CHARACTERISATION OF LUNG EDEMA OVER TIME BY 1H MRI USING PREFERENTIAL AVERAGING OF K-SPACE

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Introduction: Endothelin-1 (ET-1) drives plasma leakage and pulmonary edema which is associated with Chronic Obstructive Pulmonary Disease (COPD). This study investigated with MRI the development of lung edema over time following administration of big endothelin-1 (BET), precursor of ET-1. In order to characterise edema formation with adequate time resolution while reducing motion artifacts, we investigated and used preferential averaging of k-space. The image quality was not compromised and the increase in edema formation corresponded with an increase in Evans blue dye extravasation and a reduction of lung function observed in other studies (Bell *et al.*, submitted for publication [1]). Lung edema was prevented by administration of bosentan, an endothelin receptor antagonist and SM-19712 an endothelin converting enzyme inhibitor.

Methods: Rats were anaesthetised and the thorax imaged on a Varian 4.7T MR system. A set of short TE multislices images (625*470*2000μm^3) covering the whole lung was obtained in 13 min before injection with BET. No gating was used and physiological motion artifacts were removed by averaging each slice 8 times. In order to further reduce artifacts without increasing significantly the imaging scan time, the central lines of k-space were acquired twice and averaged. Immediately after the i.v. injection of BET, three additional set of MR images were acquired. Three doses of BET were investigated (1, 2 and 4 nmol/kg). The measurements were repeated at the highest dose of BET in animals pre-treated with either bosentan (100mg/kg p.o.) or SM-19712 (10mg/kg i.v); doses that were effective against lung function decline and Evans blue leakage (Bell *et al.*, submitted for publication). For analysis, a region of interest (ROI) was drawn manually around the lungs on the pre-BET images and applied to the images acquired after its administration. As the animals were not moved between acquisitions, in most cases image registration was not necessary as the areas outlines in the pre-BET images fitted perfectly to the lungs on the post-BET images.

Results and discussion: This study highlights the utility of MRI for monitoring the development of lung edema *invivo* and its potential for testing the efficacy of novel compounds. To perform meaningful MRI lung edema measurement [2], artifacts induced by physiological motion need to be suppressed. In this study we use a preferential averaging of the central lines of k-space to reduce the amount of physiological motion artifacts on the images without increasing significantly the scan time [3]. Out of the several possible preferential averaging regimes that were investigated, the averaging of the 21 most central lines of k-space out of 128 (16 averages of central lines, 8 averaging elsewhere) was found to offer the best compromise to reduce motion artifacts effectively in a short period of time without degrading overall image quality. Using this approach we were able to reduce the scan time by over 40% and characterise the development of edema induced by administration of BET over the entire lung with adequate time resolution. After BET injection, the increase in lung intensity associated with lung edema peaked at 26 min and was BET dose dependent (Fig.1). Treatment with bosentan (Fig.2) or SM-19172 inhibited the BET-induced MRI signal increases associated with lung edema by over 75% in this animal model and this correlated with a reduction in Evans blue dye extravasation and improvements in measured lung function.

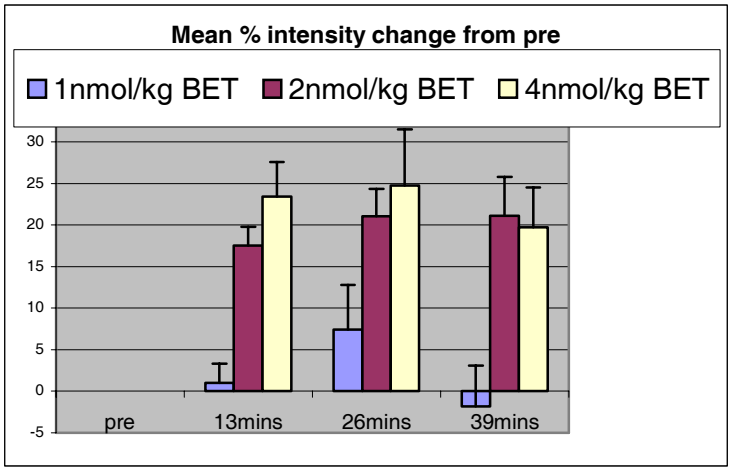

Fig 1 : Change of lung intensity associated with edema after BET injection

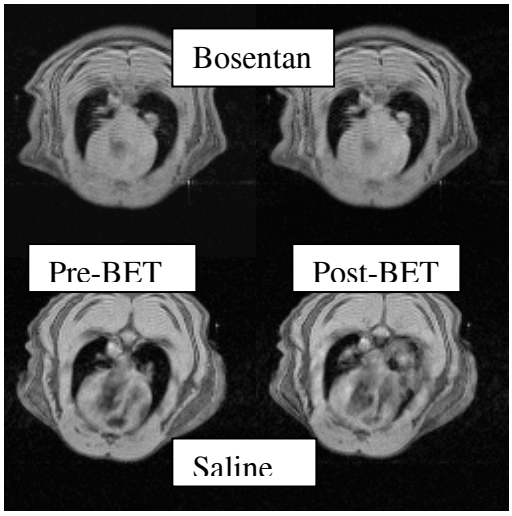

Fig 2: Effect of bosentan on lung edema

[1] Bell, American Thoracic Society, 2007, [2] Beckmann MRM 45,88,2001, [3] Nguyen MRI 19,951,2001