GC×GC-TOFMS for reliable detection of candidate biomarkers in breath analyses

R. Pesesse[1], P.-H. Stefanuto[1], F. Schleich[2], R. Louis[2], J.-F. Focant[1]

[1]Organic and Biological Analytical Chemistry, CART, Chemistry Department, University of Liège, Belgium

[2]Pneumology and Allergology Unit, University Hospital Center, Liège, Belgium

Early stage non-invasive diagnostic of diseases can possibly take place by analyzing volatile organic compounds (VOCs) released from the breath of patients [1]. Breath VOC samples are typically analyzed using one dimensional (single-column) gas chromatography coupled to mass spectrometry (1DGC-MS). In that context, a limited number (< 50) of VOCs (mainly alkane and benzene derivatives) has been identified as potential biomarkers of disease in breath VOC profile.

Because of the complexity of breath VOC mixtures, it is believed that more biomarker candidate could be found. Comprehensive two-dimensional GC coupled to time-of-flight mass spectrometry (GC×GC-TOFMS) is a powerful separation science tool and has been successfully used to separate more than one thousand of VOCs in human breath [2].

In addition to the large peak capacity, latest advances in GC×GC-TOFMS data processing tools also allows better handling of the interfering environmental VOCs to the breath signature. Supervised statistics can be applied to the GC×GC chromatograms in either a peak table-based or a pixel-based approach [3,4]. Inter-individual variations and sampling effects can therefore be minimized in order to improve the isolation of specific molecules.

In this paper, we report on practical examples of such specific data treatment procedures in the case of lung cancer screening by means of breath sampling of patients at the time of bronchoscopy.

[1] Pauling, *et al*. *Quantitative analysis of urine vapor and breath by Gas-Liquid partition chromatography.* Proc Nat Acad Sci USA, 1971. **68**(10): p. 2374-2376.

[2] Phillips, *et al*. *Detection of an Extended Human Volatome with Comprehensive Two Dimensional Gas Chromatography Time-of-Flight Mass Spectrometry.* Plos One, 2013. **8**(9): e75274.

[3] Stefanuto, *et al*. *Reading cadaveric decomposition chemistry with a new pair of glasses*. ChemPlusChem, 2014. **79**(6): p. 786-789

[4]] Stefanuto, *et al*. Exploring new dimensions in cadaveric decomposition odour analysis. *Anal. Methods*, 2015. **7**: p. 2287-2294