3D ³He and ¹H MR Imaging of Regional Pulmonary Injury Induced by Ozone

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Introduction: Ambient ozone (O₃) is a major environmental air pollutant that significantly impacts public health. Ozone exacerobates lung dysfunction in subjects with asthma and chronic obstructive pulmonary disease [1]. While much is known about the deleterious effect of O₃ on global lung function, much less is understood about its effects regionally. To this end hyperpolarized gas MRI could be an ideal means to study the effects of O₃ on regional ventilation as was first proposed by Cremillieux et al [2]. However, that study, conducted in rats, was limited to 2D imaging, and despite long ozone exposures revealed only very subtle O₃-induced lung effects. We sought to revisit the effects of ozone on pulmonary function by employing 3D ³He and ¹H MRI in C57BL/6 mice.

Methods: Male C57BL/6 mice (8 wks old, n=5) were exposed for a period of 3 hrs to air containing 1 ppm of O₃. Control animals (n=6) were naive. Approximately 16-24 hr post-exposure, all mice underwent respiratory-gated ¹H MRI at 156×156×256μm³ resolution and then underwent a 5 minute high-resolution 3D ³He MR image (156×156×256μm³) using methods outlined in [3]. Prior to ³He MRI, mice received a hyperinflation breath to clear any atelectasis. ¹H images were evaluated for edematous signals and ³He images were evaluated for ventilation abnormalities. The ¹H and ³He images for each mouse were registered to correlate fluid-filled regions of the lungs to ventilated regions.

Results: As shown in Fig 1 naive mice show homogeneous ³He ventilation and low proton signal in the thoracic cavity. By contrast, as shown in Fig 2, mice exposed to ozone showed regions of dramatically impaired ventilation, bronchial narrowing, and accumulation of edematous fluid on ¹H MRI. The ozone-exposed mouse shown in Fig 2 exhibits a ventilation defect with matching fluid accumulation in one slice (Fig 2 a,b,c) but also exhibited impaired ventilation without detectable fluid in other areas. This is illustrated in the maximum intensity projection (Fig 2 d) and was representative of what was seen in other O₃-exposed mice.

Discussion and Conclusions: Despite experiencing fairly limited O₃ exposure, equivalent to 1-day in Mexico City, the mice exhibited striking regional changes in ventilation. This stands in contrast to more subtle O₃ effects previously reported in rats [2]. This is partially attributable to our improved 3D resolution and may also reflect some degree of strain-dependent O₃ susceptibility [4]. However, the primary difference is likely to be ozone adaptation. When ozone exposure is repetitive or prolonged, the resultant inflammatory response can become attenuated [5]. Thus, both the duration of O₃ exposure and the time after exposure when imaging occurs are important factors. Our work suggests that the combination of high-resolution ¹H and ³He MRI done 24-hr after 3-hr O₃ exposure could offer a novel approach to investigate the regional pulmonary effects of this ubiquitous pollutant. Such tools should be useful for testing the efficacy of new therapeutic approaches now being developed to blunt the effects of ozone in vulnerable populations.


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