange and lung mechanics in surfactant-depleted piglets. The improvement, the physiological effect, was shown in earlier work to persist for more than 6h after therapy. Our 19F MRI measurements only could reveal that a 19F PFC signal persisted 30 min after end of the therapy but not for the 6h of increased paO2. However, since we are able to measure aerosol like PFC we could demonstrate that at 10 ml/kg/h flow rate, major parts of the lungs are filled by the PFC.

References

Persistent Improvement of Gas Exchange and Lung Mechanics by Aerosolized Perfluorocarbon
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