# Assessment of ventilation inhomogeneity in patients with alpha-1-antitrypsin deficiency- A useful tool for monitoring early lung disease

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## INTRODUCTION

The risk of developing alpha-1-antitrypsin deficiency (α1-AT deficiency) related emphysema during adulthood is high in patients with a PiZZ genotype. Currently, the $FEV_1$ is used for detecting and monitoring α1-AT deficiency related lung disease. However it is likely that the early changes occur in peripheral airways that are not accessible by spirometry. Multiple breath washout (MBW) is a sensitive test for detecting ventilation inhomogeneity (VI) within the peripheral airways. VI can be quantified by calculating several indices such as the Lung Clearance Index (LCI).

## AIM

The aim of the present study is to assess the clinical value of measuring the LCI in patients with α1-AT deficiency.

## METHOD

Patients were recruited from the German Alpha 1 registry and through patient organisations. For this preliminary analyses, data sets from 3 centers were included.

Children, adolescents and adults with confirmed α1-AT deficiency (PiZZ) and healthy controls performed 2-3 single nitrogen washout tests ($MBW_{N2}$) using the EasyOne Pro LAB™ (ndd Switzerland) with 100% oxygen.

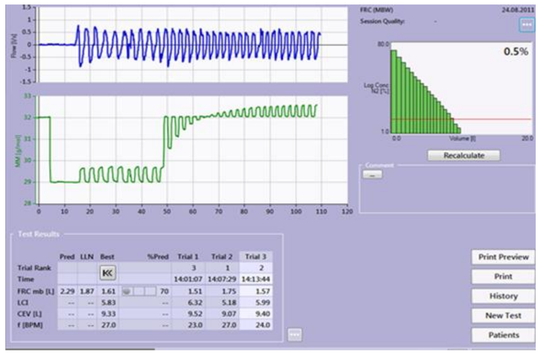


**Figure 1:** Screenshot of an MBW test in a control subject with real time traces of flow (blue) and molar mass (green) and automated analysis

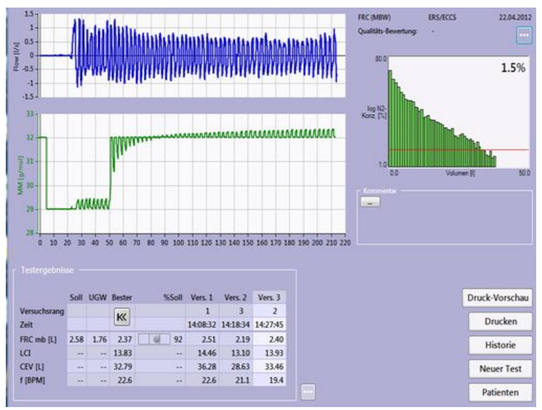


**Figure 2:** Screenshot of an MBW test in a patient with real time traces of flow (blue) and molar mass (green) and automated analysis

## RESULTS

46 patients with α1-AT deficiency and PiZZ genotype (6.4-73.4 years) and 40 healthy controls (6.9-84.4 years) were included in this preliminary analysis. Mean (SD) LCI was 10.50 (2.91) in patients with α1-AT deficiency and 6.5 (0.72) in controls. The mean difference (95% ci, p-value) of the LCI between the groups was -3.980 (-4.872;-3.089, <0.001). Within-test repeatability (CV%) was 7.2% in patients with α1-AT deficiency and 5.6% in controls. Correlation between LCI and age was significant in patients (p=<0.001) but not in controls (p= 0.076).

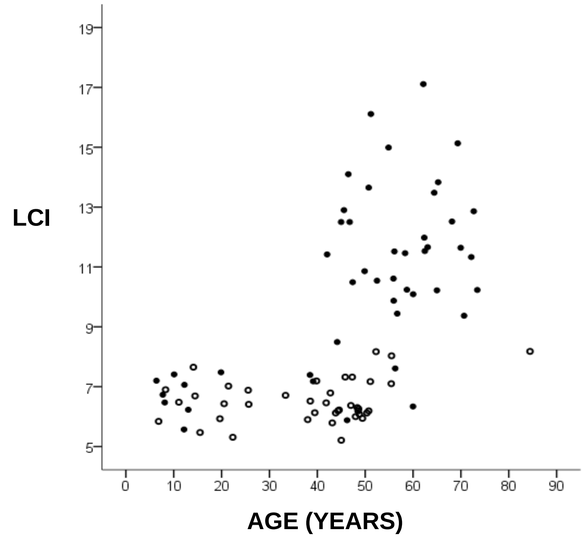


**Figure 3:** Individual Lung Clearance Index (LCI) versus age in patients (●) and controls (○)

## DISCUSSION

Assessment of LCI derived from $MBW_{N2}$ was feasible, reproducible and well tolerated in both, patients with α1-AT deficiency and controls. LCI differed significantly between patients and controls. Individual data demonstrated a marked discrimination between the groups. VI increased with age in patients. We conclude from these preliminary data that the LCI reflects the presence of VI and may be a useful additional lung function parameter in patients with α1-AT deficiency. However, further analyses will reveal the relation between LCI and other lung function parameters, particularly in early stages of disease.