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Research Article

Evaluation of a Thermal-Based Flow Meter for Assessment of Mobile Resting Metabolic Rate Measures

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This work evaluates the use of a new flow meter to assess exhalation rate. A mobile indirect calorimeter (MIC) was designed and used to measure resting metabolic rate (RMR), which relies on the measure of O_2 consumption rate (VO_2) and CO_2 production rate (VCO_2). The device was produced from a commercially available and well-established indirect calorimeter and implemented with a new flow meter for the purpose of this study. VO_2 and VCO_2 were assessed by measuring exhalation rates using the new flow meter and O_2 and CO_2 concentrations in breath using the original colorimetric sensors of the indirect calorimeter. The new flow meter was based on a thermal flow meter (TFM) affixed to an orifice with a diameter of 6.8 mm used as a passage for exhaled breath from 16 subjects. The results were compared with a metabolic cart (Medical Graphics), which was connected in series to the modified device. We found that 69% of the results had more than a 10% difference between the modified MIC device and the reference instrument, suggesting that the sensitivity of the thermal flow meter changed over time, which precluded its use as a flow meter for breath flow rate measurement.

1. Introduction

Resting metabolic rate (RMR), also known as resting energy expenditure (REE), is defined as the amount of energy expended by a person at rest [1]. RMR typically represents over 65% of total daily energy expenditure (TEE), and the percentage can be as high as 80–90% of TEE for sedentary people [2]. Therefore, evaluating an individual's RMR is important to help assess the daily caloric intake need for weight management. The most well-established method to assess RMR is indirect calorimetry, which determines RMR based on the oxygen consumption rate (VO_2) and carbon dioxide production rate (VCO_2), via the Weir equation [3]. Traditional indirect calorimetry instruments, such as metabolic carts, are expensive and bulky and require frequent calibration and trained personnel for correct use. To avoid using such equipment, equations were created to estimate RMR from a person's age, gender, weight, and height [4]. However, it has been shown that the use of these equations could result in estimations that are 600–900 kcal/day off from the true values measured with indirect calorimetry [5].

To overcome the above problem, a mobile indirect calorimeter was developed to facilitate personal use for RMR tracking [6, 7]. The device uses a differential-pressure-based flow meter and a colorimetric-based chemical sensor to determine VO_2 and VCO_2. Breath is delivered into the sensing chamber, where the O_2 and CO_2 react with a sensor chip, inducing color changes for determining exhalation O_2 and CO_2 concentrations. VO_2 and VCO_2 were calculated based on the breath O_2 and CO_2 concentrations and breath flow rate. The performance of the device and colorimetric sensor has been validated by over 300 measurements against the gold standard, the Douglas bag method [7]. In addition, this mobile indirect calorimeter has been further used in human subjects to confirm functionality [8, 9].

In order to investigate an alternative to the existing technology, we modified the commercial device to explore the utility of a new flow sensor for breath analysis.

Some commonly used flow meters are described as follows: (1) Fleisch-type meters use small capillary tubes to create laminar flow, which provide good linear relation, but they suffer from clogging and are hard to clean [10]. (2) Orifice-differential-pressure-sensor-based flow meters are simple, robust, and inexpensive, but they might offer high flow resistance [11]. (3) Variable-orifice flow meters provide less flow resistance by having an orifice size proportional to the flow [12]. However, they are prone to wearing out mechanically over time. (4) Pitot tube flow meters are inexpensive and have very low flow resistance, as their flow rate is proportional to the stagnation pressure. However, the sensitivity of this kind of tube is usually very low and is limited to low and steady flows [13]. While the field of flow meters has been well studied, flow measurement for breathing conditions with a wide range of flow rates has not been reported systematically, and it is important to investigate the direct breath flow measurement due to special conditions such as temperatures above room temperature and possible condensation from humidity.

In this work, we used an orifice plate (diameter of 6.8 m) combined with a thermal flow meter with the inlet and outlet located before and after the orifice plate for breath flow rate measurement. The thermal flow meter converted differential thermal energy change into flow rate [14]. Unlike other flow meters, a thermal flow meter enables to work at low flow resistances. A comparative study between this modified device and a metabolic cart was conducted to validate the performance of the new system.

2. Methods

2.1. The MIC from This Work. The MIC measured VO_2 and VCO_2 from breath and determined RMR according to the Weir equation [15]. When breath O_2 and CO_2 flow through the sensor chip, they induced a color change on the sensor because of specific chemical reactions. The device had a light source and photodiodes to determine the absorbance change during the chemical reaction. The photodiodes transduced the absorbance of the sensor to a digital signal, which was wirelessly transmitted to a smart device for data processing. The absorbance was calculated by taking the negative logarithm of the signal response from the sensing area ($S_{\text{sens.}}$) divided by the signal response from the reference area ($S_{\text{ref.}}$) as follows:

$$\text{Absorbance} = -\log\left(\frac{S_{\text{sens.}}}{S_{\text{ref.}}}\right). \tag{1}$$

A built-in calibration curve converted the absorbance to corresponding fraction of exhaled O_2 concentration (FEO_2) and fraction of exhaled CO_2 concentration ($FECO_2$). As mentioned above, our new flow meter implemented into the device allowed the measurement of the exhalation breath rate (VE), which was used to calculate the oxygen consumption rate (VO_2), carbon dioxide production rate (VCO_2), and RMR through the following equations:

$$\begin{aligned} VO_2 &= (0.2093 - FEO_2)\cdot VE, \\ VCO_2 &= (FECO_2 - 0.0003)\cdot VE, \\ \text{RMR (kcal/day)} &= [3.941(VO_2\ (\text{L/min})) \\ &\quad + 1.11(VCO_2\ (\text{L/min}))] * 1.440, \end{aligned} \tag{2}$$

where FEO_2 is the breath O_2 concentration typically measured between 0.13 and 0.19 and $FECO_2$ is the breath CO_2 concentration typically measured between 0.03 and 0.06. The fraction concentration of O_2 in the atmosphere is assumed to be 0.2093, and that of CO_2 to be 0.0003 based on the typical atmospheric condition [16]. Since the inhalation volume and exhalation volume are very close, we also assumed that they were the same in the calculation. Lastly, a built-in fan dried the flow tube to avoid water condensation buildup between measurements.

2.2. The Flow Meter on This Work's MIC. The flow meter of the MIC, TFM, was an off-the-shelf electronic component obtained from Omron® (part number: D6F-P0010A2 [17]). It was located with the inlet and outlet connected to the exhaled breath channel in the upstream and downstream portion at each side of the 6.8 mm orifice plate. The temperature output from a thermopile or thermistor in the TFM is based on its electrical voltage change, which was subsequently measured by the microcontroller analog-to-digital converter. The TFM utilized the transduction of energy change to voltage change to measure flow rate. Usually in a TFM, there are two thermistors in the flow tube: the reference thermistor, which measures the temperature of the incoming gas called the reference temperature (T_0), and the hot thermistor, which is driven by a current to raise its temperature (T_R) to some fixed level above the temperature of the gas [14]. In still gas, the hot thermistor loses heat due to energy dissipation (both radiation and convection) to balance the electrical energy that heats the thermistor, stabilizing the hot thermistor's temperature. When the gas is flowing, the heat dissipation constant (K) of the hot thermistor increases and T_R decreases, resulting in an increase in the flow of current. The driving circuit senses the change in the current and raises the voltage (V) across the hot thermistor to maintain a fixed temperature difference between the reference thermistor and the hot thermistor, which is described by the following equation [18, 19].

$$V = \sqrt{KR[T_R - T_0]}, \tag{3}$$

where R is the resistance.

Alternatively, two thermopiles (one upstream and the other downstream of the gas flow) and a heating element in between the thermopiles can be used. This approach can simplify the required circuitry. When there is no gas flow, the temperature as measured by the two thermopiles is the same. As gas flows, the upstream temperature (T_0) is expected to be lower than the downstream temperature (T_R). The resulting temperature profile converted to voltages will allow gas flow

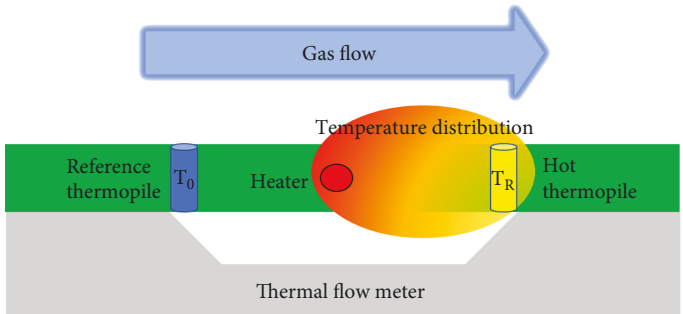

Figure 1: Schematic of a thermal flow meter.

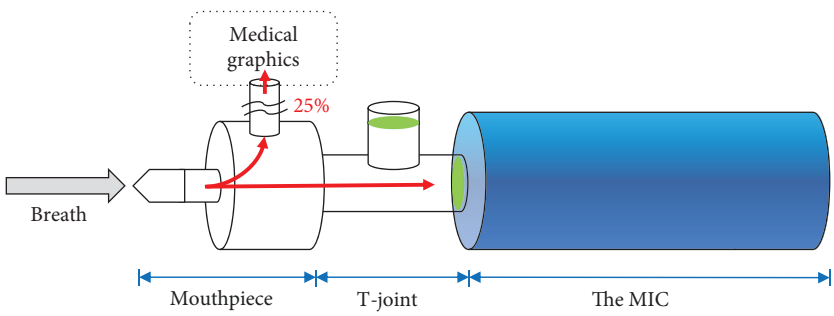

Figure 2: The schematic of sequence of how the MIC is connected to the MG.

rate to be determined. The TFM used in this project uses the thermopile approach (Figure 1).

After placing the new TMF in the MIC, a calibration curve was built between the voltage and flow rate for a range from 20 L/min to 120 L/min, using dry air. The flow rate was integrated over time to assess the total volume which was used as the criteria to determine the amount of breath to be used. The measurement of flow was set to be stopped when a total volume of 30 L was collected. The reference flow used in the calibration was a commercial flow sensor (Mass Flow Sensor SFM3000, Sensirion).

2.3. Metabolic Cart Used as a Reference Instrument. Metabolic carts are commonly used in hospitals to measure the individual's RMR. Here, we used Medical Graphics (MG) Ultima™ Cardi® as the reference equipment. This instrument provides RMR measurement based on breath-by-breath analysis, is FDA-cleared, and is typically used for assessments of patients' RMR or energy expenditure under exercise conditions at institutions such as Mayo Clinic. To validate the new MIC, 16 subjects were recruited (see details below) and measured by connecting the mouthpiece of the MG to the MIC in sequence with a T-joint, which only allowed exhalation breath to go through (Figure 2). Unlike the MIC, the MG only samples in an average of ~25% of the breath for breath O_2 and CO_2 measurement. Therefore, a factor of 1.25 was applied to the exhalation rate (VE) measured by the MIC (accordingly to VO_2, VCO_2, and RMR) to compensate for the loss of the breath.

2.4. Subjects. Sixteen (16) healthy adults, including 9 males and 6 females, were included in the study. The number of subjects was chosen to discriminate average RMR of 1800 and 2000 kcal/day with a standard deviation of 200 kcal/day (typical clinical variability) and to reach a power of 0.80 and an alpha of 0.05. The subjects' age ranged from 27 to 57 years, and BMIs ranged from 18 to 46 kg/m^2. The measurements of the resting metabolic rate were performed early in the morning following a standard clinical protocol approved by the Institutional Review Board of Mayo Clinic (IRB protocol number 16-003321). The protocol required subjects to fast with no strenuous exercise for the last 12 hours or no moderate exercise for 4 hours prior to the measurement. The subjects remained in a comfortable sitting position in a darkened room with room temperature at ~23°C. The subjects were asked to rest for 30 minutes before the measurement and then to breathe normally through the setup (Figure 2) and during the measurement.

3. Results

Based on the experience from other studies [5, 8, 9], predicative RMR equations such as Mifflin-St. Jeor or Harris-Benedict are average population estimations based on the physical characteristics of the subjects (age, gender, height, and weight) and do not necessarily represent actual measured RMR values. In the case of this study, similar conclusions have been found. Table 1 shows the comparison between the RMR calculated by the Mifflin-St. Jeor equation (MSJE) [20] and the RMR measured with our reference instrument, Medical Graphics (MG). As it can be observed, absolute differences ranging from 20% to 41% were observed for most of the subjects (11/16, ~68% of the subjects). These

Table 1

Subject number	Weight (kg)	Height (cm)	Age (yr)	Gender	MSJE RMR (kcal/day)	MG RMR (kcal/day)	Difference: MG RMR − MSJE RMR (kcal/day)	Differential percentage: (MG RMR − MSJE RMR) /MG RMR ∗ 100% (%)
1	68	170	46	F	1968	1758	−210	−11
2	85	190	27	M	2335	2547	211	9
3	60	163	27	F	1751	1997	246	14
4	84	189	27	M	2319	2983	664	29
5	61	164	27	F	1767	2315	548	31
6	66	161	59	F	1956	1150	−806	−41
7	111	180	47	M	2631	2133	−498	−19
8	48	161	50	F	1732	1366	−366	−21
9	83	176	58	M	2381	1694	−687	−29
10	150	183	57	M	3089	2261	−827	−27
11	66	161	54	F	1931	1218	−713	−37
12	102	182	52	M	2578	1700	−879	−34
13	102	159	45	F	2234	1706	−528	−24
14	101	175	56	M	2544	2510	−35	−1
15	78	186	57	M	2388	1808	−580	−24
16	110	186	57	M	2708	1983	−725	−27

MSJE RMR = resting metabolic rate calculated based on the Mifflin-St. Jeor equation: for women: 10 × weight (kg) + 6.25 × height (cm) − 5 × age (y) − 161; for men: 10 × weight (kg) + 6.25 × height (cm) − 5 × age (y) + 5. MG RMR = resting metabolic rate measured by Medical Graphics.

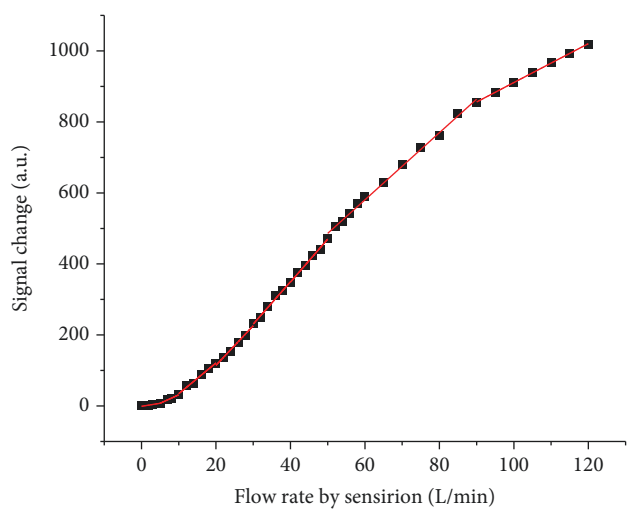

Figure 3: The calibration curve of the flow rate ranging from 0 to 120 L/min.

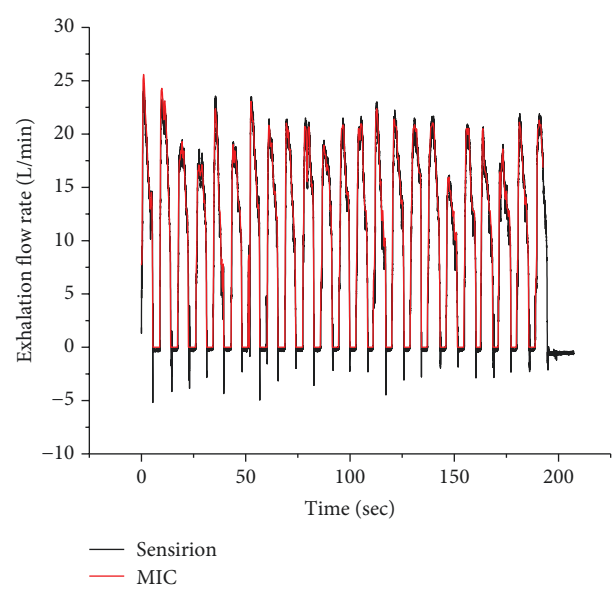

Figure 4: A breath-by-breath exhalation flow rate monitoring was measured by our modified device and Sensirion.

differences translated into energy expenditure assessments with differences between 300 and 880 kcal/day, which is a significant amount that could cause weight gain in someone targeting weight loss. For this reason, we believe that the only way to assess the true RMR of an individual is through measuring it. Indirect calorimetry is the recommended method. Therefore, the goal of this paper is to compare the results between a modified self-designed device and a solid well-established reference indirect calorimetry method.

Figure 3 shows the calibration curve of the new MIC. Since the built-in calibration curve ranging from 0 to 120 L/min was not linear, it was divided into 7 linear segments (0–10, 10–20, 20–30, 30–40, 40–50, 50–90, and 90–120 L/min) to optimize the performance of the firmware of the device and reduce calculation time.

Figure 4 shows the example of breath exhalation flow rate (VE) measured by the MIC and the reference Sensirion flow sensor. The exhalation flow rate measured by the new MIC was recovered by using the calibration curve built from the Sensirion flow sensor and corrected by standard pressure and dry conditions before the comparison. The interrogation

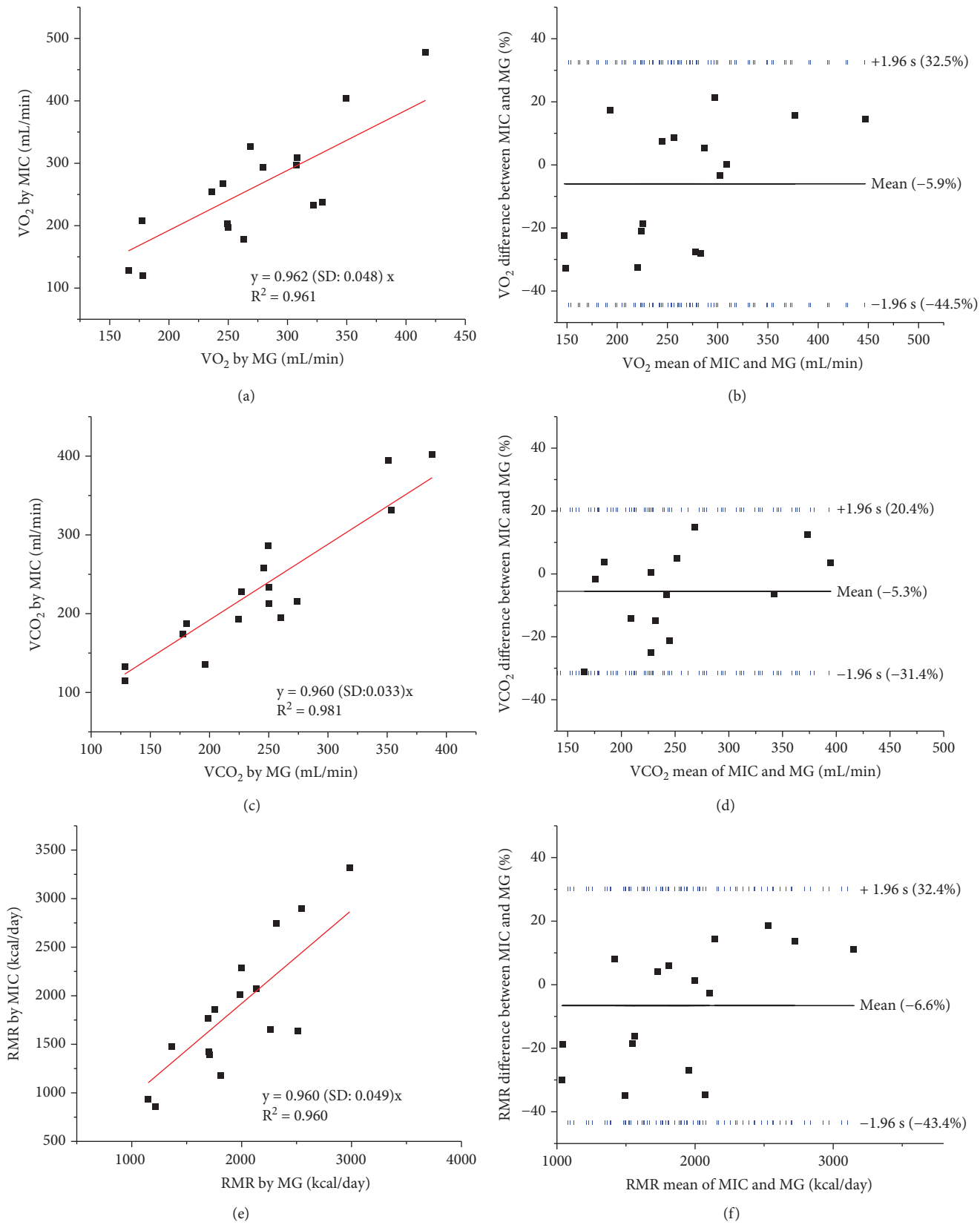

Figure 5: Comparison between the new MIC and the MG instrument. Linear correlations and Bland-Altman analysis for VO_2 (a, b), VO_2 (c, d), and RMR (e, f).

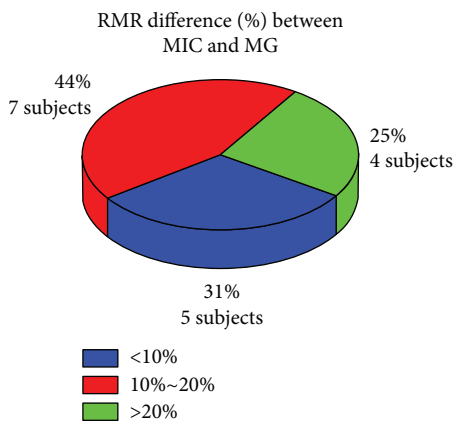

Figure 6: Pie chart distribution for RMR difference (%) between the modified MIC and MG.

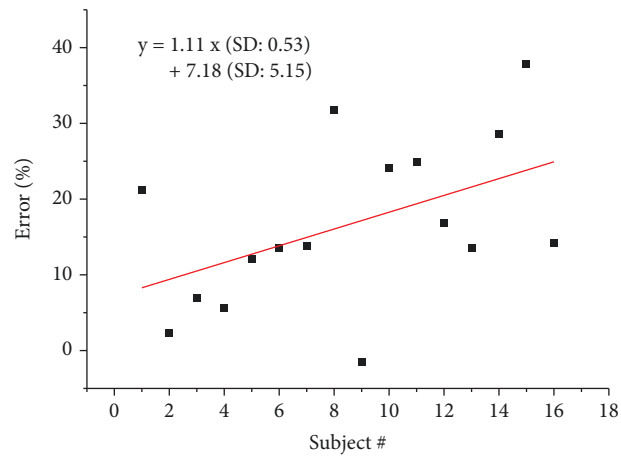

Figure 7: Absolute percentage difference of VE between the MG and MIC calculated as error (%) = $|(VE_{MIC} - VE_{MG})/VE_{MG} * 100\%|$ for each subject. The subjects 1–16 were measured between a period in time starting on February 20, 2017, and ending on February 05, 2018.

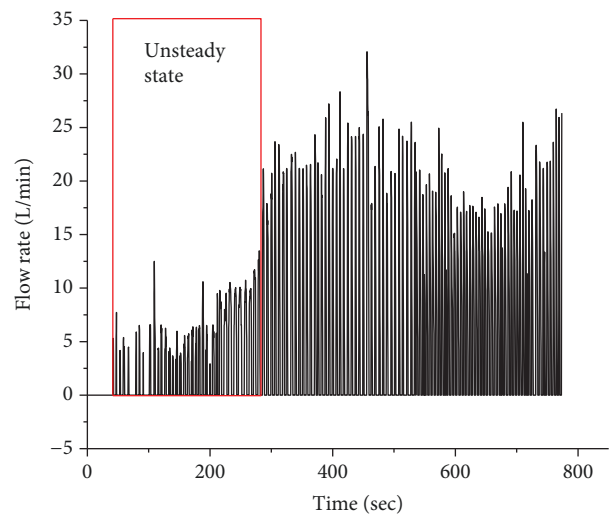

Figure 8: An example of a breath flow rate recording on the modified MIC after the performance degradation was detected.

showed the ability of the device to monitor exhalation flow rate in a breath-by-breath manner. Note that this accuracy was maintained during the first 10 weeks of the use of the flow meter. However, a degradation of performance was observed over time as shown as follows.

To evaluate the performance of the new MIC over time, 16 subjects' RMR were measured using the MIC and the MG simultaneously. As mentioned before, a factor of 1.25 was applied. Figures 5(a), 5(c), and 5(d) show that VO_2, VCO_2, and RMR measured by the new MIC and the MG correlated very well. All of them had a regression coefficient (R^2) greater than 0.96. On average, the measured RMR from the MIC were about 5.9% less than that from the MG for VO_2, 5.3% for VCO_2, and 6.6% for RMR. Figures 5(b), 5(d), and 5(f) show the Bland-Altman plot of the percentage difference between the new MIC and the MG for VO_2, VCO_2, and RMR defined as $(MIC - MG)/MG * 100\%$. All the results for VO_2, VCO_2, and RMR were within the range of the mean value ± 1.96 standard deviation, showing a reasonable performance. However, we identified that ±10% should be a practical acceptance limit of performance since ±10% is the physiological variability of RMR [16], and therefore, percentage differences larger than ±10%, which were observed for VO_2, VCO_2, and RMR, were found to be inadequate for the acceptance criteria of good performance.

In order to quantify the lack of the new MIC device's performance, we further analyzed the results, defining three categories based on absolute percentage differences: (a) <10%, (b) 10–20%, and (c) >20%. Figure 6 shows a pie chart that categorizes the absolute percentage difference between the measured results from the new MIC and the MG. Twenty-five percent (25%) of the measurements had a difference larger than 20%, 44% had a difference between 10 and 20%, and only 31% had a difference within ±10%. In summary, 69% of the measurements had a difference of over 10%.

As mentioned before, we analyzed the exhaled O_2 and CO_2 concentration outputs from the modified MIC vs. the MG, and no significant difference was found (not shown). However, we found the difference to be caused by VE (see more details below). In fact, we noticed a degradation of the VE performance from the TFM over time. Figure 7 shows the error of VE between MG and MIC on each subject over the period of use. A clear increase in error was built up over time (as the number of subjects increased), with VE measured from the modified MIC systematically lower with respect to VE from MG.

Figure 8 shows a breath-by-breath example of the measurement of a subject with the modified MIC after the performance degradation was detected. As opposite to the patterns observed before the degradation where relatively constant maximum exhalation rates were observed in each cycle from the beginning to the end of the measurement (see Figure 4), this pattern shows significantly lower exhalation rates at the beginning of the measurement. The recorded flow rate before 280 seconds was about 2 times lower than the flow rate recorded after in the remaining second portion of the measurement. Further investigation needs to be done to learn

more about this phenomenon, and only a hypothesis can be discussed at this time.

A possible reason for failure is that the condensation of moisture in breath over time may cause damage in the TFM's thermopile and the mechanisms involved to reach adequate behavior. Before the start of the measurement, the humidity around the thermopiles is the same as the humidity of the environment. After the measurement starts, a sudden disturbance from the moisture of breath condensing on the surface of thermopiles takes place.

In a new TFM, the thermopile seems to be immune to humidity condensation (probably due to hydrophobic coatings). In a used TFM, the thermopiles may suffer from a damage of their coatings and a breath humidity condensation, which is a phase change that releases heat, and may dramatically change the energy flow, changing the TFM working conditions and causing an erroneous reading. As the measurement continues, the condensation reaches a steady state and no longer perturbates the system with further heat release, and therefore, the temperature in the system would reach equilibrium so that the TFM can function correctly.

Using tubing before the flow meter inlet to trap humidity could possibly reduce the condensation onto the thermopiles. In addition, a systematical correction algorithm can also be applied to accommodate the effect of condensation. These modifications are possibilities to mitigate the abovementioned problems. However, the TFM in its current form is not suitable to be used as a flow meter for a gas sample that has high humidity or temperatures significantly different from ambient temperatures.

4. Conclusion

To conclude, we observed a 6.6% underestimation of the RMR output in the new MIC. Although the initial calibration of the TFM sensor done at a range from 0 to 120 L/min rendered accurate values with respect to reference commercial flow meters, the original calibration failed to be applied after using the TFM over a period of 3-4 months. Furthermore, VO_2 and VCO_2 were measured to render RMR measures by the modified MIC and MG in parallel, and 69% of the measurements showed a difference between the two methods that was greater than 10%, which could have been caused by moisture from the breath collection or from the degradation of the TFM sensitivity to the flow. Further investigation needs to be done to confirm this assumption. Nevertheless, the TFM is not suitable for highly humid gas sample measurement, such as human breath.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

E.F., X.J., D.B., F.T., and N.T. work for Breezing™, an indirect calorimeter tracker used as a base device of the modified indirect calorimeter device studied in this work. All other authors declare that they have no conflict of interest.

Authors' Contributions

Nai-Yuan Liu and Yue Deng contributed equally to this work.

Acknowledgments

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