VOLATOLOMICS

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INTRODUCTION

This IFCC Emerging Technology Division (ETD) is dedicated to providing current awareness for emerging technologies likely to have important clinical diagnostic applications in the near future. One of those technologies is volatolomics (breathomics) (*i.e.,* breath analysis).

This web page will provide a regularly updated perspective on the emerging clinical diagnostic applications of volatolomics over the next 3 years.

Breath analysis is not new and already has a few, but very specific applications (*e.g.,* breath alcohol testing, hydrogen, carbon monoxide, oxygen, carbon dioxide, nitric oxide, and nitrous oxide testing, ^{13}carbon/^{12}carbon-based tests)(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2990505/).

The types of breath analysis can be subdivided into:

a. Analysis of exogenous compounds, *e.g.,* ethanol, nitrous oxide (anesthesia), ^{13}carbon compounds.
b. Analysis of specific endogenous compounds, *e.g.,* oxygen, carbon dioxide, nitric oxide.
c. Analysis of mixtures of unidentified endogenous compounds (*e.g.,* Volatile Organic Compounds or VOCs) to provide a diagnostic signature.
d. Analysis of exhaled particles.

Current work on volatolomics centers on finding diagnostic utility in the pattern of compounds (VOCs) in breath. Breath analysis is an attractive proposition because this type of testing is non-invasive, applicable to the point-of-care and offers the possibility of real-time clinical management.

Already, there are more than 10 companies focused on the clinical diagnostic applications of volatolomics employing diverse analytical technologies (breath analysis analyzers are sometimes known as “electronic noses”). The broad range of diagnostic applications under investigation and development ranges from breath glucose testing to testing for different types of cancer.

Breath analysis technologies are diverse and include different types of mass spectrometry [e.g., gas isotope ratio mass spectrometry (GIRMS), selected ion flow tube mass spectrometry (SIFT-MS), field asymmetric ion-mobility spectrometry (FAIMS), secondary electro-spray ionization-MS], sensors and sensor arrays (*e.g.,* copper bromide-based sensor, colorimetric high dimensional sensor array), gas chromatography (*e.g.,* GC SAW). Further notable aspects of breath analysis technologies are the use of artificial intelligence, cloud-based analysis of data and analyzers that link to a smartphone.

The scope and content of this web page will include:

1. News items and opinion pieces from key researchers/opinion leaders about recent developments in the clinical diagnostic applications of volatolomics.
2. A directory of companies active in the clinical diagnostic applications of volatolomics.
3. Links to clinical trials involving volatolomic testing.
4. Details of analyzers and regulatory approvals of clinical diagnostic products based on volatolomic testing.
5. A literature survey updated quarterly designed to provide an educational resource and a snapshot of work since 2010.

Breath alcohol testing, and associated hand-held alcohol meters (breathalyzers), is now a mature sector of breath analysis, as is breath testing for oxygen, CO_2, and nitrous oxide, and these will not be considered here in any detail.

The web page has been developed in conjunction with key researchers and companies active in clinical applications of breath analysis. A particular feature of this webpage will be regular updates based on feedback from our readers.

Please send updates and comments to Larry Kricka:
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1. VOLATOLOMICS AND BREATH ANALYSIS IN THE NEWS

General

http://www.menssanaresearch.com/news_Menssana.html
https://www.owlstonemedical.com/about/news/
http://www.breathdiagnosticsinc.com/newsarticles/
https://www.bedfont.com/news
http://cairndiagnostics.com/news/
https://www.fossiliontech.com/in-the-media/
https://www.newenglandbreath.com/videos
www.pulmostics.com

Clinical

Breath Biopsy in the area of IPF:
https://www.owlstonemedical.com/about/news/2018/jan/25/breath-biopsy-wins-global-ipf-catalyst-challenge/

Phase II Respiratory Disease Clinical Trials for a novel drug for COPD:
https://www.owlstonemedical.com/about/news/2017/nov/27/GSK-breath-biopsy-clinical-trial/

Breath Biopsy to study disease drivers in Asthma and COPD:
https://www.owlstonemedical.com/about/news/2018/apr/9/owlstone-medical-provides-services-to-astrazeneca/

Mayo Clinic Laboratories Announce Collaboration to Develop New Diagnostic Test That Detects Lung Cancer Using Patients' Exhaled Breath:

https://news.mayocliniclabs.com/2019/03/26/breath-diagnostics-mayo-clinic-laboratories-announce-collaboration-to-develop-new-diagnostic-test-that-detects-lung-cancer-using-patients-exhaled-breath/?linkId=65319564

Blogs

https://www.owlstonemedical.com/about/blog/

Webinars

https://www.owlstonemedical.com/download/direct-breath-biopsy-webinar/?utm_source=various-zone-none&utm_medium=breath_biopsy_email&utm_campaign=00507-products-services-snippet-various-breath_biopsy_email-zone-none-20180221&mkt_tok=eyJpIjoiT0Rkak5qUm1NRFZrWlRkbSIsInQiOiIxbVU3ZGZWV1RHVmNGbHJ0RjdFUkxZbTRxTkFac0VDTzZWZ1pXdG9HUzRUVVY3a1JxbVozdzdnZlI4R1RZNThqc1RrUG41TE1KZWdubXVhOWxzNDhMRnVLalQ1S25TdU1BVXlEWDkwcmViOEkxS0ZxVFwvODdGR0hRWHJ6MU10QzgifQ%3D%3D

2. A-Z DIRECTORY OF COMPANIES ACTIVE IN THE CLINICAL DIAGNOSTIC APPLICATIONS OF VOLATOLOMICS (BREATH ANALYSIS)

Advanced Breath Diagnostics, Inc. – see Cairn Diagnostics (http://cairndiagnostics.com/)
Applied Nanodetectors Limited (www.applied-nanodetectors.com)
Bedfont Scientific (www.bedfont.com)
BreathDX (https://www.breathdx.com/about/)
Breath Diagnostics Inc (www.breathdiagnosticsinc.com)
Breathtec Biomedical Inc (breathtecbiomedical.com)
Cairn Diagnostics (http://cairndiagnostics.com/)
Circassia AB (http://www.niox.com)
Fossil Ion Technology S.L. (*www.fossiliontech.com/)*
G.A.S. Gesellschaft für analytische Sensorsysteme mbH BioMedizin Zentrum Dortmund (http://www.gas-dortmund.de)
Menssana Research Inc (www.menssanaresearch.com)
New England Breath Technologies Inc (https://www.newenglandbreath.com/)
Owlstone Medical Inc (https://www.owlstonemedical.com)
Pulmostics Inc (www.pulmostics.com)
Syft Technologies (https://www.syft.com/)

See also: https://www.nanalyze.com/2018/03/9-breath-diagnostics-companies/

3. CLINICAL TRIALS

An analysis of clinical trial data from https://clinicaltrials.gov/ between 1997 and 2017 (517 trials that have used or are using some kind of breath analysis) is available from Owlstone Medical at:

https://www.owlstonemedical.com/about/blog/2017/sep/14/breath-analysis-clinical-trials/?mkt_tok=eyJpIjoiWmpCbU5XWmpaREZrTTJNMCIsInQiOiJlNnk4K0xqbTV4Z1M2eUI1b0RDaXZsUHZKaVwvdDRZZGxXaEtVVHYrMW1Ralc1OGx3dXJNMllUMU5IQ0YwMTNDYXVRNGh6ZkU4MHZNV3N2c2xNQVU4YThENzdwSzV1akNlUktMZHNMVlwvbkhFU29mY2pcL05QM0xHSUZwTGlSd2lHMCJ9
(accessed SAT March 2)

4. ANALYZERS AND REGULATORY APPROVALS

Listed below is the current range of clinical breath analysis products with information on regulatory approvals (FDA, CE) where relevant.

Applied Nanodetectors Limited
Headquarters: Enfield Middlesex, UK
Website: http://www.applied-nanodetectors.com/wordpress/breath-analysis/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
-	Sensor array platform that can be configured and can detect multiple species.

Bedfont Scientific
Headquarters: Harrietsham, Maidstone ME17 1JA, UK
Website: https://www.bedfont.com/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
EC50 ToxCO+	Electrochemical sensor-based breath CO monitor. *FDA approved*
GastroCH_4ECK®	Portable breath methane, hydrogen and oxygen monitor to aid in the detection of gastrointestinal disorders.
Gastrolyzer®	Hydrogen and methane breath monitors to help detect gastrointestinal disorders.
iCO Smokerlyzer®	Breath CO monitor for a smartphone/tablet to track your “quit smoking” progress anytime, anywhere.
Micro+™	Breath (CO) monitors to aid smoking cessation.
NOBreath®	Fractional exhaled Nitric Oxide (FeNO) breath monitor to help improve asthma management.
piCO™	Breath carbon monoxide (CO) monitor to help stop smoking.

piCObaby™	Breath CO monitoring for pregnant women to help them stop smoking.
Smokerlyzer®	Breath CO monitor for smoking cessation.
ToxCO®	Non-invasively screening for CO poisoning through breath and ambient air testing.

BreathDX
Headquarters: UK
Website: https://www.breathdx.com/ (Accessed March 1 2019)

Product (Analyzer)	**Description of Use**
AmBeR®	Non-invasive breath ammonia monitoring system for home and hospital use.
AmBeR® Clinical	Utilized for clinical studies where large volumes of patients and sampling regimens are required.

Breath Diagnostics Inc.
Headquarters: Louisville, KY, USA
Website: http://www.breathdiagnosticsinc.com/ (Accessed March 1 2019)

Product (Analyzer)	**Description of Use**
OneBreath	A breath sample (one normal breath into a 1 L non-reactive bag) is promptly evacuated across a silicon microreactor chip that selectively and irreversibly captures exhaled carbonyl compounds produced as a result of cancer metabolism. The small microreactor volume effectively concentrates the carbonyl compounds by 10,000-fold (other components in the breath pass through the microreactor). Captured carbonyls then are eluted and analyzed using mass spectrometry (MS).

Algernon Pharmaceuticals formerly known as "Breathtec Biomedical, Inc"
Headquarters: Vancouver, BC, Canada
Website: https://algernonpharmaceuticals.com/breathtec-biomedical-is-now-algernon-pharmaceuticals/ (Accessed March 1 2019)

Product (Analyzer)	**Description of Use**
FAIMS Breathalyzer Device	In development - non-invasive, portable hand-held device to be used by clinician's in the office, clinic or hospital setting, or by agents screening for infectious diseases at national border entry points that provides early detection of, *e.g.,* lung cancer, respiratory diseases, infectious diseases, diabetes, liver disease.

Cairn Diagnostics
Headquarters: Brentwood, TN, USA

Website: https://cairndiagnostics.com/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
^{13}C-Spirulina Gastric Emptying Breath Test (GEBT)	Breath samples, collected periodically in capped glass tubes before and after test meal administration, are returned to a central laboratory for analysis by gas isotope ratio mass spectrometry (GIRMS) to determine the ratio of $^{13}CO_2$ to $^{12}CO_2$ in each sample. *FDA approved*

Circassia
Headquarters: (The Oxford Science Park, Oxford, UK; Morrisville, NC, USA; Uppsala, Sweden)
Website: https://www.circassia.com/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
NIOX MINO®	Point-of-care medical device for measuring fractional exhaled nitric oxide (FeNO), thus offering personalized asthma management. *FDA approved and CE-marked*

Fossil Ion Technology S.L.
Headquarters: Malaga, Spain
Website: https://www.fossiliontech.com/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
SUPER SESI	Online MS analysis of low volatility metabolites in breath using secondary electro-spray ionization. Measure up to 2000 species in one exhalation.

Fujitsu Laboratories Ltd.
Headquarters: Kawasaki, Japan
Website: http://www.fujitsu.com/jp/group/labs/en/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
(prototype)	Mobile copper bromide-based sensor that measures ammonia in breath.

G.A.S. Gesellschaft für analytische Sensorsysteme mbH BioMedizin Zentrum
Headquarters: Dortmund, Germany
Website: https://www.bmz-do.de/de/unternehmensverzeichnis/unternehmensverzeichnis-/gas-gesellschaft-fuer-analytische-sensorsysteme-mbh.htm (Accessed March 1 2019)

Product (Analyzer)	Description of Use
BreathSpec™	Sampling via directly exhaling into the device and samples are introduced directly in a controlled manner into the gas chromatograph linked to an ion-mobility-spectrometer. Also, breath samples in standard disposable syringes can be analyzed using the GC-IMS equipped with a Luer-adaptor

Menssana Research Inc.
Headquarters: Newark, NJ, USA
Website: http://www.menssanaresearch.com/# (Accessed March 1 2019)

Product (Analyzer)	Description of Use
BreathLink™	Mobile point-of-care internet-connected system for the collection, concentration and analysis of VOCs in human breath. A person breathes into the instrument for two minutes and their breath VOCs are rapidly analyzed with a gas chromatograph (picomolar sensitivity; GC SAW). The encrypted information is uploaded through a cloud application to a central laboratory where the chromatogram is analyzed with proprietary algorithms and a report is sent back to the point-of-care within minutes. *CE-marked*
BreathX	Fully integrated user-friendly automated analyzer (GC SAW) for collection, analysis, and interpretation of biomarkers in breath. Secure server applies algorithms and sends reports.
Heartsbreath™	A non-invasive breath test for breath biomarkers that predict the probability of grade 3 rejection in heart transplant recipients who received their transplants in the preceding year. *FDA Humanitarian Device exemption*

Metabolomx
Headquarters: Mountain View, CA, USA
Website: http://metabolomx.com/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
Breathsensor	An array of colored chemical indicators of diverse reactivities embedded in a nanoporous sol-gel matrix changes color in response to components in breath, creating a high dimensional and specific fingerprint.

New England Breath Technologies, Inc.
Headquarters: Springfield, MA, USA

Website: https://www.breathhealth.net/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
GLUCAIR™ Diabetic Monitor	Detects breath acetone concentration and this has a very high correlation to blood glucose levels.
Illume™ Diabetes Screener	Assist in the identification of diabetes through a simple, non-fasting breath test. This non-invasive test is designed to provide an instant result that will help identify when a confirmatory blood test is warranted.

Owlstone Medical, Inc.
Headquarters: Science Park, Cambridge, UK
Website: https://www.owlstonemedical.com/?utm_source=owlstone-keywords-zone-1&utm_medium=ga-search&utm_campaign=00435-corporate-brand-search-owlstone-keywords-ga-search-zone-1-20171214&gclid=CjwKCAiA8OjjBRB4EiwAMZe6y6cRJxt1g2fvxaffUjbOzMxCnO1pamMtnUwNg4WLtnoKKiCrN48ckhoCP5cQAvD_BwE (Accessed March 1 2019)

Product (Analyzer)	Description of Use
Lonestar VOC Analyzer	A non-invasive, easy to use analyzer for the detection of disease biomarkers in clinical samples using Field Asymmetric Ion Mobility Spectrometry (FAIMS) technology.
ReCIVA® Breath Sampler	Device for reliable and reproducible capture of VOCs in breath samples. *CE-marked*

Pulmostics, Inc.
Headquarters: Newbury Park, CA, USA
Website: **https://www.pulmostics.com/** (Accessed March 1 2019)

Product (Analyzer)	Description of Use
-	Integrated breath analysis systems.

Syft Technologies
Headquarters: Middleton, Christchurch, New Zealand
Website: https://www.syft.com/ (Accessed March 1 2019)

Product (Analyzer)	Description of Use
Voice200ultra	Ion flow tube mass spectrometry platform for monitoring VOCs.

5. LITERATURE BY TOPIC – DIAGNOSTIC APPLICATIONS (2010 onwards)

The following literature provides an overview of the extent and diversity of research and development in the area of volatolomics (breath analysis). A key journal in this area is the Journal of Breath Research (opscience.iop.org/journal/1752-7163) that published its first issue in 2007. In addition, several companies maintain publication archives on their web sites – see:

http://www.menssanaresearch.com/publications_Menssana.html;
http://www.breathdiagnosticsinc.com/technology/published-articles/
http://cairndiagnostics.com/resources/
http://www.niox.com/en-US/feno-asthma/publications/
https://www.fossiliontech.com/publications/
https://www.fossiliontech.com/patents/
https://www.newenglandbreath.com/articles
www.pulmostics.com
https://www.syft.com/?s=&fwp_categories=media,publications,article

5.1. ANALYZERS, SENSORS AND METHODS

2019

Lin T, Lv X, Hu Z, Xu A, Feng. Semiconductor metal oxides as chemoresistive sensors for detecting volatile organic compounds. *Sensors (Basel).* 2019;19(2):233. Available from: doi: 10.3390/s19020233.

2018

Motooka M, Uno S. Improvement in limit of detection of enzymatic biogas sensor utilizing chromatography paper for breath analysis. *Sensors (Basel).* 2018;18(2):440. Available from: doi:10.3390/s18020440.

2016

Maniscalco M, Vitale C, Vatrella A, Molino A, Bianco A, Mazzarella G. Fractional exhaled nitric oxide-measuring devices: technology update. *Med Devices (Auckl).* 2016;9:151–60. Available from: doi: 10.2147/MDER.S91201.

2014

Broza YY, Zuri L. Haick H. Combined volatolomics for monitoring of human body chemistry. *Sci Rep.* 2014;4: 4611. Available from: doi: 10.1038/srep04611.

Inyawilert K, Wisitsora-at A, Tuantranont A, Singjai P, Phanichphant S, Liewhiran C. Ultra-rapid VOCs sensors based on sparked-In_2O_3 sensing films. *Sens Actuators B Chem.* 2014;192:745–54. Available from: doi.org/10.1016/j.snb.2013.11.064.

Wolf A, Baumbach JI, Kleber A, Maurer F, Maddula S, Favrod P, et al. Multi-capillary column-ion mobility spectrometer (MCC-IMS) breath analysis in ventilated rats: a model with the feasibility of long-term measurements. *J Breath Res.* 2014;8(1):016006. Available from: doi: 10.1088/1752-7155/8/1/016006.

2013

Zrodnikov Y, Zamuruyev K, Pedersen JD, et al. Design criteria for portable point-of-care breath analysis systems. In: 2013 Transducers and Eurosensors XXVII: The 17th

International Conference on Solid-State Sensors, Actuators and Microsystems, TRANSDUCERS and EUROSENSORS 2013:*1629-32)*.

2012

Kapande KM, McConaghy LA, Douglas I, McKenna S, Hughes JL, McCance DR, et al. Comparative repeatability of two handheld fractional exhaled nitric oxide monitors. *Pediatr Pulmonol.* 2012;47(6):546–50. Available from: doi: 10.1002/ppul.21591.

King J, Unterkofler K, Teschl G, Teschl S, Mochalski P, Koç H, et al. A modeling-based evaluation of isothermal rebreathing for breath gas analyses of highly soluble volatile organic compounds. *J Breath Res.* 2012;6(1):016005. Available from: doi: 10.1088/1752-7155/6/1/016005.

Takeno S, Noda N, Hirakawa K. Measurements of nasal fractional exhaled nitric oxide with a hand-held device in patients with allergic rhinitis: relation to cedar pollen dispersion and laser surgery. *Allergol Int.* 2012;61(1):93–100. Available from: doi: 10.2332/allergolint.11-OA-0318.

2011

Hunter GW, Xu JC, Biaggi-Labiosa AM, Laskowski D, Dutta PK, Mondal SP, et al. Smart sensor systems for human health breath monitoring applications. *J Breath Res.* 2011;5(3):037111. Available from: doi: 10.1088/1752-7155/5/3/037111.

Hüttmann EM, Greulich T, Hattesohl A, Schmid S, Noeske S, Herr C, et al. Comparison of two devices and two breathing patterns for exhaled breath condensate sampling. *PLoS One.* 2011;6(11):e27467. Available from: doi: 10.1371/journal.pone.0027467.

2010

Antus B, Horvath I, Barta I. Assessment of exhaled nitric oxide by a new hand-held device. *Respir Med.* 2010;104(9):1377–80. Available from: doi: 10.1016/j.rmed.2010.06.005.

Artificial intelligence

2015

Ligor T, Pater Ł, Buszewski B. Application of an artificial neural network model for selection of potential lung cancer biomarkers. *J Breath Res*. 2015;9(2):027106. Available from: doi: 10.1088/1752-7155/9/2/027106.

Electronic nose

2016

Rocco R, Incalzi RA, Pennazza G, Santonico M, Pedone C, Bartoli IR, et al. BIONOTE e-nose technology may reduce false positives in lung cancer screening programmes. *Eur J Cardiothorac Surg*. 2016;49(4):1112–7. Available from: doi: 10.1093/ejcts/ezv328.

2015

Bikov A, Lázár Z, Horvath I. Established methodological issues in electronic nose research: how far are we from using these instruments in clinical settings of breath analysis? *J Breath Res.* 2015;9(3):034001. Available from: doi: 10.1088/1752-7155/9/3/034001.

de Vries R, Brinkman P, van der Schee MP, Fens N, Dijkers E, Bootsma SK, et al. Integration of electronic nose technology with spirometry: validation of a new approach for exhaled breath analysis. *J Breath Res.* 2015;9(4):046001. Available from: doi: 10.1088/1752-7155/9/4/046001.

Leopold JH, Bos LD, Sterk PJ, Schultz MJ, Fens N, Horvath I, et al. Comparison of classification methods in breath analysis by electronic nose. *J Breath Res*. 2015;9(4):046002. Available from: doi: 10.1088/1752-7155/9/4/046002.

McWilliams A, Beigi P, Srinidhi A, Lam S, MacAulay CE. Sex and smoking status effects on the early detection of early lung cancer in high-risk smokers using an electronic nose. *IEEE Trans Biomed Eng.* 2015;62(8):2044–54. Available from: doi: 10.1109/TBME.2015.2409092.

Seesaard T, Lorwongtragool P, Kerdcharoen T. Development of fabric-based chemical gas sensors for use as wearable electronic noses. *Sensors (Basel).* 2015;15(1):1885–1902. Available from: doi: 10.3390/s150101885.

Wilson AD. Advances in electronic-nose technologies for the detection of volatile biomarker metabolites in the human breath. *Metabolites.* 2015;5(1):140-63. Available from: doi: 10.3390/metabo5010140.

2014

Gromski PS, Correa E, Vaughan AA, Wedge DC, Turner ML, Goodacre R. A comparison of different chemometrics approaches for the robust classification of electronic nose data. *Anal Bioanal Chem*. 2014;406(29):7581–90. Available from: doi: 10.1007/s00216-014-8216-7.

2013

Fens N, van der Schee MP, Brinkman P, Sterk PJ. Exhaled breath analysis by electronic nose in airways disease. Established issues and key questions. *Clin Exp Allergy.* 2013;43(7):705–15. Available from: doi: 10.1111/cea.12052.

2012

Brinkman P, van der Schee M, Fens N, Pennazza G, Santonico M, D'Amico A, et al. Calibration of a (semi)-automatic measurement and control platform for centralized, simultaneous electronic nose (eNose) analyses in multi-centre trials. *Eur Respir J.* 2012;40(Suppl 56):P4307.

Mandon J, Högman M, Merkus PJ, van Amsterdam J, Harren FJ, Cristescu SM. Exhaled nitric oxide monitoring by quantum cascade laser: comparison with chemiluminescent and electrochemical sensors. *J Biomed Opt.* 2012;17(1):017003. Available from: doi: 10.1117/1.JBO.17.1.017003.

Kumar B, Park YT, Castro M, Grunlan JC, Feller JF. Fine control of carbon nanotubes–polyelectrolyte sensors sensitivity by electrostatic layer by layer assembly (eLbL) for the detection of volatile organic compounds (VOC). *Talanta*. 2012;88:396–402. Available from: doi: 10.1016/j.talanta.2011.11.006.

Santonico M, Pennazza G, Capuano R, Falconi C, Vink TJ, Knobel HH, et al. Electronic noses calibration procedure in the context of a multicentre medical study. *Sens*

Actuators B Chem. 2012;173:555–61. Available from: doi.org/10.1016/j.snb.2012.07.042.

2011

Bikov A, Lazar Z, Schandl K, Antus BM, Losonczy G, Horvath I. Exercise changes volatiles in exhaled breath assessed by an electronic nose. *Acta Physiol Hung.* 2011;98(3):321–8. Available from: doi: 10.1556/APhysiol.98.2011.3.9.

Immunoassay

2015

Pleil JD, Angrish MM, Madden MC. Immunochemistry for high-throughput screening of human exhaled breath condensate (EBC) media: implementation of automated Quanterix SIMOA instrumentation. *J Breath Res.* 2015;9(4):047108. Available from: doi: 10.1088/1752-7155/9/4/047108.

2012

Nunez-Naveira L, Marinas-Pardo LA, Amor-Carro O, Montero-Martinez C. Determination of ELISA reproducibility to detect protein markers in exhaled breath condensate. *J Breath Res.* 2012;6(4):046003. Available from: doi: 10.1088/1752-7155/6/4/046003.

Mass Spectrometry

2018

Singh KD, Del Miguel GV, Gaugg MT, Ibañez AJ, Zenobi R, Kohler M, et al. Translating secondary electrospray ionization–high-resolution mass spectrometry to the clinical environment. *J Breath Res*. 2018;12(2):027113. Available from: doi: 10.1088/1752-7163/aa9ee3.

2016

Clara Leigh Feider, Natalia Elizondo, Livia S. Eberlin. Ambient ionization and FAIMS mass spectrometry for enhanced imaging of multiply charged molecular ions in biological tissues. *Anal Chem.* 2016;88(23):11533-41.

2014

David S, Patrik Š, Jens H, Beauchamp J. Mass spectrometry for real-time quantitative breath analysis. *J Breath Res*. 2014;8(2):027101. Available from: doi: 10.1088/1752-7155/8/2/027101.

2013

Bikov A, Paschalaki K, Logan-Sinclair R, Horváth I, Kharitonov SA, Barnes PJ, et al. Standardised exhaled breath collection for the measurement of exhaled volatile organic compounds by proton transfer reaction mass spectrometry. *BMC Pulm Med.* 2013;13:43. Available from: doi: 10.1186/1471-2466-13-43.

Kumar S, Huang J, Abbassi-Ghadi N, Španěl P, Smith D, Hanna GB. Selected ion flow tube mass spectrometry analysis of exhaled breath for volatile organic compound profiling of esophago-gastric cancer. *Anal Chem.* 2013;85(12):6121–8. Available from: doi: 10.1021/ac4010309.

Phillips M, Cataneo RN, Chaturvedi A, Kaplan PD, Libardoni M, Mundada M, 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.

Available from: doi: 10.1371/journal.pone.0075274.

Trefz P, Schmidt M, Oertel P, Obermeier J, Brock B, Kamysek S, et al. Continuous real time breath gas monitoring in the clinical environment by proton-transfer-reaction-time-of-flight-mass spectrometry. *Anal Chem.* 2013;85(21):10321–9. Available from: doi: 10.1021/ac402298v.

2012

Janicka M, Kubica P, Kot-Wasik A, Kot J, Namieśnik J. Sensitive determination of isoprostanes in exhaled breath condensate samples with use of liquid chromatography-tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2012;893–894:144–9. Available from: doi: 10.1016/j.jchromb.2012.03.005.

2011

Turner MA, Guallar-Hoyas C, Kent AL, Wilson ID, Thomas CLP. Comparison of metabolomic profiles obtained using chemical ionization and electron ionization MS in exhaled breath. *Bioanalysis*. 2011;3(24):2731–8. Available from: doi: 10.4155/bio.11.284.

Nanotechnology

2017

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5.2. APPLICATIONS

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2017

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2018

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Lung cancer

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Pancreatic cancer

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2013

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Cystic Fibrosis

2015

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2015

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Diabetes

2013

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Environmental Health Science

2016

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Exhaled Breath Condensate

2015

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Exhaled Particles

2015

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2015

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Gastric Emptying

2015

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2012

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2016

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2015

Bodelier AG, Smolinska A, Baranska A, Dallinga JW, Mujagic Z, Vanhees K, et al. Volatile organic compounds in exhaled air as novel marker for disease activity in Crohn's disease: a metabolomic approach. *Inflamm Bowel Dis.* 2015;21(8):1776–85. Available from: doi: 10.1097/MIB.0000000000000436.

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Infectious Diseases

2015

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2010

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2010

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2012

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2012

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Liver Disease

2015

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2019

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2011

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Pulmonary Disease

2018

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2017

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Chronic Obstructive Pulmonary Disease (COPD)

2015

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2010

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Pulmonary Embolism (PE)

2010

Fens N, Douma RA, Sterk PJ, Kamphuisen PW. Breathomics as a diagnostic tool for pulmonary embolism. *J Thromb Haemost.* 2010;8(12):2831-3. Available from: doi: 10.1111/j.1538-7836.2010.04064.x.

Systemic Sclerosis

2010

Tufvesson E, Bozovic G, Hesselstrand R, Bjermer L, Scheja A, Wuttge DM. Increased cysteinyl-leukotrienes and 8-isoprostane in exhaled breath condensate from systemic sclerosis patients. *Rheumatology (Oxford).* 2010;49(12):2322–6. Available from: doi: 10.1093/rheumatology/keq271.

Therapeutic/Gamma Irradiation

2015

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Transplantation

2013

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Genetics

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Inflammation

2016

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5.3. PRACTICE GUIDELINE

2011

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5.4. REVIEWS, BOOKS & OPINIONS

2019

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