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ARTICLE

Panel study using novel sensing devices to assess associations of $PM_{2.5}$ with heart rate variability and exposure sources

Shih-Chun Candice Lung[1,2,3] · Nathan Chen[1] · Jing-Shiang Hwang[4] · Shu-Chuan Hu[1] · Wen-Cheng Vincent Wang[1] · Tzu-Yao Julia Wen[1] · Chun-Hu Liu[1]

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Abstract

Background/objective This work applied a newly developed low-cost sensing (LCS) device (AS-LUNG-P) and a certified medical LCS device (Rooti RX) to assessing $PM_{2.5}$ impacts on heart rate variability (HRV) and determining important exposure sources, with less inconvenience to subjects.

Methods Observations using AS-LUNG-P were corrected by side-by-side comparison with GRIMM instruments. Thirty-six nonsmoking healthy subjects aged 20–65 years were wearing AS-LUNG-P and Rooti RX for 2–4 days in both Summer and Winter in Taiwan.

Results $PM_{2.5}$ exposures were $12.6 \pm 8.9\ \mu g/m^3$. After adjusting for confounding factors using the general additive mixed model, the standard deviations of all normal to normal intervals reduced by 3.68% (95% confidence level (CI) = 3.06–4.29%) and the ratios of low-frequency power to high-frequency power increased by 3.86% (CI = 2.74–4.99%) for an IQR of $10.7\ \mu g/m^3$ $PM_{2.5}$, with impacts lasting for 4.5–5 h. The top three exposure sources were environmental tobacco smoke, incense burning, and cooking, contributing $PM_{2.5}$ increase of 8.53, 5.85, and $3.52\ \mu g/m^3$, respectively, during 30-min intervals.

Significance This is a pioneer in demonstrating application of novel LCS devices to assessing close-to-reality $PM_{2.5}$ exposure and exposure–health relationships. Significant HRV changes were observed in healthy adults even at low $PM_{2.5}$ levels.

Keywords PM exposure · Asian PM exposure sources · PM low-cost sensors · Particles and health

Introduction

Technologies for novel low-cost sensors have rapidly developed in recent years in both environmental sensing and bio-sensing [1, 2]. With data transmission/storage and power supply components, these sensors are integrated as low-cost sensing (LCS) devices. This panel study aims to assess impacts of $PM_{2.5}$ (particulate matter with aerodynamic diameter ≤ 2.5 μm) on heart rate variability (HRV) and explore high $PM_{2.5}$ sources using a wearable environmental LCS device for $PM_{2.5}$ and a certified medical LCS device for HRV. These two novel devices have characteristics of small size, light weight, and free of noise and vibration, thus allowing subjects to behave naturally and follow their typical daily routines, which, in turn, enable scientists to evaluate close-to-reality exposures and exposure–health relationships. The inexpensive and easy-to-use features of these novel LCS devices also facilitate their applications in developing countries where pollutant levels may be ten times higher than $10\ \mu g/m^3$, the annual $PM_{2.5}$ level recommended by World Health Organization [3, 4] and where human health is at stake [5].

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✉ Shih-Chun Candice Lung
sclung@rcec.sinica.edu.tw

1 Research Center for Environmental Changes, Academia Sinica, Taipei, Taiwan

2 Department of Atmospheric Sciences, National Taiwan University, Taipei, Taiwan

3 Institute of Environmental Health, National Taiwan University, Taipei, Taiwan

4 Institute of Statistical Science, Academia Sinica, Taipei, Taiwan

$PM_{2.5}$ is a classified human carcinogen [6]; millions of deaths worldwide were attributable to $PM_{2.5}$ [7, 8]. Long-term exposure to high $PM_{2.5}$ concentrations increases the risk of lung cancer, cardiovascular diseases, arteriosclerosis, and brain diseases [9–12]; while short-term exposure causes exacerbation of several forms of respiratory diseases and changes in HRV [13–16]. HRV is viewed as an indicator of cardiovascular mortality [17, 18]. Although previous studies have demonstrated the significant health impacts of $PM_{2.5}$, the coarsely estimated $PM_{2.5}$ exposures in most studies using ambient $PM_{2.5}$ levels as exposure surrogates face the challenge of underestimation. Studies conducted for the American Cancer Society revealed a 17% increase in all-cause mortality for 10 μg/m^3 increase in $PM_{2.5}$ using more spatially resolved exposure estimates [19], compared with a 4% increase using Environment Protection Agency (EPA) monitoring data as exposure surrogates [20]. Panel-type epidemiological studies following each subject usually assess exposure levels in greater detail than cohort studies. The newly developed wearable LCS devices facilitate close-to-reality exposure assessment for panel subjects, which would in turn yield more accurate estimates in health damages.

For personal exposure assessment, $PM_{2.5}$ levels were traditionally assessed with personal samplers such as Personal Environmental Monitors (PEM, 761-203B, SKC Ltd, Blandford Forum, UK) or personal monitors such as GRIMM 1.109 (GRIMM Aerosol Technik Ainring GmbH & Co., Ainring, German) [21–23]. PEMs are employed to collect $PM_{2.5}$ on filters, with the advantages of subsequent chemical analysis; while the integrated measurements suffered from low temporal resolution of 4–24 h [21, 23, 24]. GRIMM offers $PM_{2.5}$ levels in fine resolutions down to minutes. However, the cost limits their applications in panel studies; the heavy weight (2 kg) also restricts their being carried around the waist, slightly distant from the breathing zone for exposure assessment. In addition, the noise, vibration, and apparent outlook of PEM (plus a pump) and GRIMM often discouraged subjects from adhering to their routine daily activities on the monitoring days. The newly developed LCS devices overcome these drawbacks and allow subjects to move freely, thus enabling close-to-reality exposure assessment.

Three physiological mechanisms have been proposed for adverse cardiovascular impacts after $PM_{2.5}$ exposures [25, 26]. One of the mechanisms is that $PM_{2.5}$ activates the receptors in the lungs, which then triggers the activation of the hypothalamic pituitary adrenal axis and the domination of the sympathetic pathway in the automatic nervous system [27, 28]. This effect can occur in a matter of minutes to hours [25, 29, 30], which could be evaluated with LCS devices attached to panel subjects as the current work. It is the first to demonstrate the applicability of these novel LCS devices to $PM_{2.5}$ exposure assessment and epidemiology.

In this study, a newly developed wearable LCS device for $PM_{2.5}$ and a certified noninvasive medical LCS device for HRV were applied to assessing the impacts of $PM_{2.5}$ exposure on HRV and determining important $PM_{2.5}$ exposure sources. Data quality, stability, and wearability of these devices were evaluated. The $PM_{2.5}$ exposure–HRV relationship with 5-min resolution and the lagged effects up to 18 h were investigated. The important exposure sources at 30-min intervals were assessed. The advantages and limitations of applying these novel LCS devices in $PM_{2.5}$ environmental health research were also discussed.

Methods

Personal wearable LCS devices for environmental observations

The LCS device used in this study, AS-LUNG-P (Fig. 1), was modified from a prototype LASS-FT [1]. AS stands for Academia Sinica, the research institute supporting its development; LUNG indicates the human organ most affected by air pollutants; and P stands for portable version. Sensors for PM (PMS3003, Plantower, Beijing, China), CO_2 (S8, Senseair AB, Sweden), temperature/humidity (SHT31, Sensirion AG, Switzerland), GPS (u-blox, Switzerland), motion (Analog Devices, Inc., USA), and real-time-clock module are integrated for research purpose. Its size is 135 × 70 × 40 mm, weighing around 153 g. The basic manufacturing cost is around USD 270, without considering research and development. Real-time data are transmitted wirelessly with the built-in WiFi module through a 4 G router back to the cloud database at one of the three log intervals, namely, 15 sec, 1 min, and 5 min. An SD card is added as a complement to avoid data loss.

PMS3003 has been introduced and evaluated previously [1, 31]. In brief, PMS3003 uses a fan to draw air through a

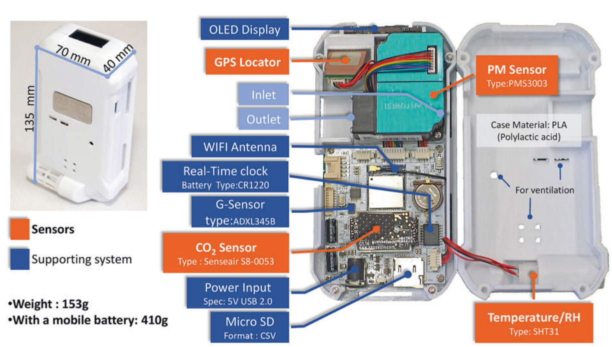

Fig. 1 Low-cost PM sensing device, AS-LUNG-P. Left panel is the outlook and right panel is the inside of the AS-LUNG-P.

chamber where it is exposed to a laser-induced light, and 90° scattered light is detected by a photo-diode detector. This laser wavelength was estimated at 650 ± 10 nm, close to that of GRIMM 1.109 (655 nm) [31]. GRIMM 1.109 is an aerosol spectrometer detecting aerosols in the size range of 0.25–32 µm in 31 size channels. In laboratory testing, R^2 between PMS3003 and GRIMM is as high as 0.9825 for PM_1, 0.9843 for $PM_{2.5}$, and 0.9760 for PM_{10} [1]. The current work focused on $PM_{2.5}$ only.

In our laboratory, each AS-LUNG-P underwent individual side-by-side comparison with GRIMM following the procedures described in Lung et al. [32]. In short, correction equations were established using data collected from collocated AS-LUNG-P and GRIMM during the concentration decay period (well mixed) after incense burning inside an almost closed hood. Then, one correction curve for each AS-LUNG-P set was employed to obtain GRIMM comparable measurements. The linear range of these curves could be up to 400–500 µg/m^3. To reduce conversion errors in lower concentration range, this work used correction equations up to 150 µg/m^3 to obtain GRIMM comparable data. Although AS-LUNG-P overestimated $PM_{2.5}$ with slopes of 1.94–3.01 (with GRIMM as X and AS-LUNG-P as Y), the good R^2 (0.978–0.989) of all the correction curves indicated high precision of the devices, thus granting their potential applications to researches after data correction with a research-grade instrument.

These correction equations of $PM_{2.5}$ were obtained in the range of 0.1–150 µg/m^3 under the conditions of 26.2–40.6 °C and 39.7–81.2% relative humidity (RH). GRIMM has the limit of detection around 0.1 µg/m^3; AS-LUNG-P overestimates $PM_{2.5}$ about 2–3 folds with intercepts of the correction equations around 2.5–3.5 µg/m^3. Thus, the limit of detection of AS-LUNG-P for $PM_{2.5}$ is probably around 3 µg/m^3. Moreover, this PMS3003 PM sensor could provide PM_{10} readings as well. Nevertheless, PM_{10} readings showed much higher variability than $PM_{2.5}$ in previous evaluations; inter-sensor variability of 16 sensors, assessed as the percent coefficient of variation (%CV = standard deviation/mean (%)) of the 5-min averages, was found to be 41 ± 21% [33]. The evaluation of PM_{10} in fields showed a lot of outliers [33]. Thus, PM_{10} was not assessed with AS-LUNG-P.

In addition to AS-LUNG-P, HOBO UA and U12 sensors (ONSET Computer Corporation, USA) were carried by the subjects. The temperature (°C) and RH (%) from U12 were used in data analysis, which had high correlation with those of AS-LUNG-P, 0.91 and 0.84, respectively. For UA, light intensity (lux) was employed to differentiate whether microenvironments are with or without solar radiation. According to prior results, light intensity had high correlation with solar radiation; and durations with 1000 lux or above were classified as outdoor conditions with solar radiation.

LCS device for heart rate variability (HRV)

Rooti RX (shorten as Rooti) is a portable single lead electrocardiogram (ECG) event recorder (RootiCare®, Rooti Labs Ltd, Taipei, Taiwan) with medical-device certifications from EU, US, and Taiwan (www.rooticare.com). It is a water-resistant compact ECG patch of smaller size (62 × 22.5 × 8.45 mm) and lighter weight (14 ± 1 g) compared with a Holter monitor, with operation range of 0–40 °C and 20–93% RH. It is attached to an electrode sticker of 32.7 × 115 × 5.2 mm in size and only 3.2 g in weight. Noninvasive Rooti provides observations for various parameters such as heart rate, HRV indicators, three-dimension motions, and sleep stages (www.rooticare.com). Rooti has been evaluated against a standard 12-lead Holter monitor [34]. The overall average beat per minute correlation between them was 0.98 in 33 healthy subjects. The mean percentage of invalid measurements was 1.6% for Rooti and 1.7% for Holter. Rooti worn by another panel of 67 subjects had mean analyzable wear time of 93.6% [34]. In view of its being a certified medical device with good performance in prior tests, Rooti was employed in this study to assess HRV.

Panel study design

Recruitment was carried out in the northern, central, southern, and eastern Taiwan since different regions have different $PM_{2.5}$ levels and major sources. Thirty-six subjects were recruited, who were at age > 20 years and willing to follow our instructions to carry sensors, respond to the questionnaire, and record time-activity diaries (TADs) every 30 min for at least 2 days in two seasons (preestablished inclusion criteria) without smoking and preexisting cardiovascular diseases (preestablished exclusion criteria). Informed consent was obtained from all subjects. Each subject was required to wear AS-LUNG-P, UA, and U12 near the chest with a strap or carry them in a handbag with inlet protruding out for 2–4 days in both Summer and Winter. Subjects were asked to keep their daily routines as usual. During shower and sleep, devices were placed outside the bathroom and at the bedside, respectively. In addition, each subject was asked to wear a Rooti on their chest on the same days, even during shower and sleep.

Before wearing the devices, subjects were also asked questions regarding their basic characteristics (including height and weight), health status, habits, and potential exposure sources. In addition, on the monitoring days, subjects had to fill out a TAD at 30-min intervals regarding their microenvironments, activities, ventilation status if indoors, and two major exposure sources if encountered, during that 30-min period. Exposure sources listed include vehicle emission, environmental tobacco smoke (ETS), cooking, incense burning, paper-money burning, agriculture-waste burning, mosquito-coil burning, community factories, and others (please specify). This question probes into nearby sources encountered, rather than distant sources like industrial parks (unless there was a clear indication that subjects were exposed to pollution from distant sources, such as visible fires). Daily reminding phone calls were made during the monitoring periods and checking for each cell of TAD with each subject was performed when the subjects handed in TADs to ensure the validity and completeness of the TADs. The study design was reviewed and approved by the Institutional Review Board of AS (IRB No. AS-IRB01-17018).

Data analysis

$PM_{2.5}$ from AS-LUNG-P was in 15-sec intervals. One-min averages of $PM_{2.5}$ from AS-LUNG-P were converted into GRIMM comparable observations with correction curves obtained in laboratory for the range up to 150 μg/m^3. All ECG signals collected at 500 samples per second from Rooti were downloaded and analyzed using previously validated proprietary algorithms provided by Rooti Labs Limited [34]. One of the time domain parameters, the standard deviation of all normal to normal RR intervals (SDNNs), and one of the frequency domain parameters, the ratio of low-frequency power (LF; 0.04–0.15 Hz) to high-frequency power (HF; 0.15–0.4 Hz), were calculated in 5-min epochs. SDNN > 250 and LF/HF smaller than 0.1 were discarded since these data were abnormal. Data for $PM_{2.5}$ and HRV indicators were matched at 5-min intervals in non-sleeping periods for exposure–health evaluation because of different HRV between sleeping and non-sleeping periods, which were determined according to the Rooti output. $PM_{2.5}$, SDNN, and LF/HF were compared under different classifications using two-sample *t*-test and analysis of variance with unequal variance.

Since movement intensity of subjects would affect their heart conditions, observations of subjects' motions in *X*-, *Y*-, and *Z*- directions with the unit of mG (milli-gravitational constant, 6.674×10^{-14} m^3/kg × s^2) from Rooti were used in health evaluation because Rooti was patched onto the chest for all subjects, while AS-LUNG-P, also with motion sensor, could be carried in different ways. The maximum acceleration in each of the three dimensions in every 5-min epoch was calculated as the activity intensity using the following equation, $\text{activity intensity} = \sqrt{X^2 + Y^2 + Z^2}$, where *X*, *Y*, and *Z* represent the maximum acceleration in left–right, cranio-caudal, and dorso-ventral dimensions, respectively. The intensities were classified into low and high, with 1500 mG as the criteria according to preliminary results. Resting, sitting, and gentle actions usually have intensity below 1500 mG.

The association between $PM_{2.5}$ and $\log_{10}$-transformed HRV indicators with 5-min resolutions was analyzed using the general additive mixed model (R Version 3.5.0). All models were adjusted for gender, age (<30/30–44/≥45), body mass index (BMI, <24/≥24), season (May–October/November–April), microenvironment (others/outdoor with solar radiation), temperature, activity intensity (<1500/≥1500), time of day, and the interaction term of age and activity intensity. The details of model setting are in Supplementary Materials. The effect estimate (β) was transformed into percentage change of HRV indicator per interquartile range (IQR) of the corresponding covariate, which can be presented as $[10^{(\beta \times \mathrm{IQR})} - 1] \times 100\%$. The corresponding 95% confidence interval (CI) was presented as $[10^{(\beta \pm 1.96 \times \mathrm{SE}) \times \mathrm{IQR}} - 1] \times 100\%$, where SE is standard error of the β estimate.

Furthermore, whether $PM_{2.5}$ impacts on HRV become even more severe above certain thresholds were explored. Since the majority of our observations were below 30 μg/m^3, a model with a threshold value of 30 μg/m^3 was established (the threshold model). In addition, to investigate the lagged effects, a model with both main-effect variable (real-time $PM_{2.5}$ exposure) and one of the lagged effect variables (30-, 60-, …, and 1080-min after exposure) was established. All other parameters were the same as those of the main model.

Besides investigating $PM_{2.5}$ impacts on HRV, matching $PM_{2.5}$ observations from AS-LUNG-P with TAD records at 30-min intervals allows the contribution of high-exposure sources to be identified and quantified. Multiple regression was applied with dependent variable as $PM_{2.5}$ and independent variables as exposure sources listed in the TAD records including sleeping and non-sleeping periods. In order to focus on essential exposure sources, sources encountered <30 times (sample size of the total valid 30-min records is 6176) were not incorporated into the model.

$PM_{2.5}$ data from Taiwan EPA represent ambient air quality, while personal $PM_{2.5}$ exposure level is the sum of ambient $PM_{2.5}$ level and $PM_{2.5}$ exposure increments due to sources encountered. The hourly $PM_{2.5}$ means in the nearest monitoring stations of Taiwan EPA were put into the model as an independent variable to adjust for day-to-day variation, with the assumption that the means of the first and second half hours were the same as the hourly means. To account for instrument differences, EPA data were also converted into GRIMM comparable measurements using conversion equations from previous side-by-side comparisons of GRIMM with EPA instrument (using beta-gauge principals) at 25.7–39.5 °C and 39.0–85.7% RH, with a correlation coefficient of 0.86.

Table 1 $PM_{2.5}$ levels, SDNN, and LF/HF according to (a) subjects' characteristics and (b) important exposure features at 30-min intervals from TAD.

	$PM_{2.5}$ (μg/m^3)				SDNN (millisecond)				LF/HF			
	Mean	SD	*n*	*p* value	Mean	SD	*n*	*p* value	Mean	SD	*n*	*p* value
Panel a: characteristics												
Gender												
Male (13)[a]	12.8	11.1	7047		60.8	25.9	7047		2.56	2.28	7047	
Female (20)	13.5	8.7	13,820	$<2\times10^{-16}$	66.4	29.1	13,820	$<2\times10^{-16}$	1.51	1.43	13,820	$<2\times10^{-16}$
Age (year)												
<30 (16)	12.8	9.2	9862		59.8	24.8	9862		2.2	2.2	9862	
30–44 (10)	14.3	11.0	5868		67.6	27.3	5868		1.8	1.5	5868	
≥45 (7)	12.8	8.4	5137	$<2\times10^{-16}$	70.0	33.3	5137	$<2\times10^{-16}$	1.4	1.3	5137	$<2\times10^{-16}$
BMI (kg/m^2)												
<24 (21)	12.9	9.4	13,051		67.9	28.8	13,051		1.6	1.6	13,051	
≥24 (12)	13.8	9.8	7816	2.374×10^{-9}	58.9	26.2	7816	$<2\times10^{-16}$	2.3	2.1	7816	$<2\times10^{-16}$
Season												
Summer (28)	12.7	10.2	9427		61.9	28.7	9427		2.0	1.9	9427	
Winter (31)	13.7	9.0	11,440	1.154×10^{-15}	66.7	27.6	11,440	$<2\times10^{-16}$	1.7	1.8	11,440	$<2\times10^{-16}$
Area												
Northern (21)	12.8	9.4	12,941		65.6	28.8	12,941		1.7	1.6	12,941	
Central (4)	11.3	8.2	2590		59.6	25.1	2590		2.4	2.8	2590	
Southern (5)	18.7	9.9	3487		63.5	27.1	3487		2.1	1.7	3487	
Eastern (3)	8.8	7.5	1849	$<2\times10^{-16}$	65.8	29.0	1849	$<2\times10^{-16}$	1.7	1.6	1849	$<2\times10^{-16}$
$PM_{2.5}$												
<30	12.1	6.3	20,104		64.5	28.3	20,104		1.8	1.8	20,104	
30–49	35.7	4.8	628		65.5	25.8	628		2.1	2.2	628	
50–99	67.8	14.4	98		57.7	24.5	98		2.8	3.1	98	
≥100	121.9	13.4	37	$<2\times10^{-16}$	45.1	23.7	37	2.44×10^{-5}	2.3	1.6	37	9.07×10^{-10}
Activity intensity (mG)												
<1500	12.6	8.9	5022		53.5	23.9	5022		1.9	1.9	5022	
≥1500	13.4	9.8	15,845	8.16×10^{-8}	68.0	28.6	15,845	$<2\times10^{-16}$	1.9	1.8	15,845	0.915
Microenvironment												
Outdoor with solar radiation	17.5	9.4	1060		63.1	28.5	1060		2.0	1.8	1060	
Others	13.0	9.5	19,807	$<2\times10^{-16}$	64.6	28.2	19,807	0.101	1.9	1.8	19,807	0.009
Panel b: exposure features												
Exposure source[b]												
Vehicle emission (5.8 ± 4.6%)[a]	15.8	7.7	333		63.7	21.6	333		1.88	1.24	333	
Cooking[c] (5.3 ± 4.9%)	18.4	12.5	284		62.6	23	284		1.97	1.47	284	
Resuspended dust (1.8 ± 3.1%)	16.2	6.6	97		64.1	25.2	97		1.56	1.32	97	
Incense burning (1.1 ± 3.1%)	19.1	13.3	82		72.3	21.6	82		1.47	1.28	82	
Environmental tobacco smoke (1.2 ± 3.5%)	24.3	25.3	67		56.9	21.7	67		1.86	0.9	67	
Others (2.3 ± 2.8%)	14.2	8.3	137		66.7	21.5	137		1.5	0.94	137	
None (85.1 ± 9.5%)	12	7.3	4667	$<2\times10^{-16}$	67.4	24.1	4667	4.09×10^{-6}	1.58	1.28	4667	6.66×10^{-8}
Ventilation												
Indoor, closed (80.7 ± 16.3%)	12.1	8.1	4484		67	24.2	4484		1.61	1.29	4484	
Indoor, open (11.6 ± 15.0%)	15.3	8.8	601		69.9	22.7	601		1.43	1.1	601	
Outdoor (7.7 ± 5.3%)	16.7	10.6	420	$<2\times10^{-16}$	61.7	22.4	420	4.11×10^{-7}	2.07	1.45	420	1.02×10^{-14}

Table 1 (continued)

	$PM_{2.5}$ (μg/m^3)				SDNN (millisecond)				LF/HF			
	Mean	SD	*n*	*p* value	Mean	SD	*n*	*p* value	Mean	SD	*n*	*p* value
Location												
Home (65.4 ± 15.3%)	12.7	8.5	3636		67.2	24.8	3636		1.54	1.28	3636	
Office (13.2 ± 13.0%)	9.9	5.5	700		68.5	22.6	700		1.7	1.19	700	
Restaurant (4.7 ± 7.9%)	16.6	9.1	247		64.5	22.8	247		1.85	1.6	247	
Car (3.8 ± 4.2%)	11.2	7.4	220		70.5	20.6	220		1.55	1.13	220	
Park (1.1 ± 2.2%)	21.5	9.4	54		61.8	24.8	54		1.99	1.01	54	
Balcony (0.8 ± 1.6%)	22.3	21.4	40		56.5	25.5	40		2.38	1.31	40	
Hospital (0.7 ± 2.2%)	9.8	6.3	33		75.8	24.6	33		1.93	0.94	33	
Others (10.5 ± 6.4%)	14.6	8.2	575	$<2 \times 10^{-16}$	63.9	20.9	575	1.3×10^{-5}	1.88	1.38	575	1.75×10^{-12}
Activity[b]												
Sleeping (38.5 ± 10.3%)	11.2	6.6	2123		66.2	25.9	2123		1.44	1.29	2123	
Static leisure (28.4 ± 12.4%)	14.1	9.4	1616		65	22.5	1616		1.78	1.27	1616	
Commuting (10.0 ± 5.8%)	13.6	7.4	572		66.8	21.3	572		1.76	1.27	572	
Eating (7.4 ± 3.9%)	15.9	9.9	408		64.1	21.3	408		1.9	1.52	408	
Bathing (2.6 ± 1.8%)	15.1	11.7	147		71.9	22.9	147		1.64	1.45	147	
Cooking[c] (1.7 ± 3.7%)	16.6	7.6	93		76.3	23.2	93		1.19	0.7	93	
Others (23.9 ± 11.6%)	12.6	8.6	1280	$<2 \times 10^{-16}$	69.4	23.5	1280	1.67×10^{-9}	1.64	1.13	1280	$<2 \times 10^{-16}$

[a]Numbers in parentheses are (a) number of subjects in Panel a and (b) the average (±standard deviation) percentage of time spent under the specified conditions of all subjects in Panel b.

[b]Exposure source and activity at 30-min intervals include multiple sources and activities; therefore, the sum of average time spent under the specified conditions could exceed 100%.

[c]For cooking listed under "Exposure Source," the subject was asked whether there was smell/odor from cooking in his/her surroundings; while for cooking listed under "Activity," the subject had to indicate whether he/she was cooking.

Results

Distribution of $PM_{2.5}$ and HRV indicators

During the monitoring campaign, only 0.2% of 15-sec observations from AS-LUNG-P were lost, mostly due to power shortage, resulted from delayed battery replacement or unexpected battery shortage. Batteries need to be replaced every 2 days to ensure continuous monitoring. In addition, observations were plotted to check for unexpected sudden changes of concentrations (ghost peaks). No such peaks were found, indicating stable readings from AS-LUNG-P during subject movements. Moreover, features of both AS-LUNG-P and Rooti including light weight, small size, free of noise and vibration, and ease of use, which incur less inconvenience on wearer, facilitated smooth subject recruitment; subjects had no complaint about wearing them.

For Rooti, data loss rates were high in the first season due to inexperienced device handling. Signals could be lost due to loose contact of Rooti with skin resulted from a combination of subject movements, too narrow or too wide distances between two contact points of the electrode stickers on the chest, and sweating. Data with missing rate in the 5-min epochs > 20% were not used [34]. After data cleaning, three subjects with significant data loss were removed, which yielded the average analyzable wear time of 84.1%.

Regarding wearability, none of the subjects had problem wearing Rooti even during shower. However, a previous study did find that 7.3% of participants had minor skin irritation related to the Rooti electrodes [34] which was also observed in our trials. In the actual campaign, electrode patches used were specially designed for athletes to ease discomfort due to sweating and skin irritation. In addition, in view of high temperature and humidity during Summer in Taiwan, electrode patches were replaced every 1–3 days and put in slightly different spots to avoid irritation for subjects with sensitive skin. Among 36 subjects, four females and one male reported minor skin irritation; hence, the overall wearability was relatively good.

In Taiwan, $PM_{2.5}$ levels were often relatively high in Winter; however, no episode occurred during actual monitoring. Thus, $PM_{2.5}$ exposures in the entire campaign were only 12.6 ± 8.9 μg/m^3 under the condition of 10.6–44.9 °C and 33.1–94.7% RH. The majority of the 36 originally recruited subjects were white-collar workers ($n = 24$); the rest were four housewives, two students, four blue-collar and two pink-collar workers. In terms of their health status,

Table 2 Estimated percentage changes (95% confidence intervals) in (a) 5-min SDNN and (b) 5-min LF/HF per interquartile range (IQR) increase in 5-min $PM_{2.5}$ ($n = 20{,}867$), calculated as $[10^{(\beta \times \mathrm{IQR})} - 1] \times 100\%$ where β is the effect estimate; the numbers in parentheses are 95% confidence intervals (CI): $[10^{(\beta \pm 1.96 \times \text{standard error} \times \mathrm{IQR})} - 1] \times 100\%$; IQR for the main and threshold models were 10.7 and 11.2 μg/m^3, respectively.

	Coefficient estimates	
	Main model[a]	Threshold model[b]
Panel a		
	Adjusted $R^2 = 0.156$	Adjusted $R^2 = 0.149$
$PM_{2.5}$	−2.79 (−3.70 to −1.88)***	−2.33 (−3.79 to −0.853)**
Gender[c]	−1.82 (−16.1 to 14.9)	−1.43 (−15.7 to 15.3)
BMI[d]	−17.1 (−28.8 to −3.49)**	−17.3 (−28.94 to −3.67)**
Outdoor[e]	−4.32 (−7.01 to −1.55)***	−4.77 (−7.45 to −2.01)***
Season[f]	5.55 (2.38 to 8.83)***	5.34 (2.15 to 8.64)***
Panel b		
	Adjusted $R^2 = 0.181$	Adjusted $R^2 = 0.178$
$PM_{2.5}$	3.24 (1.72 to 4.77)***	1.89 (−0.546 to 4.38)
Gender[c]	60.1 (21.6 to 111)***	59.3 (21.1 to 110)***
BMI[d]	25.6 (−3.82 to 64.1)*	25.9 (−3.59 to 64.4)*
Outdoor[e]	3.46 (−1.46 to 8.62)	4.10 (−0.848 to 9.29)
Season[f]	−9.13 (−13.3 to −4.71)***	−8.94 (−13.2 to −4.50)***

[a] $PM_{2.5}$ was treated as a continuous variable

[b] "$PM_{2.5}$ minus 30" was put in the model with negative values treated as 0

[c] Genderfemale was coded as 0 and male as 1

[d] BMI < 24 was coded as 0 and BMI ≥ 24 as 1

[e] Outdoor with solar radiation was coded as 1 and the other conditions as 0

[f] Season was coded as 1 for November to April and as 0 for May to October

*$0.05 < p < 0.1$; **$0.001 < p < 0.05$; ***$p < 0.001$

they were generally healthy with some mild ailments. Sixteen had allergic rhinitis, seven atopic dermatitis, three hypertensions, one kidney-related dysfunction, and one asthma. Characteristics of the 33 subjects remained in the dataset and essential measured variables (total sample size of 5-min $PM_{2.5}$ measurements = 32,719) are listed in Table S1 (Supplementary Material). The range of correction equations for AS-LUNG-P was up to 150 μg/m^3 only; hence, 43 data points above 150 μg/m^3 were removed, accounting for a very small percentage (0.13%) of the total samples.

Table 1 displays the descriptive statistics of $PM_{2.5}$, SDNN, and LF/HF according to subjects' characteristics and actual exposure conditions. Of 33 subjects remained in the dataset, there were 13 male and 20 female subjects with age of 20–65. There were significant differences in $PM_{2.5}$, SDNN, and LF/HF among subjects under different classifications (Table 1, Panel a). The majority of observations were recorded at exposure levels below 30 μg/m^3 and activity intensity above 1500 mG. Moreover, observations were mostly taken in indoor microenvironments. The different categories of exposure sources, ventilation statuses, locations, and activities of subjects were solicited from the TADs (Table 1, Panel b). After preliminary exploration on important factors affecting $PM_{2.5}$, only categories listed under exposure source and ventilation status were included in the final model for exposure-factor evaluation.

Impacts of $PM_{2.5}$ exposure on HRV

Table 2 shows the 5-min percentage changes of HRV indicators per IQR increase of $PM_{2.5}$ in the main and threshold models. After adjusting for the aforementioned factors, SDNN reduced by 3.68% (with 95% CI = (3.06, 4.29%)) and LF/HF increased by 3.86% (2.74, 4.99%) per 10.7 μg/m^3 of $PM_{2.5}$. When $PM_{2.5}$ exceeds 30 μg/m^3, the threshold model shows reduction in SDNN by 3.76% (2.67, 4.84%) and increase in LF/HF by 2.55% (0.60, 4.53%) per 11.2 μg/m^3 of $PM_{2.5}$. In terms of per 10 μg/m^3 increase in $PM_{2.5}$, SDNN would reduce by 3.44 and 3.51%, while LF/HF would increase by 3.61 and 2.38% for the main and threshold models, respectively. In short, the impacts of $PM_{2.5}$ above 30 μg/m^3 were slightly greater for SDNN but smaller for LF/HF. Moreover, the main model shows that subjects with BMI ≥ 24 had 17.9% (4.36, 29.6%) lower SDNN than those with BMI < 24, while LF/HF had marginally significant difference between these two groups. These results show that BMI ≥ 24 would aggravate the changes on SDNN.

Gender affected only LF/HF but not SDNN. Moreover, season and staying in outdoor microenvironments with solar radiation influenced both SDNN and LF/HF. Exposing to solar radiation reduced SDNN and increased LF/HF significantly. During May–October, SDNN reduced while LF/HF increased significantly in comparison with those from November to April. In other words, Summer and exposing to solar radiation would have impacts on HRV as the same direction as $PM_{2.5}$ does. Thus, a person with BMI > 24 in Summer exposing to solar radiation and $PM_{2.5}$ at the same time would experience aggravated impacts on HRV compare to another one without those conditions.

Figure 2 shows the lagged effect of $PM_{2.5}$ on HRV indicators at 30-min intervals. The impacts of $PM_{2.5}$ on SDNN and LF/HF lasted for 4.5 and 5 h after exposure, respectively. The greatest reduction of 2.85% (1.97, 3.72%) in SDNN occurred in 1 h, while the greatest increase in LF/HF of 3.56% (1.90, 5.24%) occurred at 2.5 h after exposure. The coefficient estimates of the lagged effects at hourly intervals are listed in Supplementary Materials Table S2.

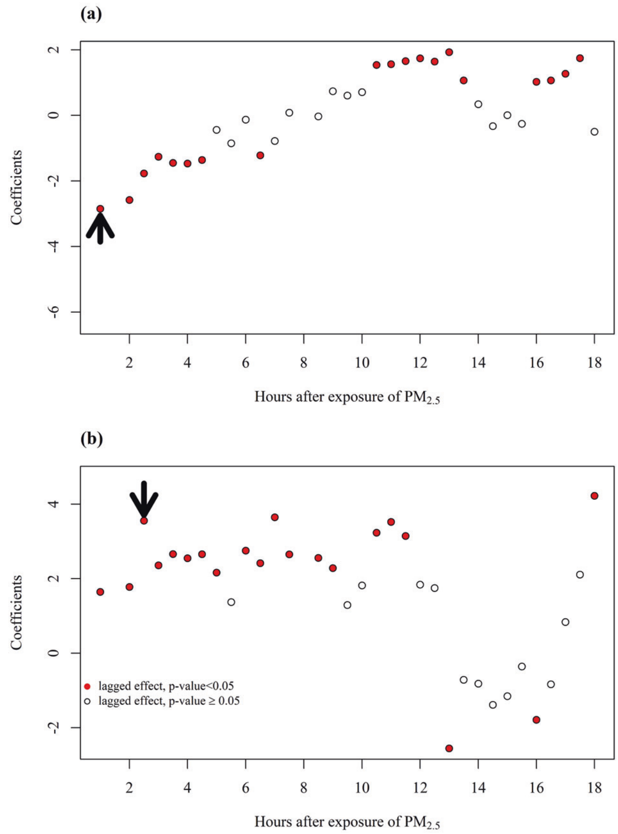

Fig. 2 Lagged effect of PM2.5. Panel **a** effect on SDNN and panel **b** effect on LF/HF. Arrows indicate the greatest changes, and data points in certain time periods were not shown since the model was not convergent.

Exposure sources and high $PM_{2.5}$ activities

Table 3 shows the results of exposure-factor evaluation. Except for ambient $PM_{2.5}$ levels (from Taiwan EPA stations), the top three important exposure sources were ETS, incense burning, and cooking, with statistically significant. In other words, subjects who encountered ETS, incense burning, and cooking would have on average 8.53 (6.98–10.1), 5.85 (4.45–7.24), and 3.52 (2.74–4.29) μg/m^3 higher $PM_{2.5}$ exposures, respectively, during that 30-min period. On the other hand, staying indoor has protection effects; the exposure was 1.32 (0.34–2.31) μg/m^3 lower with windows open and 3.08 (2.19–3.97) μg/m^3 lower with window closed.

For vehicle emission, it was unexpected that $PM_{2.5}$ exposures when outdoors during riding on vehicles and walking were lower. A possible reason is that peak exposure to vehicle emission can occur in a very short instant (Fig. 3a), which may not be captured by analysis with 30-min resolution of TADs. Examples of exposure to vehicle emission, cooking, and incense burning are shown in Fig. 3a–c; with the periods indicated by subjects when exposed to these sources marked in red. For cooking and

Table 3 Important factors of $PM_{2.5}$ exposure (μg/m^3) at 30-min resolution. Exposure sources are dummy variables with no-source as the base case and indoor ventilation statuses are also dummy variables with outdoor as the base case.

Adjusted $R^2 = 0.453$	Coefficient estimates (95% confidence interval)
(Intercept)	5.90 (4.96 to 6.83)***
Ambient $PM_{2.5}$	0.43 (0.42 to 0.44)***
Vehicle emission smelled indoor	−0.27 (−1.53 to 0.99)
Vehicle emission smelled outdoor when riding on vehicles	−1.47 (−3.02 to 0.08)*
Vehicle emission smelled outdoor when walking	−1.79 (−3.22 to −0.36)**
Cooking	3.52 (2.74 to 4.29)***
Environmental tobacco smoke	8.53 (6.98 to 10.1)***
Resuspended dust	1.38 (0.01 to 2.75)**
Incense burning	5.85 (4.45 to 7.24)***
Others	1.29 (−0.19 to 2.77)
Indoor, windows closed	−3.08 (−3.97 to −2.19)***
Indoor, windows open	−1.32 (−2.31 to −0.34)**

*$0.05 < p < 0.1$; **$0.001 < p < 0.05$; ***$p < 0.001$.

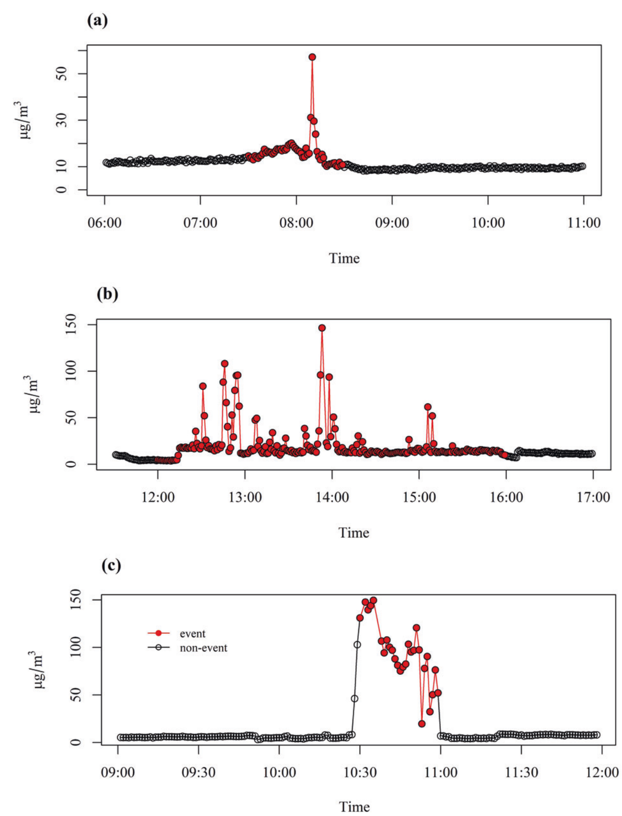

Fig. 3 Examples of PM2.5 peak exposures measured using AS-LUNG-P with subjects indicating exposure to a certain source. Panel **a** vehicle emission, **b** cooking, and **c** incense burning.

incense burning, the exposure periods were longer than 30 min; their exposure contributions were quantifiable with our statistical analysis. For vehicle emission, the TAD of that subject indicated exposure to vehicle emission between 7:30 and 8:30 a.m., with $PM_{2.5}$ levels slightly elevated compared to those at 6:00–7:30 a.m. except for the peak around 8:09 a.m. The contribution of that peak was much diluted by the 30-min average. Therefore, it is difficult to capture peak contributions from vehicle emission in our analysis.

To further identify microenvironments and activities when exposed to these important exposure sources, Figs. S1 and S2 in Supplementary Materials plotted the distribution of microenvironments and activities, respectively. As expected, the main microenvironment was road with the main activity being commuting when exposed to vehicle emission. For cooking, the two major microenvironments were restaurant and home while the two major activities were eating and cooking. For incense burning, subjects mostly had exposures at home with various activities such as static leisure, eating, and worshiping. For ETS exposure, the top three microenvironments were home, office, and others; while the top three activities were working, commuting, and static leisure. Understanding these exposure microenvironments and activities could facilitate designing better health promotion strategies to reduce $PM_{2.5}$ exposure and associated health risks.

Discussion

$PM_{2.5}$ exposure assessment and exposure–health evaluation were successfully conducted using newly developed non-invasive LCS devices for $PM_{2.5}$ and HRV. Results showed that SDNN reduced by 3.68% and LF/HF increased by 3.86% per 10.7 $\mu g/m^3$ increase in $PM_{2.5}$, which were consistent with previous findings [13, 23, 35–39]. A previous study in 2016 with meta-analysis on panel studies found that the percent reduction in SDNN per 10 $\mu g/m^3$ $PM_{2.5}$ increase was 2.11% [13]. These works used TSI DustTrak, SidePak, or GRIMM instruments for PM exposure and Holter monitors for HRV. Carrying heavy-weight instruments may affect subjects' behaviors and pose burden on their bodies. Instead, light-weight sensors with research-grade data quality were used in this study. Their being low cost allows more subjects to be recruited and their being easy-to-use also enhances participation willingness and compliance to the research protocol, both contributing to higher statistical power. This work is a pioneer in demonstrating the applicability of newly developed $PM_{2.5}$ and HRV LCS devices to $PM_{2.5}$ environmental health studies.

Moreover, previous studies assessing impacts of $PM_{2.5}$ on HRV focused either on certain susceptible population like the elderly or on certain high-exposure activities such as secondhand smoke or traffic exposure [23, 29, 36–41]. In the current study, healthy adults were recruited; and their average $PM_{2.5}$ exposure levels were only 12.6 ± 8.9 $\mu g/m^3$. Even for these non-susceptible non-high-exposure subjects during non-episodic periods, the $PM_{2.5}$ impacts on HRV are still statistically significant. These findings support further reduction in $PM_{2.5}$ and demonstrate clearly the significant impacts of $PM_{2.5}$ at low levels on healthy adults.

Analysis results revealed that impacts of $PM_{2.5}$ on HRV lasted for about 4.5–5 h with the greatest reduction in SDNN at 1 h and increase in LF/HF at 2.5 h after exposures. Lagged effects of $PM_{2.5}$ on HRV were also observed in previous studies, but with wide variations in impact-lasting duration and time point of peak impact due to different study designs in different climate zones [23, 39–41]. For example, when assessing $PM_{2.5}$ impacts on HRV, studies have observed the largest reduction in SDNN at 30 min for 11 and 9 taxi drivers in Beijing, China, respectively [23, 41]; while another one found the largest reduction in SDNN at 90 min for 16 researchers doing traffic-pollutant studies on the streets of Mexico City [39].

Our work used 5-min averages to demonstrate the advantages of fine time resolution of AS-LUNG-P to assess the lagged effect. However, hourly moving averages of pollutants were used previously to observe their "cumulative" health effects [40]. Since several studies found the largest lagged effect of $PM_{2.5}$ occurred at 30 min [23, 41], fine-resolution data such as 5-min averages shall be used at first to evaluate the lagged effect. If the health impacts were lasting for hours, 30-min or hourly averages could be used to conduct further investigation. Our work focuses on demonstrating the applicability of LCS sensors on $PM_{2.5}$ exposure and epidemiological studies. Thus, applying 30-min or hourly averages for further evaluation is outside our scope. The health damage coefficients of the lagged effects presented in this work may be slightly different if 30-min or hourly averages were used; however, the patterns of the lagged effect shall remain.

It is noteworthy that most environmental epidemiological studies assessed $PM_{2.5}$ impacts on health without considering sources, activities, or microenvironments causing exposures. Thus, no recommendations were put forward to people on actions for reducing their exposures. In particular, many nearby $PM_{2.5}$ exposure sources in Asian environments are located in residential areas and originate from people's daily activities [21]. However, ordinary citizens have little idea on what high $PM_{2.5}$ activities are. In this study, high-exposure sources were identified and their exposure contributions quantified; these scientific evidences could be used for source control strategies and behavioral change advices. In addition, more unknown or suspected sources could be quantified with this method, especially in developing countries with sources different from those in developed countries.

Reducing ETS has been a big social movement in Taiwan for the past 30 years; Taiwan has banned smoking in any public buildings with more than three persons in a room. Smokers have to smoke in designated areas outside the office buildings or in their private offices. Therefore, talking in or passing by smokers' offices at work was the top microenvironments with ETS exposure, followed by waiting for buses and passing by smokers during commute. Although the exposure frequency of these subjects was low (Table 1, Panel b), ETS was identified to be the exposure source with the highest $PM_{2.5}$ increment.

Our previous work found that the contribution of restaurants and temples 2–3 m away to $PM_{2.5}$ levels were 6.33 and 15.1 μg/m^3, respectively [42], which are higher than the current estimations. Different study designs may result in discrepancy, with previous observations made 2–3 m away from the sources and current exposure assessed with subjects perhaps more distant from the sources. The numerical differences between such observations were not huge; and both indicated statistically significant $PM_{2.5}$ contributions of these exposure sources in the vicinity.

AS-LUNG-P could also be employed to assess certain suspected exposure sources with challenging characteristics that expensive research-grade instruments cannot handle. For example, emissions from wax candles containing $PM_{2.5}$ would condense on the mirrors and interfere with measurements made according to light-scattering principles. This contamination on mirrors necessitates professional cleaning or even replacement. Cooking fumes also contain oily materials which may contaminate sophisticated instruments. Researchers using AS-LUNG-P are less inhibited from studying these challenging sources due to budget consideration as the replacement cost is low. The fine time resolution of AS-LUNG-P down to 15 s also allows detailed assessment on those understudied sources.

The characteristics of these novel sensing devices including small size, light weight, and free of noise and vibration allow subjects to behave naturally following their routine daily activities and enable scientists to evaluate close-to-reality exposure patterns and exposure–health relationship. Nevertheless, due to inexperienced handling, subjects' movement, and sweating, loss rate of Rooti data was relatively high (15.9%). After practice and improvement in using Rooti, the average data loss rate in subsequent studies reduced to <10%. For AS-LUNG-P, only 0.2% of data were lost and no ghost peaks found. Low data loss rates indicate good applicability of these LCS devices.

There is always a concern whether temperature and humidity would affect our findings. In this work, PM data were corrected based on side-by-side comparisons with GRIMM; the correction equations were not depending on temperature and humidity within the conditions of side-by-side comparisons. R^2 of side-by-side comparisons were very good (0.978–0.989) in the range of 26.2–40.6 °C and 39.7–81.2% RH. Detailed discussion about the impacts of humidity on PM data of AS-LUNG was presented in another recent publication [32]. In short, there exists an intrinsic difference in $PM_{2.5}$ concentrations obtained using sensors with light-scattering principles and those measured by filter-weighing sampling devices with dehumidifiers installed before filter collection. Water droplet by definition is an aerosol. USEPA has specified controlling filter weighing within 30–40% RH for regulatory purpose [43]. Nevertheless, another USEPA document pointed out that LCS devices can also serve purposes other than regulatory such as personal exposure research [44]. Actually, we argue against the need for humidity control in exposure assessment because the $PM_{2.5}$ inhaled contains water droplets which should be taken into account in view of its health impact. As $PM_{2.5}$ exposure assessment conducted in this study is not for regulatory purpose, the humidity level is thus not controlled for. We specified the actual temperature and humidity conditions during the field campaigns in the "Results" section and Supplementary Materials Table S1 and our findings were obtained under those conditions.

This study has several limitations. First, some AS-LUNG-P sets were carried by the subjects in handbags, near the waist or even lower while walking; $PM_{2.5}$ exposure assessed may be slightly different from that in the breathing zone. To resolve this issue, a proper chest strap customized for AS-LUNG-P was designed to allow exposure sensing in breathing zones for future research. Second, 43 points (0.13% of the total sample size) with higher values (>150 μg/m^3) were removed due to the limited range of the correction curves. It was decided that higher levels shall be covered in future side-by-side comparison of AS-LUNG-P and GRIMM. In the current work, removing these observations may result in underestimating $PM_{2.5}$ contribution of certain exposure sources, which may be negligible due to small percentages. Third, the overall data loss rate for Rooti was 15.9%. However, the final analysis results shall not be affected because data loss occurred randomly and was not associated with $PM_{2.5}$ levels.

Fourth, psychological factors such as stress and anxiety and nutrition would affect HRV [45–47]. The HRV impact of nutrition was somewhat represented by the impact of BMI evaluated in this work, while the impacts of psychological factors were not assessed. Nevertheless, unless the HRV impacts of psychological factors occurred always concurrently with $PM_{2.5}$ exposures and increased along with $PM_{2.5}$ increase, the obtained coefficients of exposure–health relationships would not be affected by these factors. Finally, other co-pollutants were not measured; thus, their impacts on HRV cannot be adjusted. The obtained coefficients of exposure–health relationships may represent the synergic effects of $PM_{2.5}$ plus those co-pollutants, as discussed in literatures [39, 48]. Nevertheless, since the levels of other co-pollutants (such as CO and NO_2) in Taiwan were much lower than the air quality standards [49], the observed HRV impacts were most likely due to $PM_{2.5}$ rather than other co-pollutants.

Application of LCS devices to $PM_{2.5}$ environmental health research has been limited due to skepticism on data quality. This study used $PM_{2.5}$ obtained from LCS devices, AS-LUNG-P, after correction with research-grade instruments, and measured health indicators with certified non-invasive medical devices, Rooti. Our results demonstrated good applicability (such as stability and wearability) of these devices. In addition, for mean $PM_{2.5}$ exposure levels of $12.6 \pm 8.9\ \mu g/m^3$, statistically significant reduction in SDNN (3.68%) and increase in LF/HF (3.86%) were found for these 33 healthy adults. Above $30\ \mu g/m^3$, the impacts on SDNN were even stronger. Moreover, subjects with BMI ≥ 24 would experience much stronger reduction of 17.9% (4.36, 29.6%) in SDNN than those with BMI < 24. Summer and exposing to solar radiation would also enhance impacts on HRV. Furthermore, the top three exposure sources identified were ETS, incense burning, and cooking with contributions to $PM_{2.5}$ increments ranging from 3.52 to $8.53\ \mu g/m^3$ at 30-min intervals.

In summary, this work is a pioneer in using newly developed LCS environmental and biological devices to quantify incremental $PM_{2.5}$ contributions from sources and to evaluate exposure–health relationships. To overcome the limitation of $PM_{2.5}$ from AS-LUNG-P in data accuracy, individual side-by-side comparison with research-grade instruments needs to be carried out, which was somewhat labor intensive and time consuming. Nevertheless, this work demonstrates that these devices have great potentials in wide applications to exposure assessment and environmental epidemiology, especially for developing countries with high $PM_{2.5}$ levels, distinctive understudied sources, and limited resources. Significant breakthrough in exposure assessment and environmental epidemiology is expected with these new scientific tools.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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