

# Measurement of $T_1$ relaxation time in lungs

## Preclinical and clinical MRI applications to COPD

Akademisk avhandling

som för avläggande av medicine doktorexamen vid Sahlgrenska akademien vid Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, fredagen den 9 Oktober 2015 kl 13.00

av

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Avhandlingen baseras på följande arbeten:

- I. **Alamidi D**, Morgan A, Hubbard Cristinacce P, Nordenmark L, Hockings P, Lagerstrand K.M, Young S, Naish J, Waterton J, Maguire N, Olsson L E., Parker G. *COPD patients have short lung magnetic resonance  $T_1$  relaxation time*. COPD: Journal of Chronic Obstructive Pulmonary Disease, In press, doi: 10.3109/15412555.2015.1048851 (2015).
- II. **Alamidi D**, Kindvall S, Hubbard Cristinacce P, McGrath D, Young S, Naish J, Waterton J, Diaz S, Wollmer P, Olsson M, Hockings P, Lagerstrand K.M, Parker G, Olsson L E.  *$T_1$  in lungs of healthy smokers*. Manuscript.
- III. **Alamidi D**, Smailagic A, Bidar A, Parker N, Olsson M, Hockings P, Lagerstrand K.M, Olsson L E. *Variable flip angle 3D-UTE  $T_1$  mapping of mouse lung: a repeatability assessment*. Manuscript.
- IV. **Alamidi D**, Smailagic A, Bidar A, Parker N, Olsson M, Jacksson S, Swedin L, Hockings P, Lagerstrand K.M, Olsson L E. *Tobacco smoke shortens  $T_1$  in a mouse model of COPD*. Manuscript.



UNIVERSITY OF GOTHENBURG

Göteborg 2015

# Measurement of $T_1$ relaxation time in lungs

## Preclinical and clinical MRI applications to COPD

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Monitoring of regional lung function in clinical trials of chronic obstructive pulmonary disease (COPD) requires alternative endpoints beyond global pulmonary function tests (PFTs), which is the most common approach for diagnosing lung function abnormalities in humans. A promising magnetic resonance imaging (MRI) biomarker of lung disease in humans and animals is the  $T_1$  relaxation parameter. Only a limited amount of data on native  $T_1$  behaviour in COPD patients and animal models of COPD are available, especially in relation to other relevant markers such as computed tomography (CT) and PFTs in humans; and bronchoalveolar lavage (BAL) fluid analysis and histology in animals. The smoking history in humans and tobacco smoke (TS) exposure in animals are important factors that need to be investigated in relation to lung  $T_1$  since tobacco smoking is the major cause for development of COPD. Therefore, we have investigated whether lung  $T_1$  can be used as a biomarker of COPD in man, if there is a direct effect of TS on lung  $T_1$  in healthy current smokers, and the repeatability of  $T_1$  measurements acquired at two visits.  $T_1$  was also related to smoking history, CT and PFTs. Subsequently, lung  $T_1$  was investigated in a mouse model of COPD and correlated to BAL, lung mechanics and histology to increase the understanding of how  $T_1$  relates to the pathophysiological aspects of COPD. A preclinical three dimensional (3D) ultra-short echo time (UTE)  $T_1$  mapping protocol was developed to enable the COPD study in mouse. We found from the human studies that: lung  $T_1$  shortens in COPD patients, ageing shortens  $T_1$  and that TS exposure does not affect  $T_1$  in healthy smokers. Additionally, lung  $T_1$  was repeatable and correlated with CT lung density and PFT parameters. Lung  $T_1$  was also shortened in the TS exposed mice, most likely due to early signs of disease. In naive mice, high lung  $T_1$  repeatability over one month was found. In conclusion, lung  $T_1$  mapping is an attractive imaging biomarker of COPD in mouse and man for future longitudinal studies. The potential of MRI-based  $T_1$  mapping to evaluate early COPD has been enhanced by the advances in this thesis.

**Keywords:** Magnetic Resonance Imaging, biomarker, tobacco smoke, mouse, smoking, lung imaging, Chronic Obstructive Pulmonary Disease, ultrashort echo time (UTE), T1 mapping, longitudinal relaxation time

**ISBN:** 978-91-628-9525-9 (print)

**ISBN:** 978-91-628-9526-6 (e-pub)

**E-publication:** <http://hdl.handle.net/2077/39543>