

## Assessment of pulmonary inflammation in allergic rats after antigen challenge by MRI

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### Introduction

Allergic rats develop pulmonary inflammation after antigen challenge, and this can be detected by proton MRI using sequences with short echo time (TE). Allergic rats developed mild inflammation after one antigen challenge and marked inflammation after two challenges. The increase in inflammation assessed by MRI imaging paralleled the increase in eosinophils in the broncho-alveolar lavage. The inflammation was largely confined to the anterior part of the lung.

### Methods

Male Brown-Norway rats were sensitised to ovalbumin (OVA) by subcutaneous injection of OVA with aluminium hydroxide adjuvant. 14 days later the rats were exposed to aerosolised 0.9% w/v saline (saline group, n=6) or 1% OVA in saline (1 x OVA group, n=6). A third group of rats (2 x OVA, n=6) were re-challenged with OVA aerosol on day 15. 24h following challenge the rats were anaesthetised and the thorax imaged on a Varian 4.7T MR system. First, a high resolution (230\*230\*2000 $\mu\text{m}^3$ ) set of images covering the whole lung was obtained using a multislice gradient echo sequence TR=650ms, TE = 2.5ms. No gating was used and physiological motion artefacts were removed by averaging each slice 20 times. Next, a set of short (0.86ms) TE multislice images (625\*470\*2000 $\mu\text{m}^3$ ) covering the whole lung was obtained with 16 averages per slice. At the end of imaging the rats were killed and a bronchoalveolar lavage (BAL) performed. The cells were stained with Kimura's stain and differential counts of BAL cells were performed manually. Cell counts were expressed as number of cells per mL of BAL fluid. Image quantification was performed on the 0.8ms TE images. A region of interest was drawn manually around the lungs. The large vessels were removed by thresholding and the density map of the remaining lung field was stored.

### Results and discussion

Antigen challenge produced an increase in eosinophils in the BAL which was more pronounced after two antigen challenges (figure 1). An influx of eosinophils into the BAL is a characteristic feature of this model of asthma [1] and is a useful marker of the inflammatory response of the lung. The high resolution MR images showed patches of increased signal in the lungs of the 2 x OVA challenged rats (figure 2). This increased signal is due to airway oedema, lung tissue inflammation [2] and possibly airway collapse. Beckmann et al. described this increased signal as oedema and showed that it was maximal 24h after antigen challenge, the time point used in this study. In the Beckmann study [3] the animals were challenged by intratracheal injection and the oedema signal was bright; in contrast, with our animal model the signal intensity was similar to that from muscle (myocardium and chest wall) and less than that from the large blood vessels, which allowed the latter to be removed by thresholding. There was little oedema signal after one OVA challenge and none in the saline challenged group. The oedema signal was most prominent in the anterior part of the lung and decreased in more caudal slices (figure 3).

Although the lung environment is challenging to MRI, the present study showed that with the use of short TE and analysis of the overall lung signal intensity it is possible to detect early sign of inflammation in rats without the need for intratracheal injection of antigen.

### References

- [1] Elwood W et al. *J Allergy Clin Immunol* **88**, 951-960, 1991
- [2] Underwood SL et al. *British Journal of Pharmacology* **137**, 263-275, 2002
- [3] Beckmann N et al. *Magn Reson Med* **45**, 88-95, 2001

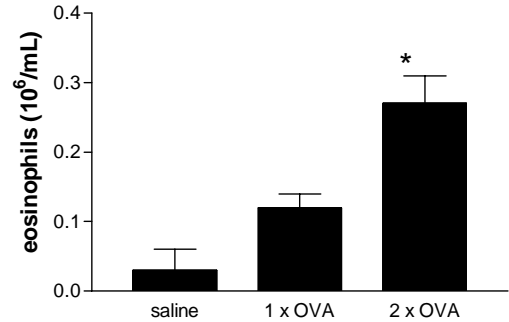


Figure 1. Eosinophil levels in the BAL \*p<0.05 compared to saline

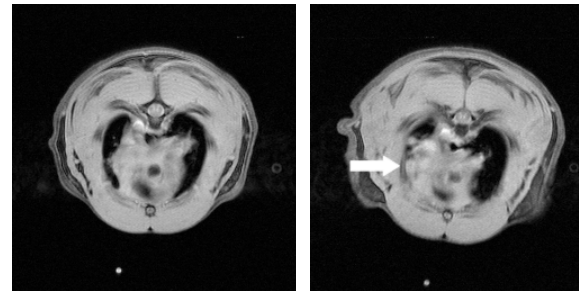


Figure 2. Transverse section of the thorax. Rats were challenged with saline (left) or 2 x OVA (right). OVA challenged rat shows oedema in the right lung (arrow) with hyperinflation of the left lung.

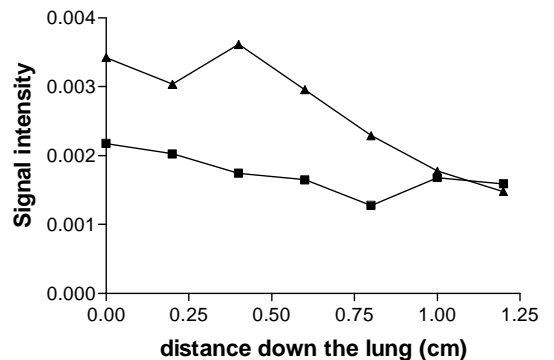


Figure 3. Mean pixel intensity is greater in 2 x OVA rats (triangles) compared to saline challenged rats (squares).