Comparison of breath VOC collected from healthy controls, healthy smokers, smokers with COPD, and ex-smokers with COPD at two German centers for lung research (DZL)

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Introduction

Several studies investigated breath patterns of volatile organic compounds (VOC) in COPD patients. The majority were single site studies with limited numbers of subjects, often not adequately controlled for active smoking or applying only an eNose analysis. The aim of this two-center collaboration study (Marburg, Hannover) was to include sufficiently high numbers of patients and controls to partition the data into different training and independent test sets to identify specific COPD related VOC biomarker signals and to assess the influence of study site. The major analysis was performed by TD-GC/MS, however, also several other analysis platforms were used.

Methods

Breath collection was performed at both sites using the same sampling device (inhalation through an A2 filter and exhalation into a stainless steel reservoir (Fig. 1) from which 3L of breath are continuously drawn onto 2 separate Tenax adsorption tubes). All samples were analyzed centrally in Hannover by TD-GC/MS. For subsets of patients we also used locally available additional analysis platforms like GC-IMS, eNose, and TD-GC-APCI-MS. This analysis is based on 101 subjects from Hannover and 66 subjects from Marburg. Table 1 lists the demographic data separately for both DZL sites. 81 selected VOCs including alkanes, aldehydes, acids, sulfides and other common substance groups, were analyzed using peak count values of the substance specific base peaks.

![Fig. 1: VOC sampling device for loading several Tenax sample tubes simultaneously.](image)

![Fig. 2: Median and IQR and individual datapoints of VOC levels for selected compounds are displayed separately for Hannover (H, left) and Marburg (M, right) and for the 4 different groups of subjects.](image)

![Fig. 3: Correlation between data of the 2 separately collected and analysed Tenax tubes. For most VOC the agreement was good (top). For some VOCs the correlations indicate that our analysis based on specific target-ions needs further optimisation.](image)

![Fig. 4: Examples for the relationship between COHb and VOC levels in actively smoking subjects (Hannover data).](image)

Results

As expected, we observed significantly higher values of carboxyhemoglobin as well as lower NO values in actively smoking subjects compared to non- and ex-smokers. COPD patients were significantly older than healthy control subjects, but no clear relationship between age and the level of exhaled VOCs could be detected. Active smokers could also be clearly discriminated by higher values for combustion products like furans as well as BTX hydrocarbons. There were clear relationships between COHb values and most smoking related VOCs (e.g. Fig. 4). VOC levels derived from the two independently loaded TENAX tubes were generally highly reproducible (e.g. Fig. 3).

Only few VOCs discriminated healthy controls from COPD patients in the univariate analysis (Fig. 2). Such a difference was clearer in not actively smoking subjects.

Conclusion

This first univariate analysis shows that comparable levels of VOCs can be found in subjects from different sites. The expected differences between smokers and non-smokers, the good correlation between samples, and the relationship to COHb levels suggests a sufficient quality of the data. There appeared to be only few COPD specific VOCs and the data clearly shows the importance to control for active smoking.

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