# $^{1}$H and HP $^{3}$He MR imaging of LPS treated mice

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Chronic obstructive pulmonary disease (COPD) is characterized by a multitude of inflammatory processes. The inflammation induced by lipopolysaccharide (LPS) is a well-established COPD model in rodents, and the model has been used in MRI respiratory research[1]. Proton MR imaging has been used to quantify edema in this model but the effect of LPS on lung function by MRI has not been explored. Recently, hyperpolarized (HP) $^{3}$He has emerged as a technique for respiratory MRI. HP $^{3}$He can assess functional parameters such as ventilation. The aim of the present study was to evaluate $^{1}$H and HP $^{3}$He MR imaging in a LPS mouse model.

**Materials and Methods:** Mice (n=8) were placed in inhalation boxes and exposed to an aerosol of LPS (5 mg/mL) for 10 minutes. Unexposed mice (n=6) were used as controls. 48h after LPS inhalation the animals were anaesthetized and a tracheal intubation was performed. Additionally, a muscle relaxant was administered to enable breath-hold imaging. The animals were connected to a ventilator (Servicios de Eléctrónica y Programación Dedicados, Madrid, Spain) set to 90 breaths/minute at a tidal volume of 0.25 ml.

All MRI experiments were performed using a BioSpec 47/40 4.7 T MR scanner (Bruker BioSpin, Ettlingen, Germany) and a double tuned $^{1}$H and $^{3}$He coil. HP $^{3}$He was delivered from the University of Mainz, Germany. After setting the ventilator to HP $^{3}$He administration, an axial 3D FLASH sequence covering the lung volume was completed over 6 breath-hold cycles. Then, the ventilator was set to air and $^{1}$H 2D slices matching the slices of the 3D $^{3}$He volume were acquired. Finally, a 2D coronal HP $^{3}$He was acquired in breath-hold after the mouse was ventilated by 3 consecutive $^{3}$He breaths. The procedure was repeated with imaging after 10 consecutive $^{3}$He breaths. After the imaging procedure a broncho alveolar lavage (BAL) for a cell count was performed.

In the axial images the number of lesions ($^{3}$He:ventilation defect, $^{1}$H:edema) were counted manually in each slice. The total volume occupied by the $^{3}$He gas and the average signal from HP $^{3}$He from the lungs was calculated. A quantitative ventilation index was obtained from the coronal images by dividing the signal in the image acquired after 10 breaths with image acquired after 3 breaths. The signals were corrected for T1-decay in the HP $^{3}$He reservoir.

**Results and Discussion:**

The LPS treatment resulted in a significant increase of granulocytes, macrophages and lymphocytes. Lesions on $^{3}$He images were characterized by a ventilation defect while lesions on $^{1}$H images were hyperintense and attributed to edema (Fig.1). For both $^{3}$He and $^{1}$H the number of lesion was significantly ($p<0.01$) higher for the LPS treated mice compared to controls (Fig. 2). The ventilation defects were often larger than the corresponding edema. However, there was no difference found in the number of lesions between the imaging methods. The lung volume ($p<0.01$), the average 3He signal ($p<0.05$), and the ventilation index ($p<0.01$) all obtained from the $^{3}$He data, were smaller for the LPS treated animals compared to controls. The functional data by HP $^{3}$He provide new and additional information about LPS induced inflammation but in this study the imaging methods were equally sensitive.

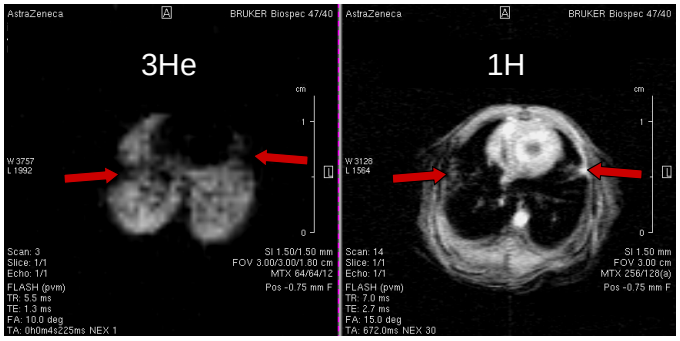


Figure 1. HP $^{3}$He image of a LPS treated mouse (left), and corresponding proton image (right). Red arrows indicate the lesions.

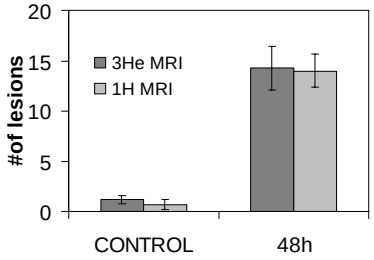


Figure 2. The number of lesions is higher ($p<0.01$) in the LPS treated mice than controls.

**Acknowledgement:** We are very grateful to professors E. Otten and W. Heil and the group at Institut für Physik, Johannes Gutenberg-Universität Mainz, for providing the HP $^{3}$He and very valuable scientific discussions.

**Reference:** 1) Quintana HK et al., Am J Physiol Lung Cell Mol Physiol 291:651-657,2006.