Breath analysis as a diagnostic tool for early disease detection

Adriaan M.H. van der Veen[1], Stefan T. Persijn[1], Jan C. Petersen[2], Florbela Dias[3], Jean-Jacques Zondy[4], Malo Cadoret[4], Olav Werhahn[5], Javis A. Nwaboh[5]
[1]VSL, Thijsseweg 11, 2629 JA Delft, the Netherlands
[2]Danish institute for Fundamental Metrology, Matematiktorvet 307, DK-2800 Kongens Lyngby, Denmark
[3]Portuguese Institute for Quality, Rua António Gião, 2, 2829-513 Caparica, Portugal
[4] Institut National de Métrologie, Conservatoire National des Arts et Métiers, 61 rue du Landy, F-93210 La Plaine Saint Denis (France)
[5]Physikalisch-Technische Bundesanstalt (PTB), Bundesallee 100, D-38116 Braunschweig, Germany

Project summary

Early disease detection is getting increased attention in the medical sector. In early stages, many diseases know little or no suffering at all, and the prospects of curing are much better. Less suffering means often that people will stay less away from work, thus reducing labour costs. For diseases like cancer, early disease detection can literally mean the difference between life and death.

Breath analysis is one of the clinical tests that can be used for early disease detection. It is non-invasive, and once operational, relatively easy to maintain and handle “on-site”. Recent developments in laser absorption spectroscopy techniques, and in particular cavity ring down spectroscopy (CRDS) and tuneable diode laser absorption spectroscopy (TDLAS), allow developing small, calibration-free devices for performing these tests. The devices must of course have a high level of accuracy, robustness, and reliability with respect to measurement of extremely low levels of trace gas components usually encountered in human breath.

Although the development of suitable (parts of) equipment is well underway, there is still a long way to go, not in the least because of a lack of accuracy and reliability in measurement results. The project addresses in particular these issues by aiming to make reliable identification of the species present in the exhaled breath, and for a selected set of biomarkers to reduce the uncertainty of measurement of the amount of substance from the current typical 10% down to at most 1-2%, taking into consideration the presence of interfering components in breath. The project output consists of

- high-accuracy spectroscopic data
- measurement methods
- and reports.

The development of the instrumentation for breath analysis has progressed very well. Recent highlights include:

- constructed frequency-stabilized optical parametric oscillator pumped by an extended cavity diode laser (1050-1670nm) with 3-4 µm idler tuning and up to 1.8 Watt power.
- a complete fibre-based system at 1.5 µm is operational and has been tested with several gases.
- articles on the developed instrumentation have been accepted for publication in Applied Physics B: Laser and Optics (2x) and Applied Optics.

The developed instrumentation will be used to analyse gas mixtures that have been gravimetrically prepared in cylinders. Gas mixtures contain up to 5 components like methane, ammonia, and carbon monoxide and have been distributed to the partners. Studies done so far with the instrumentation include:

- extensive line shape analyses of acetylene and ammonia spectra with fitting routines including almost all known line shapes.
- study on optimising the measurement of strongly adsorbing gases (in particular ammonia).
- comparison measurements with Institut für Lasermedizin (Düsseldorf, Germany) analysing amount fractions of CO and CO_2 of the gas mixture provided by IPQ.
- comparison measured infrared spectra with Fourier Transform Infrared (FTIR) spectra from NIST and PNNL database. Data agree within the measurement uncertainty for propane, ethane, formaldehyde, and benzene.
- use of chemical and physical techniques to remove moisture from human breath

Activities that have been undertaken in dissemination, exploitation and knowledge transfer include:

- established contacts with equipment manufacturers and medical hospitals in Portugal, the Netherlands, Germany, and France.
- HC Photonics, a Taiwanese manufacturer of periodically poled non-linear crystals, joined the consortium as an external collaborator.

Another recent highlight is a document on line strength measurements including uncertainty budget and the documentation of a technical method for calibration-free amount fraction measurements based on spectroscopic absorption techniques.

The project started 1 May 2008 and its duration is 3 years. A scientific committee containing experts from equipment manufacturers, medical and clinical research groups, and spectroscopists will support the organisation of the closing symposium.

JRP Contract Number:	T2JO2
JRP Title - JRP Acronym:	Breath analysis as a diagnostic tool for early disease detection – Breath analysis
JRP start date and duration:	1 May 2008; 36 months
Date of this Publishable JRP Summary:	10 June 2010

JRP-Coordinator:

Name, Title, Organisation:	Dr. A.M.H. van der Veen
	VSL
Tel.:	+31 15 2691 500
E-mail:	avdveen@vsl.nl
JRP website address:	http://www.vsl.nl/knowledge/breath-analysis-project/425

Other JRP partners:

Organisation, Country:	Danish institute for Fundamental Metrology, DK;
	Portuguese Institute for Quality, PT;
	Institut National de Métrologie, Conservatoire National des Arts et Métiers, FR;
	Physikalisch-Technische Bundesanstalt, DE

The research within this EURAMET joint research project receives funding from the European Union Seventh Framework Programme, ERA-NET Plus, under the iMERA-Plus Project – Grant Agreement No. 217257.