Therapeutic lipolysis monitoring with an aerosol-made sensing device

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A major concern of today's society is metabolic health (e.g. obesity) that can be responsible for several diseases (e.g., diabetes, cardiovascular illnesses). Various diet strategies as well as exercising are explored, but the assessment of treatment effectiveness on an individual level remains difficult. Desired are simple and accurate devices that monitor metabolic changes conveniently and guide therapeutic action at the point-of-care. One such possibility is through non-invasive acetone detection in the human breath, a metabolic marker of lipolysis that correlates well with its "gold standard" in the blood, β-hydroxybutyrate (BOHB [Anderson, 2015]). Specifically, acetone is formed during hepatic β-oxidation of fatty acids that further divide into acetoacetate that undergoes decarboxylation and enzymatic degradation to acetone [Evans *et al.*, 2017], which is volatile and measureable in exhaled breath.

To monitor lipolysis, most important is the accurate detection of *fine differences* in breath acetone, for example during exercise (e.g., to indicate anaerobic thresholds or distinguish cardiorespiratory fitness) or dieting (e.g., to assess diet effectiveness). Promising for this are low-cost metal oxide sensing devices [Righettoni *et al.*, 2015). However, these are typically limited by insufficient selectivity, particularly in breath analysis applications, where acetone needs to be detected in the presence of endogenous (e.g., isoprene spikes during exercise) and background interferants (e.g., ethanol from sanitizers [Güntner *et al.*, 2020]).

Here, we present a low-cost and compact device [Weber *et al.*, 2020] based on an aerosol-made catalytic filter [Van den Broek *et al.*, 2021] and chemo-resistive sensor for rapid and highly selective breath acetone detection [Weber *et al.*, 2021]. This device is tested on end-tidal breath during and after a standardized exercise protocol [Königstein *et al.*, 2020]. Figure 1 shows acetone concentrations of a single volunteer as detected by bench-top mass spectrometry (triangles) and the aerosol-made sensing device (circles). Most impressively, the device detects even fine acetone differences with high accuracy (i.e., bias of 25 ppb for 146 breath samples of 9 volunteers) and is robust also against endogenous interferants such as isoprene that spikes at the onset of exercise [King *et al.*, 2009] and is not detected by the sensor here (i.e., between 0 – 60 min, Fig. 1) even though it reaches up to 0.5 ppm as confirmed by mass spectrometry! Furthermore, the detection of acetone is not affected by orders of magnitude higher ethanol concentrations in the background air that came from hand disinfection in the same room. The steady increase in acetone (Fig. 1) is indicative for enhanced lipolysis, as confirmed also by blood BOHB measurements. This device is used to monitor the metabolism of 72 volunteers in a randomized clinical trial at ETH Zurich.

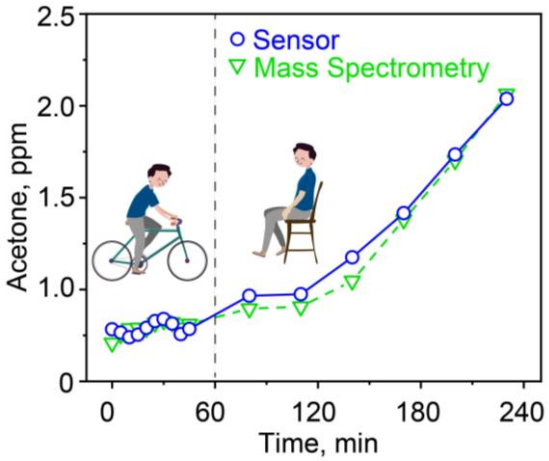

Figure 1: End-tidal acetone increases during exercise and rest, indicating enhanced lipolysis, as detected by the aerosol-made sensing device (circles) and mass spectrometry (triangles).

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