Physiological modelling of a dynamic contrast-enhanced MRI extended time series in COPD

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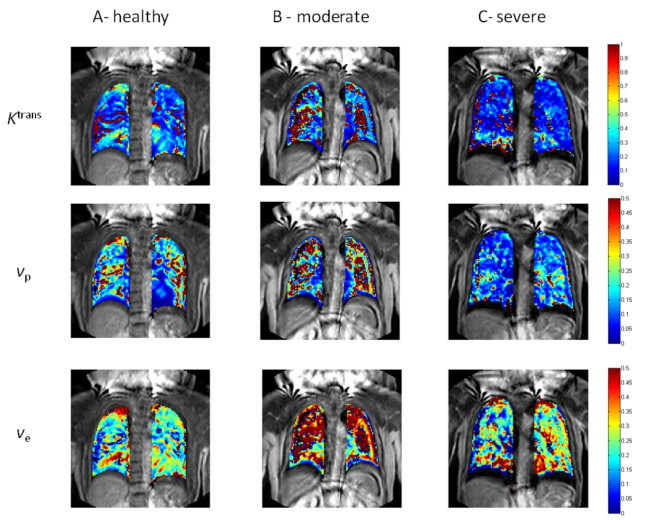
Introduction We present the results of a dynamic contrast-enhanced (DCE-) MRI study in subjects with Chronic Obstructive Pulmonary Disease (COPD) and age-matched healthy subjects. To our knowledge this is the first study to fit a pharmacokinetic model to an extended dynamic contrast-enhanced time series in this patient group. Similar studies to date have applied a first-pass technique, either presenting qualitative curves [1, 2] or using the indicator dilution theory to extract pulmonary blood volume (PBV), pulmonary blood flow (PBF) and mean transit times [3]. This model that we apply here allows for extravasation of the contrast agent and can therefore be used to probe pulmonary capillary permeability.

Methods DCE-MRI was carried out on a 1.5 T Philips Achieva system (Philips Medical Systems, Best, NL) on a group of 12 subjects with moderate COPD (GOLD Stage 1-2 [4]), 12 with severe COPD (GOLD stage 3-4) and 12 age-matched healthy subjects (mean age 65±9). The DCE-MRI acquisition used a high temporal resolution 3D short echo time T_1-weighted spoiled gradient echo time series. A variable flip angle acquisition (FA = 2°, 10° and 20°, 5 average volumes) was employed to determine T_1. Contrast agent (Gd-DOTA, Dotarem®) was administered on the 10th dynamic acquisition of 180 single average volumes (20 slices, FA = 20°) at a temporal resolution of 1.9 s. The details for the DCE procedure have been reported in [5]. A single posterior slice was chosen for further analysis. The acquisition was made during gentle free-breathing and registered as described in [6] to warp to the position of maximum expiration. T_1 maps were calculated for the baseline data, used to estimate T_1 for each time point of the dynamic acquisition and the change in T_1 then converted into the contrast agent concentration, assuming a contrast agent longitudinal relaxivity of 3.4 $s^{-1}mM^{-1}$. Hematocrit was assumed to be 0.42 for all subjects. Individual subject arterial input functions were obtained by manual definition of a region of interest (ROI) in the pulmonary artery. Function fitting for the extended Kety model [5] was all carried out using a non-linear least squares fit algorithm from the Matlab Optimization Toolbox to extract: v_e, the fractional extracellular-extravascular space (mL/(mL tissue)), v_p, the fractional vascular plasma space (mL/(mL tissue)), and K^{trans}, the volume transfer coefficient between v_p and v_e (mL/(mL tissue)/min).



	A- healthy	B - moderate	C- severe
K^{trans} (ml/ml tissue)/min	0.31±0.16	0.29±0.13	0.21±0.05†
v_p, ml/ml tissue	0.22±0.11	0.22±0.09	0.14±0.04†‡
v_e, ml/ml tissue	0.27±0.07	0.32±0.09	0.25±0.05

Figure 1 Representative extended Kety model fit parameter maps for a) healthy, b) moderate and c) severe COPD.

Table 1 Median group values for 3 groups.

Results Significant differences were not observed between healthy and moderate COPD groups any of the DCE-MRI parameters. Significant differences were observed between the healthy and severe COPD groups in two of the DCE-MRI parameters, revealing lower v_p and K^{trans} in severe COPD (Fig. 1). Significant differences were observed in v_p between moderate and severe COPD.

Conclusions K^{trans} is related to perfusion and/or capillary permeability and is observed to decrease in severe COPD. v_p (pulmonary blood volume) also decreases with disease severity and, when considered in combination with decreased K^{trans}, is suggestive of reduced perfusion in the ROI analysed. The extracellular–extravascular fraction, v_e, shows similar median values in healthy and severe COPD, with an increase in moderate COPD (although the differences are not statistically significant). This may suggest increased inflammation in moderate COPD, which is superseded by tissue breakdown with disease progression. This tentative interpretation requires confirmation with larger studies and histological measurement but suggests that DCE-MRI may provide a novel window on the progression of COPD.

References **1.** Amundsen, T., et al., *JMRI*, 2000. 12: p. 224-31. **2.** Amundsen, T., et al., *JMRI*, 2002. 15: p. 386-394. **3.** Jang, Y.M., et al., *Investigative Radiology,* 2008. 43(6): p. 403-410. **4.** *GOLD: Global Initiative for Chronic Obstructive Pulmonary Disease, www.goldcopd.com*. **5.** Naish, J.H., et al., *MRM*, 2009. 61: p. 1507-14. **6.** Naish, J.H., et al., *MRM*, 2005. 469: p. 464-469.

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