

## Noninvasive Measurement of Plasma Triglycerides and Free Fatty Acids from Exhaled Breath

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### Abstract

#### Background:

Although altered metabolism has long been known to affect human breath, generating clinically usable metabolic tests from exhaled compounds has proven challenging. If developed, a breath-based lipid test would greatly simplify management of diabetes and serious pathological conditions (e.g., obesity, familial hyperlipidemia, and coronary artery disease), in which systemic lipid levels are a critical risk factor for onset and development of future cardiovascular events.

#### Methods:

We, therefore, induced controlled fluctuations of plasma lipids (insulin-induced lipid suppression or intravenous infusion of Intralipid) during 4-h *in vivo* experiments on 23 healthy volunteers (12 males/11 females,  $28.0 \pm 0.3$  years) to find correlations between exhaled volatile organic compounds and plasma lipids. In each subject, plasma triglycerides (TG) and free fatty acids (FFA) concentrations were both directly measured and calculated via individualized prediction equations based on the multiple linear regression analysis of a cluster of 4 gases. In the lipid infusion protocol, we also generated common prediction equations using a maximum of 10 gases.

#### Results:

This analysis yielded strong correlations between measured and predicted values during both lipid suppression ( $r = 0.97$  for TG;  $r = 0.90$  for FFA) and lipid infusion ( $r = 0.97$  for TG;  $r = 0.94$  for FFA) studies. In our most accurate common prediction model, measured and predicted TG and FFA values also displayed very strong statistical agreement ( $r = 0.86$  and  $r = 0.81$ , respectively).

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**Abbreviations:** (2-BuONO<sub>2</sub>) 2-butyl nitrate, (2-PeONO<sub>2</sub>) 2-pentyl nitrate, (C<sub>2</sub>Cl<sub>4</sub>) tetrachloroethylene, (C<sub>2</sub>HCl<sub>3</sub>) trichloroethylene, (CHBr<sub>3</sub>) bromoform, (CH<sub>3</sub>Br) bromomethane, (CH<sub>3</sub>I) methyl iodide, (CH<sub>3</sub>ONO<sub>2</sub>) methyl nitrate, (CH<sub>4</sub>) methane, (CO<sub>2</sub>) carbon dioxide, (DMDS) dimethyl disulfide, (ECD) electron-capture detectors, (EtONO<sub>2</sub>) ethyl nitrate, (F) female, (FFA) free fatty acids, (FID) flame-ionization detectors, (GC) gas chromatograph, (ICTS) Institute for Clinical and Translational Science, (IV) intravenous, (M) male, (MSD) mass spectrometer detector, (MTBE) methyl tert-butyl ether, (RMSE) root mean square errors, (SCD) sulfur chemiluminescence detector, (TG) triglycerides, (UCI) University of California, Irvine, (VOC) volatile organic compounds

**Keywords:** breath tests, diabetes mellitus, diagnostic techniques and procedures, gases, lipid metabolism, volatile organic compounds

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**Abstract cont.****Conclusions:**

Our results demonstrate the feasibility of measuring plasma lipids through breath analysis. Optimization of this technology may ultimately lead to the development of portable breath analyzers for plasma lipids, replacing blood-based bioassays.

*J Diabetes Sci Technol* 2012;6(1):86-101