# Inhalation of Heat-Not-Burn Tobacco Aerosol Impairs Vascular Endothelial Function

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**Introduction:** "Heat-not-burn" (HNB) tobacco devices heat tobacco at temperatures that avoid combustion but cause the nicotine to aerosolize, leaving the leaf material intact but depleted of volatile substances. A new HNB product, iQOS, from Philip Morris, has been test marketed in several non-US countries and has been considerably more successful than previously introduced HNB products[1]. Despite harm reduction claims by the tobacco industry[2], the health effects of HNB products are incompletely understood. Notably, industry-supported studies of potential cardiovascular consequences of HNB aerosol exposure published to date[3] have not included some common measures of adverse effects of smoke exposure, such as vascular endothelial function tested in vivo[4].

**Figure 1. iQOS.** *iQOS is composed of three main parts: HeatStick, holder, and pocket charger. HeatSticks are inserted in the holder, which contains an electronic heating blade to heat tobacco and release aerosol. HeatSticks contain strips of processed and reformed tobacco. (Photo: M. Springer)*

**Methods:** We exposed rats (n=8/group) via nose cone to iQOS aerosol, Marlboro cigarette mainstream smoke, or clean air as a control, ten times over 5 min to approximate the consumption of a single iQOS HeatStick. Exposure conditions were 15 seconds and 5 seconds twice per minute. To generate the aerosol and mainstream smoke, we used a manual system for the 15-second and an analytical vaping machine for the 5-second exposure (Figure 2). Arterial flow-mediated dilation (FMD) was quantitated pre- and post-exposure by measuring femoral artery diameter with micro-ultrasound before and after 5 min of transient surgically induced ischemia, and expressed as the percent vasodilation[5,6] (Figure 3). Serum samples were collected after the exposure and assessed for nicotine and cotinine levels.

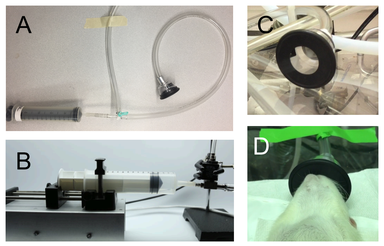


**Figure 2. Aerosol generator and exposure systems.** *A. Manual exposure system; B. Analytical vaping machine made by Gram Research Technology; C. iQOS aerosol coming out of nose cone; D. Rat's nose placed in the nose cone.*

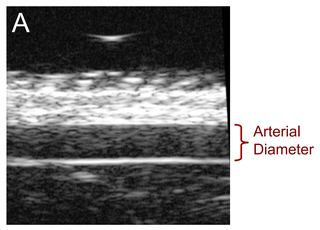


**Figure 3. Arterial Flow-Mediated Dilation.** *A. Ultrasound imaging of rat femoral artery; B. FMD experimental design.*

**Results:** FMD was impaired comparably by 5-second exposures to iQOS aerosol (9.6±1.0(SD)% pre-exposure vs. 3.8±2.6% post-exposure, p=.0001 by 2-tailed paired t-test) and cigarette smoke (11.2±2.6% pre-exposure vs. 4.2±2.3% post-exposure, p=.0005). 15-second exposures to iQOS aerosol and cigarette smoke impaired FMD to a similar extent (10.6±2.9% pre-exposure vs. 4.5±1.9% post-exposure, p=.0008; and 10.6±2.0% pre-exposure vs. 4.6±1.3% post-exposure, p=.0004, respectively). FMD was not affected in the clean air control group (8.3±1.9% vs. 8.8±4.5%, p=.82) (Figure 4). The percent FMD impairment was not significantly different in groups exposed for 5 seconds compared to 15 seconds (p=.27).

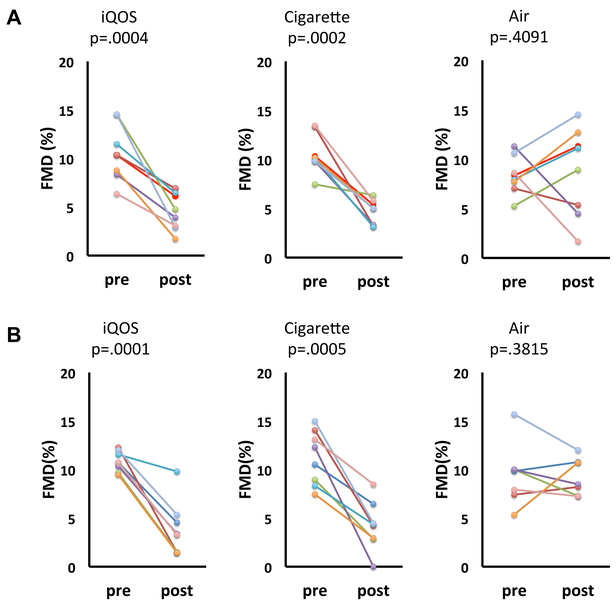


**Figure 4. FMD was impaired by mainstream cigarette smoke and iQOS aerosol.** *A. Ten 15-second exposures. B. Ten 5-second exposures.*

**Results (continued):** Nicotine levels in the 5-second cigarette group were similar to the amount in blood after humans have smoked one cigarette, confirming that the exposure conditions were relevant to real-world smoking. Serum nicotine and cotinine levels were significantly higher in the iQOS-exposed group compared to the cigarette-exposed group (Figure 5).

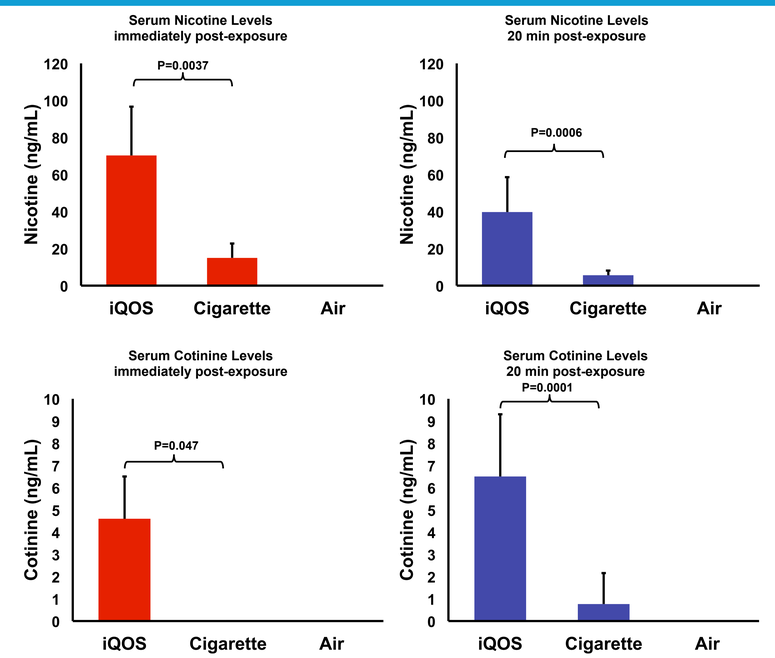


**Figure 5. Serum nicotine and cotinine levels immediately and 20 min post-exposure.**

**Conclusion:** We conclude that acute exposure to iQOS aerosol at doses relevant to real world use can substantially impair endothelial function in rats comparably to cigarette smoke despite the absence of combustion. Use of HNB tobacco products does not necessarily avoid the adverse cardiovascular effects of smoking cigarettes.

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**Disclosures:** none

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