MAGNETIC RESONANCE IMAGING (MRI) CHARACTERIZATION OF THE FUNCTIONAL AND MORPHOLOGICAL CHANGES IN HEART AND LUNG AFTER MYOCARDIAL INFARCTION IN MICE

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Introduction: Pulmonary congestion secondary to heart failure is a major cause of dyspnea and exercise intolerance in the congestive heart failure patient population. In the following study, we developed an MRI method to non-invasively and serially assess cardiac dysfunction and lung congestion in a chronic heart failure model (1), myocardial infarction (MI), in mice.

Method: C57BL/6 mice, were subjected to sham (n=6) or MI (n=19). Due to the increased mortality in the MI mice, mice were divided into three groups: 1) MI mice (MI-A) n=6 that died between day six and day nine (before imaging); 2) MI mice (MI-B) n=6 that survived to the final time point on day thirteen. MI mice (n=7) that died between day two and day six (before imaging), are excluded from the results.

Cardiac and lung MRI were performed at baseline then every three days up to 13 days post-surgery. For lung imaging, a 2D FLASH sequence without gating (2) was used to acquire oblique coronal slices and axial slices (7-10 slices covering the entire lung) using the following parameters: TR/TE =6.7/2.2 ms, Flip Angle =10 deg, Band Width =100KHz, FOV =3X3cm, Matrix =256X128, slice thickness =1 mm, and NEX = 60. For cardiac imaging, a Bruker IntraGate Flash sequence was used to acquire long-axis slices and 6 to 9 short-axis slices. In addition, whole body plethysmography, lung mechanics, lung wet weight and histological analysis were evaluated.

Results: MRI results revealed that MI induced significant pulmonary congestion/edema (Fig 1) as detected by increased MRI signal intensity (Fig 2) as early as D2 and was associated with increased lung volume (MI-A: ↑72%, MI-B: ↑26% at D6 vs D0) and decreased cardiac function (ejection fraction, MI-A: ↓61%, MI-B: ↓52% at D2 vs D0). Ventilatory function was also depressed in MI-mice, reflected by a reduced tidal volume and low minute ventilation rate. Lung mechanics analysis indicated that MI significantly increased lung resistance, and markedly reduced lung compliance and total lung capacity. Blood gas analysis showed that MI significantly reduced the level of pO2. Postmortem analysis showed that lung weights were significantly increased by 57% in MI-mice. Additionally, significant correlations were observed between lung signal intensity and each of the following parameters: lung volume (r=0.95), ejection fraction (r=-0.82), left ventricular mass (r=0.86) and lung wet weight/body weight ratio (r=0.93).

Conclusion: MRI was used for the first time to assess cardiac dysfunction and lung congestion simultaneously in-vivo in a heart failure model. MRI, lung mechanics and blood gas analysis are useful tools for accurately assessing pulmonary congestion, lung function and the efficacy of drug-treatment post-MI.

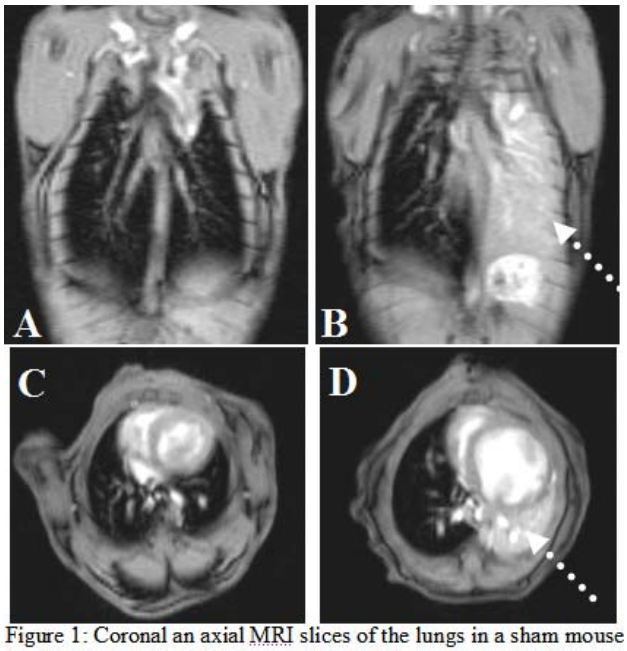

Figure 1: Coronal an axial MRI slices of the lungs in a sham mouse (A & C) and in a MI mouse (B & D). Lung congestion was observed as increased signal intensity in the MI mice (Arrow)

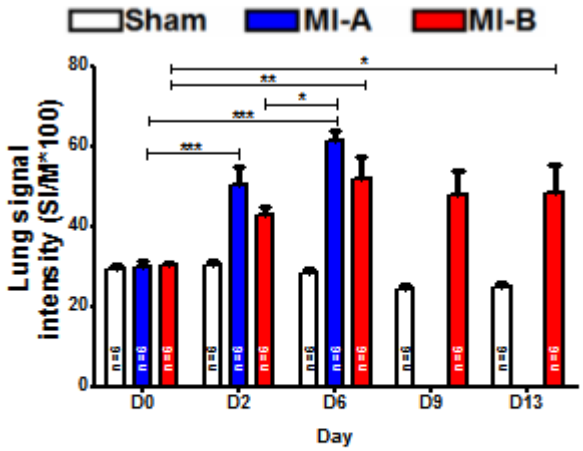

Figure 2: Lung (left & right lobes) signal intensity (SI) measured by MRI. Baseline (D0) measurements confirm that groups were similar at the start. Increased SI was observed in both MI-groups (MI-A & MI-B) but were more apparent in MI-A mice which died earlier, *p<0.05; **p<0.01; ***p<0.001

References:

1. Patten RD et al. Am J Physiol 1998;274:1812-1820.
2. Ble FX et al. Radiology 2008;248(3):834-843.