235. Imaging in COPD

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Assessment of relative regional lung compliance in patients with COPD

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Pathologically altered lung mechanical properties are difficult to assess regionally. A method has been developed utilising structural proton MRI in conjunction with post-processing and image registration techniques to provide measures of relative regional lung compliance [1].

This method was applied in 23 COPD patients and 11 healthy controls. Each subject had two supine scans, 1 week apart. Compliance maps were found to be reproducible, with increased spatial heterogeneity seen in patients compared to controls (Figure 1).

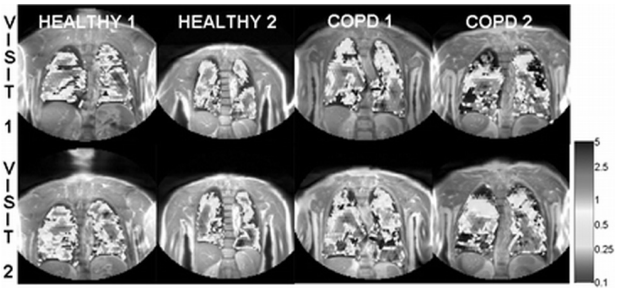

Figure 1. Relative regional compliance maps for healthy controls and COPD patients (mapped on log scale).

The gradient of relative compliance from lung apex to diaphragm was calculated. An increased compliance gradient was seen in moderate COPD ($p<0.05$), with a more significant increase in severe COPD ($p<0.001$) (Figure 2).

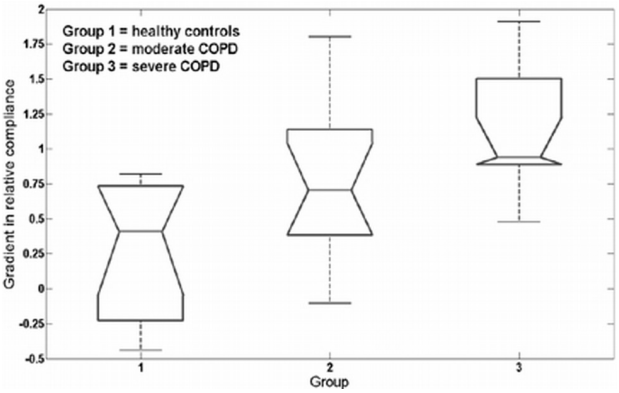

Figure 2. Box plot of relative compliance gradients (found using regional relative compliance and position as fraction of lung length).

The method shows significant differences between COPD patients and healthy controls with areas of altered relative regional compliance indicating likely regions of disease.

Reference:

[1] Morgan, A.R. et al. Proc ISMRM 2010; p.2520.

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Novel ventilation-perfusion ratio measurements in COPD using MRI

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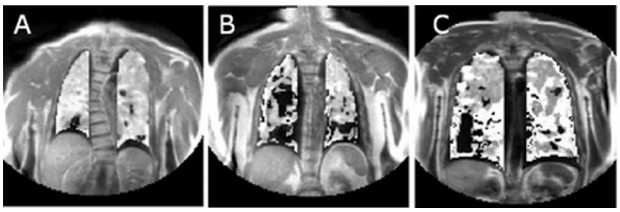
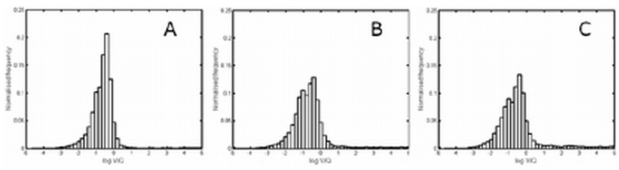
We present a novel analysis of oxygen-enhanced (OE)MRI data in COPD that allows quantitative ventilation-perfusion ratio (V/Q) maps to be determined. Representative V/Q maps of: *A* healthy; *B* moderate & *C* severe COPD subjects reveal homogeneous maps for *A* and considerable heterogeneity in *B/C*.



Group-average histograms (labelled as above) show a narrow peak in *A*; the peak broadens and a lower V/Q peak becomes evident in *B/C*. A high V/Q tail is also seen in *C*.



OEMRI parameters, enhancing fraction (EF) and interquartile range (IQR) V/Q, show significant differences between *A* & *B/C*. Each group had 12 subjects, data averaged over 2 scans. Using a single slice, minimum group sizes to detect a 50% difference of the healthy group window are 27 (EF) & 14 (IQR V/Q). Power calculations are specific to this implementation of the methods, we envisage improvements with further development.

Group mean and SD for OEMRI parameters

	Healthy	Moderate	Severe
EF	0.87±0.06	0.70±0.09*	0.68±0.11*
IQR-V/Q	0.55±0.13	0.80±0.16*	0.81±0.12*

*Significantly different to healthy ($p<0.05$).

The results show strong similarities to published literature using more invasive techniques and enable powering of future intervention studies.

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Repeatability of MR imaging in chronic obstructive pulmonary disease (COPD)

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Purpose: COPD is a broad disease entity defined by PFT, however providing only a global measure of the disease. With the increasing number of therapeutic options, particularly when it is advanced, there is a high demand for a non-invasive imaging test to identify different phenotypes providing regional information on structural and functional changes in order to target therapies accordingly. Recent developments have opened the way for introduction of proton MRI of the lung into the clinical arena. This technique allows for radiation free assessment of the above mentioned issues. So far, no data regarding the repeatability of this technique is available.

Materials/Methods: A comprehensive MR protocol (1.5T) was developed to investigate different aspects of the disease. The protocol consisted of morphological, pulmonary perfusion, cardiac function and respiratory dynamics sequences. Overall, 9 patients (COPD stages III&IV) were investigated twice in a 24h interval.

Results: The mean examination time was 64min and all patients tolerated the examination well. Visual evaluation of morphological and perfusion sequences demonstrated a good repeatability of the visualization of the parenchymal loss and perfusion defects. Quantitative evaluation of flow measurements revealed considerable variations (interexamination difference for the PA flow: 7-64ml). Evaluation of the respiratory dynamics showed a broad variation allowing for no meaningful interpretation.

Conclusions: Overall, the proposed imaging protocol is feasible and applicable even in significantly ill COPD patients. The protocol is easy to use and shows a high repeatability in the key aspects for assessment of morphological and functional disease components.

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Ventilation-perfusion mismatch in COPD with or without emphysema: Comparison of structural CT and functional OE-MRI

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Single-slice conoral oxygen-enhanced MRI (OE-MRI) images were acquired in 24 patients with chronic obstructive pulmonary disease (COPD) and 12 healthy subjects, from which color-coded V/Q maps were extracted by pixelwise model fitting. COPD were structurally classified by percentage of low attenuation areas under -950 HU (LAA%) in matched single-slice CT images: LAA%≤1%–non-emphysema (n=8), >1%–emphysema (n=16).

V/Q maps in COPD were much more heterogeneous than those in healthy subjects, while they showed similar or mildly lower heterogeneity in non-emphysematous COPD than in emphysematous COPD, which demonstrates that comparative V/Q mismatch exists in COPD even if there is no emphysema. To explore potentially different structure-function relationship in two COPD types, correlation between CT and OE-MRI parameters was measured. Median V/Q did not correlate with LLA% in COPD. However, inter-quartile range of V/Q, representing the extent of heterogeneity, was fairly correlated with LLA% in emphysematous COPD (r=0.449, p=0.017), indicating V/Q mismatch in COPD gets worse as emphysema increases. However, the correlation was not found in non-emphysematous COPD.

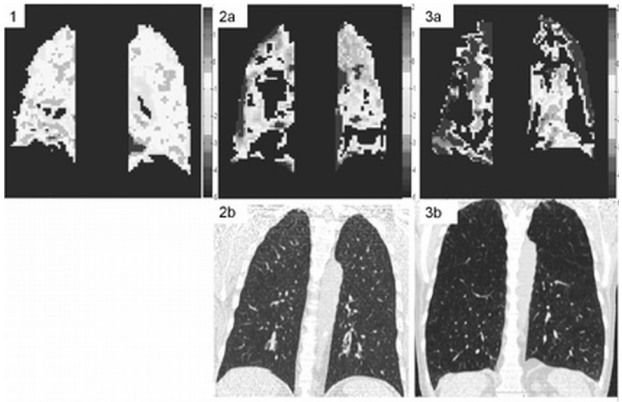

Fig1: V/Q map of a male healthy subject (69 yrs, FEV1%=117%,). Fig 2a and 2b: the V/Q map and matched CT image of a male COPD patient without emphysema (64yrs, FEV1%=65%, LAA%=0.74%). Fig 3a and 3b: the V/Q map and matched CT slice of a male COPD patient with emphysema (63yrs, FEV1%=26%, LAA%=41.78%). CT was not performed in healthy subjects.

This study elucidates that distinction between emphysematous COPD and non-emphysematous COPD does not affect the presence of V/Q imbalance substantially but that the relationship between V/Q and CT measures does vary between these two types.

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Decline in lung density is accelerated in active smokers

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Background: Emphysema is associated with rapid decline in lung density; however, this decline may be influenced by other factors including smoking habits.
Objective: To compare the annual decline in lung density between current and ex-smokers with or without airflow obstruction (AFO).
Material and methods: As part of the Danish Lung Cancer Screening Trial, 2,052 current or ex-smokers aged 50-70 years were screened annually for 5 years (2005-2009) with low dose CT. At annual screening rounds, smoking habits were recorded; carbon monoxide level in exhaled breath was measured; and spirometry was performed. CT lung density was measured as the volume-adjusted 15th percentile density (PD15). The influence of sex, age, smoking and AFO on PD15 was analysed in a mixed effects model with random intercept and random slope of time effect. Former smoking men with less than 30 pack-years and with no AFO at entry were chosen as reference group.
Results: Data were analysed for all subjects throughout the study although censored after they changed their smoking habit. At study entry, 1075 subjects did not have AFO and 843 subjects had AFO based on GOLD spirometry criteria. For the reference group, PD15 was (mean±SE) 72.4±0.8 g/L, and was higher in women (17.0±0.6 g/L); and in active smokers (10.5±0.7 g/L); and lower in subjects with AFO (–3.4±0.6 g/L). Annual decline in PD15 for the reference group was –0.38±0.08 g/L/yr and was higher in women, with additional (0.30±0.07 g/L/yr), current smokers with additional (0.53±0.08 g/L/yr) and for subjects with AFO with additional (0.34±0.07 g/L/yr).
Conclusion: Active smoking, female sex and the presence of airflow obstruction are associated with accelerated decline in lung density.

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The relationship between airflow limitation and quantitative computed tomographic assessment of air trapping and emphysema

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Background: Small airways disease and emphysema are the main components of airflow limitation in COPD. The independent contribution of quantitative CT measurements of these components to airflow limitation in COPD is yet unknown.
Purpose: To determine to what extent the combination of quantitative CT measurements of air trapping and emphysema can explain the variance in lung function in a population that covers the total spectrum of airflow limitation.
Methods: We studied 248 subjects (50 without airflow limitation; 50 GOLD 1; 50 GOLD 2; 50 GOLD 3; 48 GOLD 4) with paired inspiratory and expiratory CT scans and pulmonary function tests. We calculated CT emphysema (2 methods) and CT air trapping (4 methods), and used univariate and multivariate linear regression analysis to relate the quantitative CT measurements to lung function parameters (FEV_1, FEV_1/FVC, RV/TLC and Kco).
Results: Quantitative CT measurements were strongly related to airflow limitation; the best univariate R-square value was 0.72 ($p<0.001$) for percentage of voxels <-850 Hounsfield units (EXP_{-850}) and FEV_1/FVC. In multivariate analysis (corrected for sex, age and height) the combination of CT emphysema and CT air trapping explained 68% to 83% ($p<0.001$) of the variance in lung function parameters of airflow limitation (FEV_1 and FEV_1/FVC).
Conclusion: Quantitative CT air trapping and CT emphysema measurements are strongly associated with lung function impairment, and when combined they explain a large part of the variance in airflow limitation. Our results may prove useful in automated detection and phenotyping of COPD cases.

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Computer modelling and visualisation of the microscopic distributions of hyperpolarised gas diffusivity in models of acinar airways

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Diffusion MRI using hyperpolarized gases is sensitive to lung microstructure. Computer simulations used to investigate the relationship between diffusivity (ADC) and airway dimensions are generally limited by non-realistic geometric assumptions (e.g. infinite cylindrical airways). In this work, we use histology sections to generate realistic models of acinar airways that are used in finite element computer simulations of ^{3}He and ^{129}Xe gas diffusion and ^{129}Xe exchange between gas and tissue.
Results:

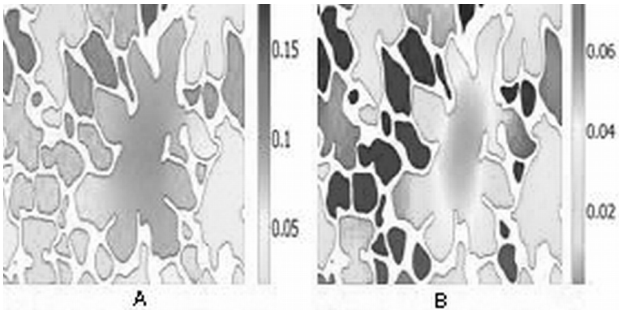

Figure 1. The different diffusivities of ^{3}He (A) and ^{129}Xe (B) result in different ADC (in cm^2/s) distributions.

For ^{3}He, the distribution over the largest airway is nearly uniform due to motional averaging. For ^{129}Xe, its reduced diffusivity limits the mixing between intra and extra-alveolar gas resulting in a non-uniform distribution, which can be described with a two-compartment analytical model.
These results suggest that ^{129}Xe MRI may be more sensitive to alveolar structure than ^{3}He, while being less sensitive to branching and localized diffusion effects.

Conclusion: Computer simulation and visualization of maps of microscopic diffusivity distributions in realistic acinar geometries have helped provide a better understanding of the length scales and diffusion regimes relevant to hyperpolarized gas lung MRI and may help simplify the development of ^{129}Xe-based MR lung morphometry techniques.