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Title: Phenotyping of patients with COPD from exhaled air by ion mobility spectrometry

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Body: Background: COPD is a heterogeneous disease including several comorbidities. Different phenotypes have been proposed, among them patients with frequent exacerbations. We investigated whether an electronic nose is sensitive in the detection of such characteristics. Methods: Thirty stable COPD patients and 26 control subjects breathed at rest into a special 6.5L tube via a valve. Analysis for VOCs was done online by ion-mobility spectrometry (IMS, Sionex). It turned out that data could be condensed into 23 voltage bins (columns) and 693 reading points (rows) of retention time yielding a matrix of 23x693 signals. For each matrix element values were compared between groups or within COPD patients by Mann-Whitney-U-test at p=0.005. Columns with at least 10 significant row differences were considered as different. This handling of multiple testing of correlated data was based on bootstrap results indicating <2 differences occurring by chance at p=0.005. Results: Ten columns differed between COPD patients and controls, 2 between COPD I/II versus III, and 2 between patients with (n=14) and without at least one exacerbation during the last year, while the distribution of COPD stages (FEV_1) was similar in the latter patients. In single columns the number of significant rows much exceeded the threshold of 10. The analysis of comorbidities also suggested differences in IMS signals. Conclusion: Breath profiles from a highly sensitive electronic nose correlated with COPD disease severity and characteristics. This might help in the non-invasive differentiation between COPD phenotypes. Supported by the Competence Network Asthma/COPD funded by the Federal Ministry of Education and Research (FKZ 01GI0881-0888).