BREATH® BIOPSY

Breath Biopsy Conference

13th - 14th NOVEMBER 2019

Welcome

I'm very pleased to welcome you to the Breath Biopsy Conference 2019. It's been an exciting year for breath analysis with fascinating new research in a number of areas including respiratory and liver diseases and we're pleased to be reflecting some of these latest discoveries in our program.

This year's conference celebrates the intrinsically collaborative nature of breath research, with speakers and sessions representing a range of specialisms and related research areas that make breathomics possible. We're also looking forward to sharing some of the progress we've made at Owlstone Medical, particularly the launch of our updated Breath Biopsy product line and EVOC® Probes, a novel approach to probing metabolism.

Thank you for joining us this year, we hope you enjoy the packed program we have prepared and we look forward to discussing your latest discoveries with you.

Best,

Billy Boyle
CEO, Owlstone Medical Ltd.

DAY 1

Wednesday 13th of November 2019

TIME	EVENT
8:30-9:15	**Registration**
9:15-9:25	**Welcome to the Breath Biopsy Conference**
9:25-11:00	**Session 1: Breath Biopsy Applications**
	Max Wilkinson, University of Manchester *Effects of humidity, dry purging and sorbent choice on VOC recovery during breath sampling*
	Chris Mayhew, Institute of Breath Research, University of Innsbruck *Applications of ion-molecule reactions to breath analysis: use for discovery and real-time measurements*
	Olaf Holz, Fraunhofer Institute for Toxicology and Experimental Medicine *Breath analysis following experimental endotoxin challenge in healthy volunteers*
11:00-11:30	**Coffee Break**
11:30-11:50	**Kayleigh Arthur, Owlstone Medical** *A new approach to Breath Biopsy using TD-GC Orbitrap*
11:50-12:35	**Keynote Speaker**
	Jane Hill, Thayer School of Engineering, Dartmouth *Toward breath tests for infectious diseases*
12:35-14:00	**Lunch** **Poster session**
14:00-15:40	**Session 2: EVOC and stable isotopes**
	Isabel Orf, Owlstone Medical *Breath Limonene and Liver Disease – Using EVOC® Probes to Assess Metabolic Pathways*
	Douglas Morrison, University of Glasgow *Stable Isotope Breath Tests: Applications, Challenges and Opportunities*
	Anil Modak, Owlstone Medical Scientific Advisory Board *Diagnostic breath tests for unmet clinical needs with labelled and unlabelled probes*
15:40-16:15	**Coffee Break**
16:15-17:00	**Keynote Speaker**
	Jessica Lasky-Su, Brigham and Women's Hospital, Boston *Metabolomics in the multi-omic era: the key component for clinical translation in asthma*
17:00-18:30	**Networking, canapés and drinks**

DAY 2

Thursday 14th of November 2019

TIME	EVENT
8:30-9:00	**Coffee and Networking**
9:00-9:45	**Keynote speaker**
	George Hanna, Imperial College London *Talk title not available*
9:45-10:05	Laura McGregor, Markes International *Delivering quality data in biomarker discovery*
10:05-10:30	Huw Davies, Owlstone Medical *Introduction to Breath Biopsy Services*
10:30-11:00	**Coffee Break**
11:00-12:40	**Session 3: Breath Biopsy and Breathomics**
	Renaud Louis, University of Liege *Biomarkers in asthma monitoring*
	João Rufo, University of Porto *Breathomics in asthma diagnosis and monitoring*
	Jose Torrecilla, Complutense University of Madrid *Artificial intelligence in the early diagnosis of diseases through breath analysis*
12:40-14:00	**Lunch** **Poster session**
14:00-15:15	**Expert panel discussion: the next 5 years in breath research**
	Renaud Louis Jose Torrecilla Marc van-der-Schee Jonathan Beauchamp
15:15	**Breath Biopsy Conference Wrap-up** **Coffee + Networking**

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Posters

Exhaled Gas Analysis by GC-MS, Sampled from Flexible Bronchoscopy, for Finding Lung Cancer Biomarker

Yunghee Lee, Seoul National University Bundang Hospital

Multi-centre cross-validation study in the search for volatile colorectal cancer biomarkers in breath and faeces

Y Lan Pham, Fraunhofer Institute

Using Exhaled Breath Analysis as a Biomonitoring Tool - Determining Smoking Status Using Breath Biomarkers

Will Murch, Owlstone Medical

Detecting CH_4 in breath and its related diseases

Tahereh Shah, Ulster University

Volatile profiles of MSTO-211H malignant mesothelioma cells

Liam Little, Sheffield Hallam University

Development of a Compact, IoT-enabled Electronic Nose for Breath Analysis

James Covington, School of Engineering (University of Warwick)

Detection and quantification of lung cancer biomarkers using a micro-analytical device

Igor Bezverkhyy, CNRS - University of Burgundy

Human chemosignals elicited from emotional states

Fabio Di Francesco, University of Pisa

Evaluation of non-invasive approaches for the analysis of exogenous and endogenous VOCs

Beate Gruber, Research Institute for Chromatography (Kortrijk, Belgium)

Breath-holding times distinguish gases diffusing from lungs, arteries, veins and the average of all tissues

Albert Donnay, Johns Hopkins University

Pectin supplementation did not alter profiles of exhaled breath in young adults and elderly

Agnieszka Smolinska, Maastricht University

ZnO nanowires-based Sensors for Methane detection in Breath

Niyanta Datta, Aoife Morrin

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DAY 1

Max Wilkinson

University of Manchester

Biography

Max Wilkinson has recently been awarded a PhD at the University of Manchester under the supervision of Steve Fowler and will be continuing to work with the group for the next two years. His research has been focussed on the optimisation of breath sampling to improve the reproducibility of results. Max is currently working on the analysis of GC-MS data from clinical studies investigating asthma and COPD.

Effects of humidity, dry purging and sorbent choice on VOC recovery during breath sampling

Abstract

Background: Offline breath analysis by GC-MS requires the use of sorbent traps to concentrate and store volatile compounds. The selection of which sorbent to use and best practices for managing water retention are important considerations to allow for reproducible, untargeted, biomarker discovery in water saturated breath samples.

Objective: To assess three commonly used sorbent materials for their use in breath volatile sampling and determine how the high relative humidity inherent in such samples effects the capture of volatile compounds of interest.

Methods: One single bed sorbent (TenaxGR) and two dual bed sorbents (TenaxTA / Carbograph1TD and TenaxTA / Carbograph5TD) were selected as they are the most commonly used sorbents in the breath sampling literature. Water retention and dry purge rates were determined. The recovery of 29 compounds in a standard mix loaded using high humidity gas was tested for each sorbent and compared to loading in dry gas. Finally, breath samples were sampled simultaneously on to each sorbent type using the ReCIVA, a proprietary breath sampler, and analysed by TD-GC-MS.

Results: All three sorbents exhibited acceptable reproducibility when loaded with the standard mix in dry gas. Loading the standard mix in humid gas led to reduced recovery of compounds based on their chemical properties. Dry purging performance for each sorbent material was assessed and was shown to be 1.14, 1.13 and 0.89 mg H_2O min^{-1} for TenaxGR, TenaxTA/Carbograph1TD and TenaxTA/Carbograph5TD respectively. A comparison of breath profiles on different sorbents showed differences in background artefacts (sulfur dioxide, cyclopenten-1-one and 3-nonene) and endogenous breath compounds (2-methyl-furan and furfural).

Conclusions: All three sorbents performed equally well when the standard mix was loaded onto them. High relative humidity during sampling reduces the ability of sorbent tubes to capture volatile compounds. This effect is dependent on the chemical properties of the compound and could impact method detection limits during breath sampling studies. Sufficient water to impair accurate analysis was retained on all tube and dry purging times are suggested. Minimal differences were observed between sorbent materials when used to sample breath, however, suggestions are provided for sorbent selection for future studies.

Chris Mayhew

Institute of Breath Research,
University of Innsbruck

Biography

Chris Mayhew is Professor of Molecular Physics at the University of Birmingham, UK, and Professor of Analytical Chemistry and Director of the Institute for Breath Research at the University of Innsbruck, Austria. Over a period of 30 years, he has established a unique suite of instrumentation used for the study of electron attachment and ion-molecule processes. His applied multidisciplinary research programmes include technological plasma physics and analytical chemistry using soft chemical ionisation techniques, with the latter predominantly focusing on Health Sciences (breath analysis), Atmospheric Chemistry, and Homeland Security. His research also addresses the many current challenges of applying soft chemical ionisation mass spectrometric techniques for breath analysis for the benefit of clinical non-invasive diagnosis procedures and for detecting hidden or entrapped people. This research is paving the way for the development of analytical techniques and instrumentation applied to the identification of a pattern of biomarkers specific to a given disease and to human presence.

Applications of ion-molecule reactions to breath analysis: use for discovery and real-time measurements

Abstract

Soft chemical ionization mass spectrometric techniques, which include proton transfer reaction mass spectrometry, selected ion flow tube mass spectrometry, and ion mobility spectrometry, employ ions as sensitive analytical probes for use in the identification, detection and monitoring of trace compounds in complex chemical surroundings. These techniques have opened up new and exciting possibilities for applied areas of research to identify trace volatiles in human breath, emitted from the skin and present in bodily fluids for diagnosing and monitoring diseases, monitoring treatments and examining health in general. The research being undertaken at the Institute for Breath Research in Dornbirn, Austria is addressing the many current challenges of applying soft chemical ionization mass spectrometry for the analysis of the human volatilome for the benefit of clinical non-invasive diagnostic procedures; including discovery programmes and real-time measurements. The main focus of the talk will be on our applications of proton transfer reaction mass spectrometry to breath analysis, but details on health sciences and search and rescue operations will also be included.

Olaf Holz
Fraunhofer Institute for Toxicology and Experimental Medicine

Biography

Olaf Holz is a bioengineer, trained at the Hamburg University of Applied Sciences. After working in toxicogenetics in the Department of Occupational and Environmental Health at the University of Hamburg and the Department of Occupational Health at the University of Vienna for 4 years, he changed to respiratory health and worked in the Hospital Grosshansdorf in the research group of Professor Magnussen for 18 years. Here the focus was on research in non-invasive methods to monitor airway inflammation, especially induced sputum and exhaled nitric oxide. He achieved his PhD in environmental Sciences from the University of Lüneburg in 2006. The work on human experimental challenge models (ozone, LPS), and their use in pharmaceutical proof of concept studies continued after changing to the Fraunhofer Institute for Toxicology and Experimental Medicine ITEM in 2010, were he is now a group leader for non-invasive clinical method development in the department of Clinical Airway Research.

Breath analysis following experimental endotoxin challenge in healthy volunteers

Abstract

It´s still unclear how airway inflammation effects the breath VOC profile. We therefore analyzed breath volatile organic compounds (VOC) following experimental endotoxin (LPS) challenge of healthy human volunteer subjects.
10 healthy, non-smoking volunteers were recruited for this study. Breath was collected during the following visits: screening (V1), baseline (V2), following overnight fasting in the morning before (V3a), in the late afternoon following a segmental LPS challenge (V3b), and following an overnight fasting period approximately 22 h after the segmental challenge (V4). After a 4 week washout period the subjects underwent a whole lung LPS inhalation challenge. A breath sample was collected about 1 week before (V5), the morning before (V6a) and in the early afternoon (V6b) following the inhalation challenge. Airway inflammation was assessed by bronchoscopy (BAL) after the segmental challenge and using sputum analysis after the inhalation challenge. Patients inhaled room air through a VOC and sterile filter and exhaled into an aluminum reservoir tube. Breath was loaded simultaneously onto 4 Tenax and 2 carbon adsorption tubes and analyzed by GC-MS.
The segmental and the inhalation LPS challenge caused a clear inflammatory response characterized by a massive influx of neutrophils and monocytes into the airways (BAL median (IQR): 3.0(4.2) vs. 64.0(7.3), sputum: 33.9(26.8) vs. 78.3(13.5), respectively). We observed changes in VOC patterns related to food intake during the study days. Among these were terpens, acetone, and ethanol, which increased in the samples taken after the lunch break (V3b and V6b). There were also study procedure related changes in the VOC profile. Propanol-1 and propanol-2, compounds of hand and skin disinfection solutions, increased with the duration of time spend in our institute and were found increased on days when ECG and skin prick test were performed. For a number of aldehydes we observed changes which could be related to the change in airway inflammation.
The longitudinal breath analysis in this study shows that metabolic and environmental processes clearly affect the VOC patterns, therefore an identification of VOCs is strongly recommended as pattern changes detected by eNOSE or other sensor based instruments could be misinterpreted. It's tempting to speculate that the observed changes in breath aldehyde levels reflect oxidative stress during induced airway inflammation.

Kayleigh Arthur
Owlstone Medical

A new approach to Breath Biopsy using TD-GC Orbitrap

Abstract

Since its introduction in 2016, Breath Biopsy® has been widely adopted by academic and pharmaceutical researchers for breath biomarker discovery due to its standardized breath collection procedures, consistent sample process and analysis. In this presentation we will describe how adopting the Orbitrap™ mass analyser (Thermo Scientific, Bremen, Germany) has allowed us to address some of the widely accepted challenges associated with breath analysis.

As a high-resolution accurate mass (HRAM) instrument with high dynamic range, the Orbitrap allows detection of both high-abundance volatile organic compounds and trace-level analytes within a single analysis. Using the software package Compound Discoverer, customised feature extraction and data processing methodologies have been developed, streamlining the identification of unknowns for discovery metabolomics. The sub-ppm mass accuracy is taken advantage of to create accurate mass libraries which can be used for unambiguous biomarker identification and comparison of compounds of interest across samples and between studies.

Finally we will discuss how the implementation of Chromeleon Chromatography Data System (CDS) has provided enhancements in data acquisition, management and processing, providing the end-to-end solution required to manage the logistics of ever-increasing demand on our high throughput Breath Biopsy® laboratory and the maintenance of quality in such an environment. Combined, these new approaches demonstrate significant advancements in Breath Biopsy®.

Talk sponsored by Thermo SCIENTIFIC

Jane Hill

Thayer School of Engineering, Dartmouth

Biography

Jane Hill is an Associate Professor at Dartmouth. Her team focuses on determining cross-sectional and individualized biomarker suites for infectious diseases, particularly those of the respiratory tract. Her team has helped to mature the breath-based biomarker approach through the development and optimization of chemical data acquisition and data analysis pipeline for untargeted metabolites in clinical populations. Her team is in the process of clinical validation of biomarkers for a number of infectious etiologies in addition to working with others to miniaturize and/or commercialize current benchtop systems for direct clinical translation.

Toward breath tests for infectious disease

Abstract

The diagnosis of most infectious diseases still uses or is based on technologies from the time of Louis Pasteur! To be fair, nucleic acid amplification technologies are revolutionizing some diagnostic areas, however, many patients will not benefit, and so we must find constructive alternatives. Here, I will present our efforts to deploy metabolomics and transcriptomics to diagnose respiratory infections quickly and accurately. I will share our progress on pre-clinical applications of breath analysis for tuberculosis profiling for animal health monitoring, antibiotic testing, and vaccine development, as well as our early work translating the same into clinics in South Africa in combination with efforts to enhance diagnosis effectiveness using blood transcriptional profiling.

Douglas Morrison
University of Glasgow

Biography

With undergraduate training in Medicinal Chemistry and a PhD which focussed on developing stable isotope-based methods of measuring gut function, Dr Morrison is currently a Reader in Stable Isotope Biochemistry at the University of Glasgow. His main research activities revolve around using stable isotopes to understand biological systems and processes. His research focus is on the role of the gut in over-nutrition (obesity) and under-nutrition (stunting). Together with colleagues, he has developed a novel food ingredient that targets nutrient-sensing, appetite-regulating circuits in the gut that has demonstrated promise for the prevention of weight gain. Currently he is working on developing stable isotope approaches to measure gut function in under-nutrition (e.g. brush border enzyme activity) to improve diagnosis of gut dysfunction and monitoring of nutritional interventions that target improvement in gut barrier function in malnutrition settings.

Stable Isotope Breath Tests: Applications, Challenges and Opportunities

Abstract

Stable isotope breath tests are an attractive diagnostic modality because they are non-invasive, report functional response and can potentially offer improved sensitivity and specificity than more generic breath tests. For example, the ^{13}C-urea breath test for diagnosis of *Helicobacter pylori* infection demonstrates sensitivity and specificity of greater than 98% and is measured in breath ^{13}CO2. However, oral administration of an isotope labelled tracer also presents some challenges. Variability in gastric emptying rates and intestinal transit times, coupled with interferences from microbes that reside in different regions of the gut reduce the sensitivity and specificity of stable isotope breath tests of more distal gut function and the function of other organs. A priori choice of isotope labelled tracer is normally a prerequisite for a stable isotope breath test and judicious choice of tracer has led to several applications of stable isotope breath tests in clinical practice and research. Complimentary approaches of using targeted and untargeted breath analysis such as exogenous volatile organic compound analysis are rare but offer opportunities for target discovery and refinement of diagnostic breath tests.

Anil Modak
Owlstone Medical
Scientific Advisory Board

Biography

Anil Modak, PhD was untill recently the Associate Director of Medical Products Research & Development at Cambridge Isotope Laboratories Inc.in Tewksbury, MA in the US. He has been involved in the design, research and development of novel non invasive breath tests for personalized medicine using stable isotope substrates for the monitoring of disease severity/toxicity and the evaluation of drug metabolizing enzyme activity. He is the author of several recent patents and publications and numerous presentations at medical conferences around the world. He has authored two book chapters. He serves on the Editorial board of the Journal of Breath Research, Journal of Pharmacogenomics & Pharmacoproteomics and International Journal of Clinical Pharmacology & Toxicology.
His previous experience includes working for Ribozyme Pharmaceuticals in Boulder, CO and Monsanto in St Louis, MO. His postdoctoral research was conducted at the University of Iowa and Kings College London.

Diagnostic breath tests for unmet clinical needs with labeled and unlabeled probes

Abstract

In the modern era since Linus Pauling's VOC microanalysis in 1971, breath tests have been extensively researched both with endogenous VOC's as well as the more specific ^{13}C-probe based breath tests using $^{13}CO_2$ as a biomarker of physiological changes and genetic diversity in humans.
With the development of sensitive analytical techniques, we can now investigate for unique biomarkers in a person's breath to identify particular medical conditions. Breath analysis has the potential to become a non-invasive diagnostic tool in clinical practice.
Over the last two decades non invasive diagnostic phenotype [^{13}C]-breath tests[1] as well as tests using endogenous volatile organic compounds (VOCs) in breath[2] have been researched extensively. However, only five breath tests have been approved by the regulatory boards in the US/Europe (FDA/EMA).
Linking VOC's to specific illnesses has been extremely challenging since oxidative processes in different organs of patients afflicted with various diseases could result in the generation of the exact same VOC's lowering the ability to pinpoint one of more VOC's to reliably detect a specific disease. The origins of the VOC's due to physiological processes in the human body need to be identified for them to be useful as biomarkers of disease.
On the other hand using either stable isotope or unlabeled probes for evaluating various drug metabolizing enzyme deficiencies for personalizing medications have the potential of being the most promising breath tests that can make the transition from research to the clinic. The pros and cons of both breath test paradigms for medical applications will be discussed in great detail.

References
1 Modak AS. An Update on ^{13}C-BreathTests: The Transition to Acceptability into Clinical Practice in Volatile biomarkers: non-invasive diagnosis in physiology and medicine p 245-262. A Amann and D Smith (Eds), Elsevier 2013
2 Lourenco C. & Turner C. Breath analysis in disease diagnosis: methodological considerations and applications. Metabolites, 4, 465–498 2014

Jessica Lasky-Su
Brigham and Womens Hospital, Boston

Biography

Jessica Lasky-Su is an Associate Professor in Medicine and associate statistician at Harvard Medical School and Brigham and Women's Hospital. Over the last 20 years, Dr Lasky-Su has focused on the analysis of genetics, genomics, and metabolomics data of various complex diseases with a primary focus on respiratory disease over the last 15 years. The accumulation of these efforts has resulted in a productive track record of over 130 original research articles. Through the funding of several metabolomics-related grants, Dr Lasky-Su has developed a "metabolomics epidemiology" research program at the Channing Division of Network Medicine that has been highly successful and synergistic in nature, and has developed into one of the largest and most impactful groups of metabolomic epidemiologists with a strong national and international presence and comprehensive publication record. In addition to using metabolomics to study the etiology of several complex diseases, including body mass index, asthma, allergies, autism, bacteremia, and macular degeneration, Dr Lasky-Su has also focused on using metabolomics data in conjunction with other omics data to study disease etiology using several approaches to integrative omics. Dr Lasky-Su also serves in national and international leadership capacities, including the acting chairman of the Consortium of METabolomic Studies (COMETS), a board member of the International Metabolomics Society, and a scientific advisor to the "Metabolomics Workbench."

Metabolomics in the multi-omic era: the key component for clinical translation in asthma

Abstract

The rapid advance in scientific technology has resulted in a multi-omic era, where multiple omics data types are available for single, large population-based cohorts. For the first time, epidemiologists have the ability to study complex diseases biology through the use of multiple omics data types simultaneously, in conjunction with relevant clinical and environmental information. While multi-omic integration has the potential to provide optimal insight into disease pathogenesis, the best approaches to multi-omic integration are not clear. In this talk we describe several approaches to multi-omic data integration that can be utilized to study asthma eitiology. From a reductionist approach that relies on previous biologic and scientific knowledge to guide the analyses to a systems biology approach that integrates genomic, epigenomic, and metabolomic networks together, we review examples of each from our research focusing on asthma, allergy, and obesity phenotypes. Highlights include 1) Using 2 birth cohorts with >1,000 children to demonstrate the interplay between genetics, metabolomics, and environmental exposures in pregnancy and early life that lead to childhood asthma and allergies; 2) Applying a systems approach to integrate gene expression, methylation, and metabolomics data to identify multiomic influences on asthma phenotypes; 3) Analyzing metabolomic data in 2 large population-based cohorts totaling >12,000 to study prevalent asthma and to examine the impact of inhaled steroid use; and 4) Demonstrating the feasibility of large-scale metabolomic integration through a meta-analysis of metabolomic data in >85,000 people from multiple cohorts throughout the world. We examine these approaches and discuss the advantages and weaknesses of each and under what conditions each approach is most relevant. The talk concludes with a discussion of why metabolomics as an essential component of omics research and the scientific challenges that are imperative to address in order to continue making progress towards utilizing multi-omics in a personalized medicine framework.

DAY 2

George Hanna

Imperial College London

Biography

Professor George Hanna is the head of the Department of Surgery and Cancer at Imperial College and Consultant Upper Gastro-intestinal surgeon at Imperial College NHS Trust. He was trained in Ninewells Hospital, Dundee, Scotland and obtained a PhD (University of Dundee) in 1997 and FRCSEd (Gen Surg) in 1993. He joined Imperial College as a Clinical Senior Lecturer and Upper Gastrointestinal Consultant Surgeon in 2003. His clinical work is based at Hammersmith Hospital and includes oesophageal and gastric cancer and advanced laparoscopic surgery.
Professor Hanna leads the NIHR programme for point of care diagnostics in cancer and gastrointestinal diseases (NIHR London IVD). The current interests of his laboratory revolve around volatile organic compounds analysis for biomarker discovery and understanding the molecular drivers of volatile compounds to develop a non-invasive breath test to diagnose oesophageal and gastric cancer. His educational research aims to develop competency assessment tools for training and quality assurance of surgical performance in randomised controlled trials.

Challenges in external clinical validation studies

Abstract

The breath field research has many small scale discovery studies that lack external independent validation. The clinical environment and quality control demands present a set of challenges that need to be taken into consideration in the design and execution of clinical studies. Wide-scale studies, quality control measures and the design for external validation will be discussed.

Laura McGregor
Markes International

Delivering quality data in biomarker discovery

Abstract

Many breath analysis studies target the broadest possible range of vapour-phase compounds, particularly during biomarker discovery phases, and rely on thermal desorption coupled with gas chromatography / mass spectrometry (GC-MS) as the 'gold standard' analytical tool. The high water content, wide analyte concentration range and the unique, precious nature of the samples present significant challenges to breath researchers and it is vital to ensure the quality and integrity of such samples throughout the sampling and analytical workflows. In this presentation we present recent advances in thermal desorption and GC-MS technology for optimising data quality in breath analysis.

Talk sponsored by SepSolve Analytical MARKES international

Renaud Louis
University of Liege

Biography

Prof Renaud Louis is a professor and academic head of the department of respiratory medicine at University of Liege and CHU of Liege, Belgium since 2004. He was president of the Belgian Thoracic Society from 2013 until 2014. He served as secretary of the group 5.3 allergy and Immunology of the assembly 5 “Airway diseases” at the ERS from 2002 until 2005. He currently sits in the steering committee of the SHARP (ERS research project on Severe Asthma) and is co-chair of the current ERS task force on “Diagnosis in asthma in adults”. He has focused his clinical research on asthma for 30 years, developing the technique of induced sputum as a research tool to investigate mechanisms of airway inflammation but also applying it in clinical practice as an aid to asthma management. He is currently running, together with Prof Schleich, a busy asthma clinic at CHU Liege with more than 150 hundreds of severe asthma patients receiving regular biologics. He has 307 peer reviewed publications in Scopus with an H Index of 39. He was associate editor of International Journal of clinical practice (section respiratory medicine) and current associate editor of the European Respiratory Review.

Biomarkers in asthma monitoring

Abstract

Asthma is chronic airway disease characterized by symptoms of dyspnea, cough and wheezing associated with excessive fluctuation in airway caliber. Asthma was once considered as a homogeneous disease with a treatment strategy one size fits all. It is now recognized that different phenotypes exist under the asthma umbrella, which may give insights on prognosis and treatment responsiveness. This concept of asthma phenotype is in particular crucial for predicting response to inhaled corticoids and costly biologicals which have recently emerged in the treatment of the most severe cases of the disease. So far the most popular and clinically useful classification of inflammatory phenotype has been relying on sputum cell counts. This technique is however difficult to apply on a large scale because it is technically demanding and not yielding immediate results. Exhaled breath may be alternative. Measuring exhaled fraction of nitric oxide has proved to be useful in some extent and has open the way towards more complex breath assessment. There has been growing interest on breathomic as a means to approach airway cellular content and, perhaps, as a tool to drive treatment choice.

João Rufo
University of Porto

Biography

João Cavaleiro Rufo is an Integrated Postdoc Researcher at the Institute of Public Health of the University of Porto and an expert in breathomics applied to clinical immunology.
João obtained his Master's degree in Biomedical Sciences at the University of Beira Interior, Portugal, in 2013. During the same year, he started working on the ARIA project in order to comprehend the exposure mechanisms behind allergic diseases and asthma development in children. The strict collaboration with the Laboratory of Indoor Air Quality, between 2013 and 2015, resulted in several published studies concerning environmental exposure in a public health perspective, as well as the coordination of the Indoor Air Quality Assessment and Public Health courses at the Institute of Public Health.
During his PhD, awarded by the University of Porto in 2018, João managed to identify specific patterns of volatile organic compounds in patients with persistent asthma, which lead to the creation of the first laboratory in Portugal dedicated exclusively to breathomics.
In 2019, João Rufo was elected as a board member of the Epidemiology Work Group of the European Academy of Allergy and Clinical Immunology, where he is working to implement breathomics as a novel screening method for asthma studies.

Breathomics in asthma diagnosis and monitoring

Abstract

Asthma is a non-communicable chronic disease that is highly prevalent in developed countries. The diagnosis and phenotyping of asthma are particularly complex due to the lack of currently available sensitive diagnostic tools. This often results in inappropriate or untargeted inhaled steroid therapy prescription, which may consequently result in poor disease treatment and more frequent exacerbations. However, several studies have shown that exhaled breath analysis may become the solution to improve point-of-care diagnosis of asthma.
In this talk, the most recent scientific advances concerning asthma diagnosis through exhaled breath analysis will be discussed, with special focus given to applications compatible with real clinical scenarios. Moreover, original research performed in an outpatient allergology clinic, using medical diagnosis of asthma as the reference test, will not only demonstrate that breathomics allow the distinction of paediatric individuals with a medical diagnosis of asthma, but also allow the identification of individuals in need of corticosteroid therapy.

José Torrecilla
Complutense University of Madrid

Biography

José Torrecilla is currently an Associate Professor and Researcher at the Chemical Engineering Department of the Complutense University of Madrid (UCM), Spain. He is the principal investigator of the AlgoReach Research group. Dr Torrecilla received his MBA, B.Sc., and Ph.D. (with honors) in Chemical Engineering from the UCM and carried out his postdoctoral studies at Queen's University of Belfast (UK) and the Spanish Ministry of Science and Technology. He has been working for more than 25 years in the development of chemometric tools and intelligent machine learning models to interpret complex systems and reach applications in different sectors such as health (non-invasive early diagnosis), food technology (quality control and adulteration detection), chemical engineering, and more. He has written technological books and patents. Additionally, Dr Torrecilla has published over one hundred articles in prestigious journals and has participated as a principal investigator in a high number of collaborations and projects at national and international levels.

Challenges in external clinical validation studies

Abstract

The combination and growth of the fields of chemical analysis and mathematical tools and models leads to relevant and innovative alternatives within the field of disease diagnosis. In medicine, the analysis of different kinds of samples generates large amounts of patient-specific data. For this reason, the use of mathematical tools capable of pinpointing and distinguishing the most relevant information contained in such databases is crucial within the scope of medical diagnosis. This integration becomes increasingly important when it comes to the diagnosis of diseases where the prognosis depends on the time and stage at which it was diagnosed, for instance, any type of cancer.
Tools based on artificial intelligence and machine learning are designed to be able to find differences and similarities between large amounts of samples by analysis of many variables and identification of their relationships and patterns. The integration of intelligent tools in the field of diagnosis offers the ability to distinguish profiles and facilitate the association of samples with pathological or healthy patterns, leading to informed and meticulous diagnoses.
Furthermore, in many occasions, the synergy between different intelligent tools in the same algorithm offers outstanding advantages in the development of applications, including the diagnosis of diseases by means of a technique as minimally invasive as the analysis of the patient's breath. For this reason, the research group AlgoReach aims to find the best intelligent algorithms, either through a single tool or through a combination, to reveal relevant and generally hidden characteristics that offer speedy and reliable depictions of diseases intended for their early, safe, and accurate diagnosis.

Expert panel discussion
The Next 5 Years in Breath Research

In this session we invite you to ask the panel about the future of Breath Research. Where is the future of the field? What advances do we expect in the next 5 years? How can we improve the quality of our research, and therefore further validate breath research?

Panelists:

Renaud Louis, University of Liege

José Torrecilla, Complutense University of Madrid

Marc van-der-Schee, Head of Clinical at Owlstone Medical

Marc van der Schee has close to 10 years of experience in the field of volatile biomarker research. During his PhD Marc pioneered the use of exhaled breath analysis in Lung Cancer, Asthma and Colorectal Cancer amongst others. For this work he received various awards including a Marie Curie Fellowship. His background spans both medical, epidemiological, chemical analytical and data-analysis aspects of biomedical research. By building on this expertise he designs and oversees all clinical trials within Owlstone Medical helping to collect data that drives product development and implementation into clinical practice. As a trained medical doctor Marc helps prioritise medical applications and is the primary interface between clinical partners and Owlstone. Marc holds a medical degree and a doctorate in Biomedical Sciences and obtained a PhD degree by studying the use of volatile biomarkers for disease diagnosis, monitoring and prognosis prediction.

Jonathan Beauchamp, Research Associate in the Department of Sensory Analytics
Fraunhofer Institute for Process Engineering and Packaging IVV Freising (Germany)

Jonathan Beauchamp holds a physics degree from University College London, UK and a PhD in environmental physics from the University of Innsbruck, Austria. He currently works as a research associate at the Fraunhofer Institute for Process Engineering and Packaging IVV in Freising, Germany, where he is Manager of the Emissions Analytics and Diagnostics group and Deputy Head of the Department of Sensory Analytics. Jonathan's research includes investigating the emissions of volatile organic compounds (VOCs) from the human volatilome, which he has been studying for the last 15 years. Jonathan has published over 50 papers and book chapters, which have over 1000 citations. He is currently editing a breath research related reference book entitled Breathborne Biomarkers and the Human Volatilome. Jonathan is Associate Editor of Journal of Breath Research, and a board member of the International Association of Breath Research (IABR).

Posters

Exhaled Gas Analysis by GC-MS, Sampled from Flexible Bronchoscopy, for Finding Lung Cancer Biomarker

Yunghee Lee, Seoul National University Bundang Hospital

Purpose The probability of lung cancer is increased and the survival is distinct between early and late stage of lung cancer. In this study, we analyze the exhaled gas, collected by bronchoscopy, to find lung cancer biomarker by using thermal desorption of gas chromatograph time of flight mass spectrometer (TD-GC-MS, Markers, Agilent 7890B). Methods Prospective cohort study has been progressed in Seoul National University Bundang Hospital from August, 2019 for 15 patients. Gas sample was collected in cancer affected bronchus (G1), cancer non-affected contralateral bronchus (G2), and room air (G3) in bronchoscopy room. The gas was sampled by the working channel port in bronchoscopy (Olympus, BF-1T260, BF-260, BF-P260F). Results Two patients were excluded and 13 patients' results were presented. The integration value of each VOCs were calculated by characteristic retention time and 6 high ranks of VOCs in G1 were Dibutyl phthalate (P = 0.546, 3 out of 13), Acetone (P = 0.009, 12 out of 13), Ethanol (P = 0.072, 13 out of 13), Hexane, 2,3,5-trimethyl (P = 0.368, 1 out of 13), 1,4-Pentadiene (P = 0.064, 5 out of 13) and Benzaldehyde 4-methyl (P = 0.417, 9 out of 13). Further gas samples of new patients will be obtained; the aim of enrollment number of patients is 20. Conclusions The qualitative analysis of VOCs in lung cancer was done by TD-GC-MS with sample collection by bronchoscopy to select more targeted gas. There were few VOCs were suggested as lung cancer biomarker.

Multi-centre cross-validation study in the search for volatile colorectal cancer biomarkers in breath and faeces

Y Lan Pham, Fraunhofer Institute for Process Engineering and Packaging (IVV)

Non-invasive diagnostic tools based on the detection of volatile biomarkers in exhaled breath have largely failed to reach the necessary maturity for practical use. Cross-validation of large cohorts between clinical and analytical centres is imperative for developing biomarker-related screening tests with high sensitivity, specificity and low false-positive rates. Our multi-centre study will explore the presence of disease-specific volatile organic compounds (VOCs) in exhaled breath and faeces headspace of colorectal cancer (CRC) sufferers in comparison to other bowel disorders and healthy controls. In the first phase of the project, standard operating procedures (SOPs) will be established to ensure optimum sampling and analysis of the two gas matrix types. Samples will be collected onto Tenax/Carbograph sorbent tubes using a ReCIVA device for exhaled breath and a micro-chamber/thermal extractor for stool headspace. VOCs will be analysed by thermal desorption-gas chromatography-mass spectrometry. The study design is unique in that sample replicates for each patient of each cohort will be analysed at each of the centres. The project aims at recruiting approximately 300 participants for each cohort to search for CRC-specific biomarker, followed by a validation in independent patient cohorts. Datasets will be pooled for data-mining and biomarker discovery using machine learning techniques. This poster outlines the cross-validation concept, the methods being employed, and intends to spark debate and seek additional advice on searching for CRC-specific volatile biomarkers.

Using Exhaled Breath Analysis as a Biomonitoring Tool - Determining Smoking Status Using Breath Biomarkers

Will Murch, Owlstone Medical

This study aimed to discover and validate breath-based biomarkers for the discrimination of smokers and non-smokers, and to test the feasibility of breath analysis as a tool for biomonitoring and exposure research. Exhaled breath samples from 73 subjects were captured and analysed using the Breath Biopsy Platform. Each breath sample was collected over a 10-minute period using the ReCIVA Breath Sampler. Volatile organic compounds (VOCs) from breath were pre-concentrated onto sorbent tubes. A CASPER Portable Air Supply minimized contamination from environmental sources. Samples were shipped to Owlstone Medical and analysed using TD-GC-TOF-MS. 475 molecular features (MFs) with distinct mass spectrums and retention times were identified across multiple breath samples. Analysis revealed 26 MFs that were significantly different between the groups. The statistically significant features were analysed by quantifying how well the two classes separated from each other in the dimension of the feature across all samples – yielding ROC-AUCs ranging between 0.72 and 0.96. Combinations of MFs, analysed using linear discriminant analysis and random forest, discriminated between groups with an accuracy of 96% and 97% respectively, using 10-fold cross-validation. Tentative identification of MFs using the NIST library indicated that many are combustion related compounds including benzene, toluene and ethylbenzene. Verification of the validity of our observations was performed using breath samples collected from 136 individuals. A subset of the tentatively identified MFs were quantified at the parts per billion level using pure synthetic standards as VOCs surrogates. This quantitative analysis confirms BTEX compounds (benzene, toluene, ethylbenzene, xylenes) measured using Breath Biopsy can discriminate smokers from non-smokers. This study supports breath analysis as a novel technique for exposure related biomarker discovery and biomonitoring research

Detecting CH4 in breath and its related diseases

Tahereh Shah, Ulster University

Methods

Firstly, before proceeding with breath analysis, we have investigated supervised learning using Partial Least Squares Discriminant Analysis (PLS-DA) on a gas mixture dataset of He/CH4 spectra where the CH4 concentration varies from 0 – 100 ppm. He/CH4 is a complex gas mixture but is still simpler than external clinical or environmental samples. The data was collected in a matrix of 3648 variables (wavelengths), which form 9 CH4 concentration categories (0, 1, 2, 4, 6, 12, 23, 77, 100 ppm). Later, we have tried all achieved result into another experiment. In this method, exhaled breath was collected from five participants. Spectra were collected using an Ocean Optics HR4000CG-UV-NIR spectrometer in the wavelength range 194 – 1122 nm (interval 0.25 nm), with a slit width of 5 m and a minimum optical resolution >0.5 nm.

Results

From a computation perspective, the major difficulty of CH4/He spectra data is the high feature dimensionality, along with temporal instability or drift, collinearity and a high matrix component. These challenges decreased after pre-processing of spectra to include autoscaling, smoothing and baseline correction, followed by data segmentation, VIPs selection and peak concatenation. As a result, spectral features corresponding to helium, carbon, hydrogen and impurities (N, O, OH/H2O) were observed and the algorithm accuracy on this data improved to 98% with < 15 LV.

Volatile profiles of MSTO-211H malignant mesothelioma cells

Liam Little, Sheffield Hallam University

Background - Malignant mesothelioma (MM) is an incurable cancer with a poor survival rate and limited treatment options. Volatile organic compounds (VOCs) in breath have been shown to differentiate MM patients from other groups, with the ultimate intention of providing a non-invasive method of early diagnosis. Headspace analysis was performed on MSTO-211H cell cultures in order to identify the most clinically relevant VOCs released from MM cells.
Methods - Solid-phase microextraction (SPME; Supelco, DVB/CAR/PDMS) was performed on MSTO-211H cultures and controls at 24, 48 and 72 hour incubation points. The SPME fibre was transferred to a GC-MS for thermal desorption and VOC analysis. Cell viability was assessed after each time point. Principal component analysis was performed using XCMS online.
Results - Cell number increased with incubation but cell viability was maintained. Over 100 VOCs were identified from controls, with some specific changes observed in cell cultures. 2,6-Dimethyl-Octane and 2-butoxyethyl acetate were reduced in cells and 2-butoxy-Ethanol and 2-ethyl-Hexanol were increased compared to controls. PCA score plots showed separation of results after 48 and 72 hours incubation and clustering of experimental repeats.
Conclusion - 2-butoxy Ethanol was increased in cell cultures whereas 2-butoxyethyl acetate was decreased - likely to be the result of cellular metabolism through a hydrolysis reaction. The PCA plot showed separation of MSTO-211H and RPMI results, highlighting the potential of VOC analysis to be used in a diagnostic setting. Further method development is required to reduce culture-ware background signals and identify unique VOCs released from MM cells.

Development of a Compact, IoT-enabled Electronic Nose for Breath Analysis

James Covington, University of Warwick

In this work, we report on the design and development of a compact, internet-of-things (IoT) enabled electronic nose (E-nose) for use with breath analysis. It has long been suggested that applications of diagnostic breath analysis must extend beyond laboratories and pilot studies to standard clinical practice and home-use. The latter requires a compact and portable personal diagnostic device, which can sample and analyse the exhaled breath of an individual at any time or place. While no single analysis technique can provide complete diagnosis of a patient, E-nose technology has the advantages of being relatively low-cost, low-power, user-friendly and portable. The developed unit includes an integrated sampling tube for end-tidal breath, which can be heated to body-temperature (37C), and an array of 10 MEMS metal oxide (MOX) gas sensors. The selected analogue and digital sensors are produced by 7 different manufacturers and include many of the most relevant MOX sensors currently available on the market. The unit is compact (dimensions of 7x23x16 cm) and uses a microcontroller with Wi-Fi communication capabilities, for integration with future IoT infrastructure. The device has been tested with chemical standards and exhaled breath samples from volunteers. It is our intention to deploy this system in a UK hospital in upcoming breath research studies to evaluate its potential as a non-invasive diagnostic tool.

Detection and quantification of lung cancer biomarkers using a micro-analytical device

Igor Bezverkhyy, CNRS - University of Burgundy

We present a prototype system for monitoring a set of potential lung cancer biomarkers: propanol-1, toluene, o-xylene and cyclohexane. This micro-analytical system consists of silicon gas preconcentrator containing a nanoporous zeolite sorbent, silicon gas chromatographic (GC) micro-column and a miniaturized single SnO_2 -based gas sensor as detector. We show that the system can be used for quantification of traces of the mentioned biomarkers in the presence of H_2O (90% RH) and CO_2.

Human chemosignals elicited from emotional states

Fabio Di Francesco, University of Pisa

In the animal kingdom most species secrete or excrete chemical factors that trigger a social response in members of the same species. Smell provides peculiar evolutionary advantages over vision and hearing, as it works even when other senses are impaired (e.g. in the dark or during sleep) and it allows obtaining information over long distances about the possible presence of a predator or a potential sexual partner. If olfactory communication is so important for animals, what about human race? As a social species, humans rely on social interaction for their well-being and survival: are we unconsciously using olfactory clues to select our social relationships, choose a partner or communicate emotions like pain, fear or happiness? Literature does not provide any definitive answer to such questions, but more and more hints are cumulating which seem to suggest the exchange of chemical messages among humans. The POTION project (Promoting social interaction through emotional body odours, FETPROACT-01-2018, Contract n° 824153) will investigate the nature of chemosignals and their sphere of influence on social interaction. The identification of human pheromones is impressively challenging. Probably such volatile or semivolatile chemicals are released at very low concentration levels (pre-concentration step needed before analysis). Furthermore, these distinctive odours likely consist of a cocktail of multiple chemicals and the concentration pattern might be important. Finally, these odour components might belong to different chemical classes and have different properties, so that they may not be all detected with just a single method.

Evaluation of non-invasive approaches for the analysis of exogenous and endogenous VOCs

Beate Gruber, Research Institute for Chromatography

Non-invasive techniques for monitoring volatile metabolites in body fluids and exhaled breath have become increasingly established in areas such as human biomonitoring, clinical diagnostics, and forensics. Since only trace amounts of VOCs are emitted by the human body, pre-concentration is required prior to analysis. Although sampling of e.g. exhaled air offers promising advantages such as large sample quantities, this step often represents the biggest bottleneck in the analysis workflow. Therefore, different sampling approaches have been evaluated for the analysis of human-emitted VOCs in exhaled breath as well as skin emissions and subsequent thermal desorption coupled with gas chromatography – mass spectrometry. Taking into account the effects of sampling parameters such as sorbent type, sampling volume and moisture effects, various approaches have been tested in a targeted approach using reference substances and non-invasive sampling of VOCs derived from the human body in a nutritional study. Comparing the nutritional target profiles delivered by body fluids and exhaled breath, a holistic view of volatile metabolites was achieved.

Breath-holding times distinguish gases diffusing from lungs, arteries, veins and the average of all tissues

Albert Donnay, University of Maryland and Donnay Detoxicology LLC

A novel breath collection method (US patent 10,386,357) is presented that distinguishes levels of free gases diffusing from the lungs, arteries, veins and the average of all tissues. It quadruples the amount of meaningful data that can be obtained from traditional breath collection methods, revealing where gases arise and how most are not in equilibrium among lungs, blood and tissues. By repeating these measures over time, more information can be obtained about gas absorption, distribution, metabolism and excretion. In contrast, most breath collection methods used with multi-gas and single-gas analyzers specify analyzing all or one or more fractions of breath but from just one compartment. They typically involve collecting either full breaths over time with no breath-holding, such as Owlstone recommends, or collecting a single exhalation after a fixed breath-holding time. Breath alcohol testers, for example, specify a breath-hold time of zero to get an alveolar measure, while carbon monoxide testers specify 20 seconds to most closely correlate with venous carboxyhemoglobin. Comparing CO exhaled by smokers and non-smokers, we identified the optimal breath-holding time for arterial gas levels at 5 seconds and the average of all tissues at 35s. Results from these 4 compartments show that levels of alcohol diffusing from the lungs and arteries are several fold higher than from veins and tissues 30 minutes after consumption but in equilibrium after 60. Levels of CO in contrast, never reach equilibrium, even in non-smokers, with arterial normally greater than venous except after exposures when the level diffusing from tissues is highest.

Pectin supplementation did not alter profiles of exhaled breath in young adults and elderly

Agnieszka Smolinska, Maastricht University

Since ancient times, physicians valued human breath as a window of diseased and healthy organs. Thousands of volatile organic compounds (VOCs) are produced in different organs which are transported by blood to the lungs where they are released. Inflammatory and deviant metabolic processes change the composition of these compounds which can be of use for clinical diagnosis and disease monitoring. Many VOCs are also produced by intestinal microbiota. Some of these compounds are excreted into feces while others enter the systemic circulation where they can be further modified by the host. Exhaled breath analysis has been demonstrated for disease monitoring and diagnosis but also for investigating effect of various diet. In the current study, exhaled breath was used to monitor effect of prebiotics. In the study, 52 young adults and 48 elderly consumed 15g/day sugar beet pectin or maltodextrin for four weeks. Before and after the intervention period exhaled breath samples were collected. The group of individuals receiving maltodextrin was considered as placebo. Exhaled breath samples were analysed by Gas Chromatography coupled with Mass Spectrometry analysis. Different machine learning technique were used to find differences in volatile compounds. The statistical analysis revealed that pectin intervention did not significantly alter the content of exhaled breath in young adults and elderly. In both groups, the tree-based technique has led to classification model with prediction performance of random classifier. Moreover, the statistical analysis using a set of 15 volatile compounds, to determine differences in exhaled breath between young adults and elderly, showed an AUROC of 0.70 with sensitivity and specificity of 0.6 and 0.58 in the validation set, indicating relatively small differences in exhaled breath profiles. The current study showed that following four weeks of pectin implementation did not affect the content of exhaled breath.

ZnO nanowires-based Sensors for Methane detection in Breath

Niyanta Datta, Aoife Morrin School of Chemical Sciences - Dublin City University

Volatile organic compounds (VOCs) are emitted from the body in a range of ways e.g. via breath, skin. Many emitted compounds are end-stage metabolites and can potentially be used as biomarkers of different disease states or metabolic changes in the body, e.g. change in diet, or use of prescription drugs. Current research generally uses high end techniques such as mass spectrometry for the analysis of complete gas profiles. Given the literature findings, there is significant opportunity for the use of sensors to continuously monitor specific gases known to correlate directly with disease or nutrition state. For example, acetone is emitted from skin in states of acid ketosis, and may represent a new way to track glucose levels without having to sample/ test blood. Metal oxides are a well-known class of materials that can be tailored in novel ways via morphology and by the incorporation of additives in order to detect gases in the low concentration range. In the current study, we aim to realize the concept of metal oxide based chemiresistive sensors for analyte detection from breath. ZnO is chosen owing to its versatility as a functional material that has a diverse group of growth morphologies, inexpensive synthesis process, high electron mobility, high thermal conductivity, wide and direct band gap making it suitable for a wide range of devices. Hydrothermally grown ZnO nanowires were modified with Co to attain specific sensors for CH4 detection (methane levels are related to gut metabolism) in the breath relevant range (< 20 ppm). The inclusion of optimised concentration of Co (10mM) resulted in improved gas sensing properties with reduced operating temperatures and higher sensitivities as compared to pure ZnO nanowires. The interference with H2 gas was studied due to its predominance in the human breath. Also, some of the sensors were employed for direct breath measurement and were characterized as a function of operating temperature. The findings from this research will be further developed with the goal of attaining a wearable metal-oxide sensor for monitoring of breath analytes.

AI can detect more – a deep learning-based system for fast and automated analysis of raw GC-MS breath data

Angelika Skarysz, Loughborough University

Human breath carries thousands of volatile organic compounds (VOCs), measurable with gas chromatography-mass spectrometry (GC-MS), which comprehensively describe the individual's health conditions. Breath analysis has the potential to deliver a fast, accurate and non-invasive diagnostic platform. However, detection of the VOCs in GC-MS data requires time-consuming expert-driven processing, which is prone to errors and delivers operator-subjective results. We propose a system, employing deep learning -- precisely convolutional neural networks (CNNs), to learn and automatically detect VOCs' patterns directly from raw GC-MS data, bypassing expert-led processing. We evaluate this CNN-based approach on clinical samples and with four types of networks: VGG16, VGG-like, Densely-connected and Residual CNNs. All system configurations not only demonstrated high sensitivity and specificity but also detected approximately 25% more VOC occurrences than expert-led analysis. Our results indicate that the automated CNN-based method can improve accuracy and reduce the time of samples analysis, vitally contributing to the large-scale development of breath-based diagnosis. The system may support experts to put much more accurate hypothesis on the VOCs related to the specific health conditions. Moreover, by the significant acceleration of the VOC detection process, the CNN-based method allows for much quicker hypotheses validation on new GC-MS samples.