





Hospital Universitari Métua Terrassa BARCELONA



UPDATE IN EXHALED BREATH IN DETECTION OF LUNG CANCER

Ángela Guirao Montes Hospital Clínic de Barcelona

Lung cancer (LC) is the most frequent and deadly human cancer; overall survival is 10-15% at 5 years of diagnosis. Yet, LC can be cured if diagnosed early during the course of the disease, when the tumor can be removed surgically. Unfortunately, this occurs in less than 25% of patients because LC is most often asymptomatic until advanced. A large study that used computed tomography (CT) of the chest to screen smokers at risk of LC convincingly shown that mortality can be reduced by 20-40%. However, CT screening is expensive, difficult to implement logistically and not exempt of radiation exposure. Thus, alternative LC diagnostic methods suitable to use at the point of care are needed. Our proposal is to use volatile metabolomics. The rationale behind this approach rests on the fact that the human metabolome expresses distinct and immediate changes when pathological processes occur and alter the body's biochemistry via a combination of oxidative stress, cytochrome p450, liver-enzymes and carbohydrate and lipid metabolism. Volatile Metabolites are transferred from blood to breath in the alveoli. Volatile Organic Compounds (VOCs) present in human breath will originate from normal and abnormal cells, although in different mixture compositions. A subset of VOCs may appear exclusively in abnormal cells but not in healthy cells. The particularly significant feature that we will exploit in this approach is that each disease may be characterized a unique VOC pattern so that the technique may be optimized in selectivity for a certain condition irrespective of other diseases. The study of VOC integrates cutting-edge scientific and technological knowledge form multidisciplinary fields (biomedicine, analytical chemistry, gas chromatography - mass spectroscopy (GC-MS), microelectronics, nanotechnology, computational metabolomics and machine learning based on artificial intelligence (AI)). The challenge now is the development of a novel and self-contained tool for the clinical practice. This tool will be the combination of complex technologies that still face many practical challenges, including, but not limited to, the following areas: 1) the fast evolving field of the human metabolome, 2) the rapidly maturing field of nanotechnology that enables unprecedented sensing solutions for biological samples and very low detection levels, 3) the challenging analysis of omics data featuring extremely high dimensional data with limited number of examples, conditions that require the latest techniques for model development and validation to avoid false discoveries or optimistic results, therefore we are just at the begging of a very long journey.

Bibliography

1. Guirao Montes Á, Molins López-Rodó L, Ramón Rodríguez I, et al. (2017) Lung cancer diagnosis by trained dogs. Eur J Cardiothorac

Surg 52:1206–1210

2. Gaga M, Powell CA, Schraufnagel DE, et al. (2013) An Official American Thoracic Society/European Respiratory Society Statement:

The Role of the Pulmonologist in the Diagnosis and Management of Lung Cancer. Am J Respir Crit Care Med 188:503–507

3. Horeweg N, van Rosmalen J, Heuvelmans MA, et al. (2014) Lung cancer probability in patients with CT-detected pulmonary nodules:

A prespecified analysis of data from the NELSON trial of low-dose CT screening. Lancet Oncol 15:1332– 1341

4. Amann A, Smith D (2013) Volatile Biomarkers: Non-Invasive Diagnosis in Physiology and Medicine. Elsevier, Amsterdam

5. D'Amico a, Pennazza G, Santonico M, et al. (2010) An investigation on electronic nose diagnosis of lung cancer. Lung Cancer

68:170-176

6. Sivalingam Y, Martinelli E, Catini A, et al. (2012) Gas-sensitive photoconductivity of porphyrinfunctionalized ZnO nanorods. J Phys

Chem C 116:9151–9157

7. Capuano R, Santonico M, Pennazza G, et al. (2015) The lung cancer breath signature: A comparative analysis of exhaled breath and

air sampled from inside the lungs. Sci Rep 5:16491

8. Di Natale C, Macagnano A, Martinelli E, et al. (2003) Lung cancer identification by the analysis of breath by means of an array of nonselective

gas sensors. Biosens Bioelectron 18:1209–1218

9. Gasparri R, Santonico M, Valentini C, et al. (2016) Volatile signature for the early diagnosis of lung cancer. J Breath Res 10:16007

10. Paolesse R, Nardis S, Monti D, et al. (2017) Porphyrinoids for Chemical Sensor Applications. Chem. Rev. 117:2517–2583

11. Marco S, Gutierrez-Galvez A (2012) Signal and data processing for machine olfaction and chemical sensing: A review. IEEE Sens J

12:3189-3214

12. Rodríguez-Pérez R, Cortés R, Guamán A, et al. (2018) Instrumental drift removal in GC-MS data for breath analysis: the short-term

and long-term temporal validation of putative biomarkers for COPD. J Breath Res 12:36007

13. Marco S (2014) The need for external validation in machine olfaction: Emphasis on health-related applications. Anal Bioanal Chem

406:3941-3956

14. Rodríguez-Pérez R, Fernández L, Marco S (2018) Overoptimism in cross-validation when using partial least squares-discriminant

analysis for omics data: a systematic study. Anal Bioanal Chem 410:5981–5992

15. Rudnicka J, Kowalkowski T, Ligor T, et al. (2011) Determination of volatile organic compounds as biomarkers of lung cancer by

SPME-GC-TOF/MS and chemometrics. J Chromatogr B Anal Technol Biomed Life Sci 879:3360–3366 16. Spicer R, Salek RM, Moreno P, et al. (2017) Navigating freely-available software tools for metabolomics analysis. Metabolomics

13:1–16

17. Saalberg Y, Wolff M (2016) VOC breath biomarkers in lung cancer. Clin Chim Acta 459:5–9

18. Grabe V, Sachse S (2018) Fundamental principles of the olfactory code. BioSystems 164:94–101