Hyperpolarized helium-3 lung function imaging in ozone exposure experimental models

Y. Crémillieux[1], S. Servais[2], Y. Berthezène[3], D. Dupuich[1], A. Boussouar[2], P. Anfré[1], V. Stupar[1], J-M. Pequignot[2]

[1]Laboratoire de RMN, Villeurbanne, France, [2]Laboratoire de Physiologie Intégrative Cellulaire et Moleculaire, Villeurbanne, France, [3]CREATIS, Lyon, France

INTRODUCTION

Ozone (O_3) is a powerful oxidant and a major environmental pollutant in most of the large cities. Its primary target is the lung tissue with initial damage to the lung epithelial cells. As a consequence of the induced reactive processes, acute or chronic exposure to ozone results in airway injury with respiratory irritation and reduced lung function. Decrease of vital capacity and of forced expiratory volume (FEV) as well as airway resistance increase have been reported using pulmonary functional tests in humans (1) and in rats (2). Furthermore, ozone has been shown to exacerbate illness conditions in asthmatics and COPD (chronic obstructive pulmonary diseases) patients. As a non-invasive technique, ^{3}He imaging represents a unique tool for investigating the effects of ozone exposure on lung ventilation function at a regional level. In this work, we studied the effects of ozone exposure on rat lung function using ^{3}He ventilation imaging techniques.

METHODS

^{3}He was polarized using the spin-exchange method with polarisation levels ranging between 20 and 30 %. MRI experiments were performed on a 2 Tesla magnet. Five-month-old male Sprague-Dawley rats were studied (n=18). For ozone exposure, the animals were placed in a Plexiglas chamber with a constant air flow. Ozone was generated by passing the filtered air across an ultraviolet light source (3). 4 groups of animals, subjected to 0.5 ppm ozone either continuously (22 h per day) or alternately (12 h per day) were prepared: 6 days of continuous ozone exposure (n=3, group 1), 2 days of continuous ozone exposure (n=4, group 2), 6 days of alternated ozone exposure (n=5, group 3) and 2 days of alternated ozone exposure (n=3, group 4). A control group (n=3) exposed to filtered air at the same flow rate was also imaged. Anesthetized animals were tracheotomized and placed in supine position in the magnet. 6 ml of polarized helium3 were injected in the animal lungs at a controlled flow rate (2ml/s). NMR acquisitions as well as reconstruction and analysis of images were performed according to the previously proposed SPIRO technique (4). The delay between the end of ozone exposure and the imaging procedure did not exceed 3 hours.

RESULTS AND DISCUSSION

All the animals exposed to ozone during 6 days, either continuously or in an alternated way, exhibited large ventilation defects. The defects were essentially located in the upper parts of the lungs and appeared either as delayed gas-filled regions or as non-ventilated regions. The control animals and those exposed to ozone during 2 days did not exhibit visible ventilation defects (except for one animal in group 4).. Typical ventilation acquisitions are shown in figure 1. Top row images were obtained in a control animal and correspond, from left to right, to a raw image extracted from a dynamic series, to a “gas volume” map and to a “gas-arrival-time” map. Bottom row images were obtained from an animal in group 3. Regions with delayed gas-filling are clearly visible in the upper lungs and in the lower part of the left lung. These defects are confirmed by the corresponding hyper-intense regions in the “gas-arrival-time” map and by the normal appearance of the “gas volume” map. One has to mention that no lung function impairment were detected by plethysmography technique in any of the animals of group 3.

CONCLUSION

Polarized ^{3}He imaging appears to be a very sensitive technique for investigating the effects of ozone exposure on animal models. Thanks to its high spatial resolution and sensitivity, this non-invasive ventilation imaging technique could proved to be a method of choice for studying the effect of acute or chronic ozone exposure on humans. Based on comparative dose-effect studies (5) in humans and rats, 0.5 ppm ozone exposure in rats can be translated into 0.1 ppm ozone concentration exposure in human. This 0.1 ppm ozone concentration (200 $\mu g/m^3$) corresponds to the information threshold as defined by an EC directive and is frequently exceeded in most of western European countries during summer months.

References :

(1) Mudway et al., Mol. Aspect Med (2000), 21, 1-48.

(2) Costa et al., Am J Respir Crit Care Med (1995), 151, 1512-1518.

(3) Cottet-Emard et al., Eur. J. Physiol (1997), 433, 744-749.

(4) Dupuich et al., Magn Reson Med (2003), 50, 777-783.

(5) Hatch et al., Am J Respir Crit Care Med (1994), 150, 676-683

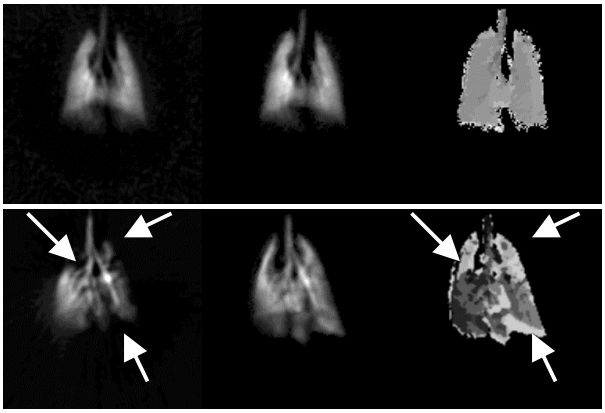

Figure 1 : Ventilation images obtained in control animal (top row) and animal exposed to ozone (bottom row). Arrows indicate regions of delayed gas arrival in dynamic image and “gas-arrival-time” map.