

Breath Analysis Using Secondary Electrospray Ionization Mass Spectrometry - Steps Towards Absolute Gas-phase Concentrations of Metabolites

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Exhaled breath contains hundreds of volatile metabolites that provide biochemical information about the health or pathophysiological state of an individual. Therefore, chemical analysis of the molecular composition of breath is a promising tool for the non-invasive and rapid diagnosis of diseases. [1]

Previous studies have shown that respiratory diseases like chronic obstructive pulmonary disease or obstructive sleep apnea can be diagnosed by analyzing exhaled breath on-line using secondary electrospray ionization mass spectrometry (SESI-MS) [2,3]. SESI coupled to a high-resolution mass spectrometer is a highly sensitive and specific technique, which allows the detection of hundreds of metabolites within a broad mass range (up to 900 Da) [4]. In terms of sensitivity and compound coverage, it is able to overcome limitations of other techniques used in breath analysis [5]. However, one main drawback of SESI-MS is the difficulty to obtain absolute gas-phase concentrations of biomarkers in breath. To overcome this limitation, a sample delivery system was developed in this study and integrated into an existing SESI-MS setup. This allows for a stable gas-phase delivery of compounds at low mixing ratios (parts per billion range), thereby enabling quantification by external calibration or standard addition.

Our results indicate that the quantification of breath biomarkers is possible with SESI-MS. The ability of standardization and absolute quantification renders the measurements more robust and environmental influences can be eliminated. Furthermore, it allows for a better correlation between levels of metabolites found in exhaled breath and in blood.

[1] B. de Lacy Costello et al., *J. Breath Res.* **2014**, 8, 014001.

[2] P. Martínez-Lozano Sinues et al., *Respiration* **2014**, 87, 301-310.

[3] E.I. Schwarz et al., *Thorax* **2015**, 71, 110-117.

[4] M. T. Gaugg et al., *J. Breath Res.* **2016**, 10, 016010.

[5] P. Martínez-Lozano Sinues et al., *J. Breath Res.* **2011**, 5, 016002.