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What do masks mask? A study on transdermal CO₂ monitoring

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ABSTRACT

Medical professionals have complained of extreme discomfort and fatigue from continuous wearing of N95 respirators (N95) overlaid with surgical masks (SM) and face shields (FS) during COVID-19 pandemic. However, there are no reports on the effect of face coverings on transdermal CO₂ (TrCO₂) levels (a measure of blood CO₂) during moderate activity. In this study, real-time monitoring of TrCO₂, heart rate and skin surface temperature was conducted for six subjects aged 20–59 years with and without personal protective equipment (PPE). We initially studied the effect of wearing PPE (N95+SM+FS) at rest. Then, the effect of moderate stepping/walking activity (120 steps per minute for 60 min) while wearing PPE was evaluated. In addition, we investigated the effect of exercising intensity with different masks. We observed a significant difference (p < 0.0001) in TrCO₂ levels between without and with PPE during moderate exercise, but not while resting. TrCO₂ levels were correlated to exercise intensity independently with masking condition and breathability of masks. For the first time, we present data showing that a properly fitting N95 worn along with SM and FS consistently leads to elevated TrCO₂ under moderate exertion, which could contribute to fatigue over long-term use.

1. Introduction

The ongoing pandemic has led to widespread implementation of mandates to wear masks especially in indoor public spaces. The WHO has similarly recommended when and how to use facemasks [1] on a daily basis, which has led to mask wearing in situations not previously considered. Recent studies have claimed that community use of facemasks and implementation of mandates [2] resulted in more than 200,000 COVID-19 cases being averted by May 22, 2020, and modelling studies [3] on universal masking forecast to save an additional 129,574 lives from September 22, 2020 through the end of February 2021. Medical professionals have routines adopted face-shields in addition to double-masking. Double-masking for the general public has been recommended as COVID-19 variants have emerged.

Even as clarity on the efficacy of facemasks in inhibiting airborne transmission of COVID-19 is emerging, [4] a Danish randomized controlled trial has found that wearing of a surgical mask (SM) in a community with modest infection rates did not reduce the infection rate by more than 50% [5]. There is even more ambiguity regarding blood gases, specifically the impact on gas exchange of carbon dioxide (CO₂) and oxygen (O₂) imposed by facemasks, under moderate exertion. A recent meta-review reported the effects of different facemasks and the cardiorespiratory response to physical activity, which suggested that dyspnea might increase and modify apparent effort with activity. However, it was concluded that the effect on blood gases imposed by facemasks during physical activity is trivial and negligible to detect, even while performing vigorous exercise [6]. Another study has presented no significant changes in gas exchange, O₂ saturation or CO₂ levels with the use of SM even in subjects with severe lung impairment [7]. Further, in a small crossover study, no decline in O₂ saturation was observed in older participants wearing a 3-layer nonmedical facemask [8]. Additionally wearing a mask for an average of 90 min during a flight-training mission does not appear to increase CO₂ retention in the body or the ability to attain O₂ [9]. However, study on the use of FFP-2 respirator with SM cover by healthcare workers during this COVID-19 outbreak has been found to

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significantly increase the end-tidal CO$_2$ and fractional inspired CO$_2$ pressure values, without any disease while in resting position \cite{10}. Another study also showed CO$_2$ in mask increase with facemasks but remains below short-term National Institute for Occupational Safety and Health limits \cite{11}. More comprehensive studies need to be undertaken for drawing meaningful conclusions in light of certain other studies that claim facemasks reduce O$_2$ availability, prevents exchange of CO$_2$ and results in hypercapnic and hypoxic conditions while exercising \cite{12,13}. Close monitoring of respiratory status is critical, especially since there has been an increase in the use of respirators with high filtering performance, (i.e., N95-type), that are also associated with several concerns relating to physiological effects \cite{14}, including silent hypoxia and poor oxygenation \cite{15} during early stages of COVID-19. Despite vaccination rates steadily increasing, experts are suggesting that mask wearing continue for everyone and certainly for frontline workers.

In the current study, we present the results from real-time measurement of transdermal CO$_2$ (TrCO$_2$) levels during exercising and resting conditions, while wearing PPE face coverings. The transdermal measurement approach was chosen as it is non-invasive and the face covering would not be impeded. It has also been previously validated to be reflective of blood CO$_2$ levels \cite{16}. Usage of the word ‘exercise’ in this study implies moderate activity/execution of routine tasks. Our study has broad implications related to health and wellbeing, especially during this COVID-19 pandemic. However, our findings are more pertinent to healthcare workers, due to their constant usage of single-use N95 covering would not be impeded. It has also been previously validated to be reflective of blood CO$_2$ levels \cite{16}. Usage of the word ‘exercise’ in this study implies moderate activity/execution of routine tasks. Our study has broad implications related to health and wellbeing, especially during this COVID-19 pandemic. However, our findings are more pertinent to healthcare workers, due to their constant usage of single-use N95 together with SM and patterns of exertion. For the first time, we present a path towards a wearable transdermal CO$_2$ sensor.

2. Experimental section

2.1. Systems and experimental design

TrCO$_2$ emission rate could be influenced not only by using PPE but also by other factors. To take these effects into account, room temperature (RT) and relative humidity (RH) sensors (GSP-6, Elitech, USA) were installed in the experimental environment, and subjects wore a a skin surface temperature (SST) sensor (GSP-6) and a TrCO$_2$ sampler on the inner side of the forearm, along with a heart rate (HR) sensor (H1, Polar, Finland) on the chest (Fig. 1A). Fig. 1B shows a simplified diagram of previously developed rate-based TrCO$_2$ measurement system \cite{17}. The system automatically repeats a purging process with pure N$_2$ aeration for 30 s and recirculation for 60 s. During recirculation, CO$_2$ continuously diffuses across the skin through the contacting aperture of the sampler using N$_2$ as the carrier. The CO$_2$ concentration in the recirculated N$_2$ increases according to various parameters, including blood CO$_2$ concentration. TrCO$_2$ emission rate can hence be monitored every 90 sec in real-time. In this system, a new design of the TrCO$_2$ sampler with a spiral channel was adopted to improve the efficiency of TrCO$_2$ extraction without heating the skin (Fig. S1). Fig. S2 presents the collection arrangement used to obtain the preliminary results which demonstrate good stability of the system. We used this experimental platform to perform a two-pronged study: static and dynamic measurements, as presented in Fig.1C. The static study examined the effect of PPE wearing on TrCO$_2$ under stable conditions. In contrast, the dynamic study examined the effect of PPE wearing upon significant changes in activity, imitating work and exercise.

This study was authorized by the Institutional Review Board at the University of Maryland, Baltimore County (Protocol Number 89) was in accordance with the latest version of the Declaration of Helsinki. Healthy volunteers (five male and one female) were enrolled in this study after obtaining a written informed consent. Table S1 provides the details on the subjects obtained using a questionnaire prior to conducting the experiments. Age (in years) and BMI (kg/m$^2$) differed by $38.7 \pm 14.5$ and $24.8 \pm 5.5$, respectively (mean ± SD). Data analysis was performed using R software (cran.project.org) version 4.0.0. The PPEs

![Fig. 1. Systems and experimental design.](image-url)
used in this study (Fig. S3) along with other experimental methods are described in the supplementary appendix. During the scheduled experiments conducted in triplicates, the six subjects were first provided with testing instructions, familiarized with the collection system and provided with quantitative fit-tested respiratory devices. The subjects maintained similar diet and fluid intake during all the testing phases of the study.

2.2. Static study

In this study, experiments were initiated within 2 h of the subjects’ meals. The study subjects first rested on a chair with the wearable sensors on and without a mask for 30 min. They were then asked to wear N95 (3 M, USA) overlaid with a SM, a face shield (FS) and asked to rest on the chair for 30 min. Finally, the subjects were asked to remove the PPE and continue to rest on the chair for another 30 min. Data acquiring was done in triplicates and each of the subjects completed the experiments on separate days.

2.3. Dynamic study

In this set of experiments, the diet conditioning of the study subjects was the same as in the case of the static study. Here, the study subjects first rested on a chair with the wearable sensors and without wearing a mask for 30 min. In the second phase involving exercise, the subjects were asked to maintain a step rate of 120 steps per minute (spm), audio click) for 60 min. The exercising phase had two patterns: controls (without PPE) and while wearing N95 overlaid with SM and FS. The mask-fitting check was manually done by the subject, and then visually inspected by the investigators. Finally, the subjects sat on the chair for 60 min without a mask for both patterns of the exercising phase. Armpit temperature (AT) and oxygen saturation (SpO2) was measured every 10 min in addition to data acquisition from the other sensors, as described in the static study design. Each subject performed two sets of experiments (exercising phase without and with masks) per day. The order of exercising patterns was randomized. The complete protocol was implemented for three days with at least one rest day in between.

3. Results

3.1. Effect of wearing PPE on TrCO$_2$ and HR while resting

Fig. 2A shows the typical time course variation of TrCO$_2$, HR, RT, RH, and SST parameters. We have defined the three 30 min phases concerning before, during, and after PPE wearing as P1, P2, and P3, respectively. The environmental parameters, HR, and SST were observed to be stable through the 1.5 h of experiments. TrCO$_2$ rate was stable in both of these conditions throughout the experiment. SST was the same as in the case of the static study. (Fig. S2). There are no significant differences in both TrCO$_2$ and HR parameters with confidence intervals of 95% (Fig. 2B). Moreover, we did not observe any differences in other study subjects beyond individual differences.

3.2. Time course studies on TrCO$_2$ emission rate without and with PPE during rest and moderate activity

The supplemental video 1 shows the record of one experiment pertaining to Section 3.4 for reference. The only PPE wearing condition and stepping rate is differed from the experiment in this section. Fig. 3A and B present the variation in TrCO$_2$ rate, HR, RT, RH, SST, and AT overtime when exercising without PPE (control) and with concurrent wearing of N95, SM, and FS. The two sets of experiments were conducted on the same day with a study subject. P1’, P2’, and P3’ are phases of resting before exercise without PPE, during exercise, and resting after exercise without PPE, respectively. Subjects performed 120 steps per minute (spm) of stepping exercise during P2’ without (Fig. 3A) and with PPE (Fig. 3B). RT and RH were similar during each experiment. AT was stable in both of these conditions throughout the experiment. SST decreased on cooling due to sweat vaporization that occurred during P2’, ΔTrCO$_2$ and ΔHR were defined as the difference between the minimum value obtained in the 0–30 min range and an average value of 80–90 min. TrCO$_2$ emission rate began to increase approximately 10 min later, after the onset of stepping, and was observed in both conditions to converge to a nearly plateau value during P2’ and then recovered to baseline in P3’.

3.3. Effect of wearing PPE on TrCO$_2$ in different study subjects while exercising moderately

Five subjects showed significant differences in TrCO$_2$ emission rate between the non-masked and masked (N95+SM+FS) conditions.

![Fig. 2. Effect of PPE on TrCO$_2$ rate and vitals while resting. (A) A typical variation in TrCO$_2$ and vitals over time in static conditions observed without and with PPE: N95, SM, and FS. P1, P2, and P3 represent the data before, during, and after PPE wearing, respectively. (B) Comparison of the average TrCO$_2$ emission rate and HR in each of the phases. n.s.: no significant difference.](image-url)
In our six study subjects, only subject 6 did not show a TrCO$_2$ emission rate without PPE, with a cloth mask (CM), and with FS indicated nearly the same value: 0.65 ± 0.05, 0.68 ± 0.07, and 0.63 ± 0.03 ppm/s, respectively. ΔTrCO$_2$ values with N95-only and SM-only was marginally higher (0.91 ± 0.04 and 1.03 ± 0.05 ppm/s) than that of without PPE, with CM, and with FS. ΔTrCO$_2$ levels with N95 covered by SM (1.21 ± 0.06 ppm/s) or SM and FS (1.58 ± 0.05 ppm/s) were higher than the ΔTrCO$_2$ levels of the N95 alone.

4. Discussion

In the resting state, there was no variation in the TrCO$_2$ emission rate, although wearing N95 overlaid with SM and FS (Fig. 2B). Hence, wearing a PPE with higher breathability (e.g., wearing only the N95 respirator) rather than N95 overlaid with SM and FS will definitely not alter the TrCO$_2$ levels while resting. This confirms that rebreathing alone, which can be caused by wearing a PPE, does not seem to have a significant effect on CO$_2$ concentration.

In contrast, during moderate exercise, the TrCO$_2$ emission rate increased even when the subject did not wear a PPE, and a larger increase was induced by wearing N95 overlaid with SM and FS. In our study, we did not use a standard instrument such as an ergometer; however, 120 spm of exercise is in the range of moderate (3 metabolic equivalents; METs) to vigorous (6 METs) exercise [18]. The threshold of exercise intensity at which the TrCO$_2$ levels increase is still debatable on account of large individual differences. Even the CDC has cited the Roberge study that concluded there was no significant difference in pCO$_2$ after 1 h of mild/moderate exercise while wearing N95 alone and in contrast to N95 overlaid with SM, where 2 out of 10 subjects showed a change in pCO$_2$ [19,20]. However, TrCO$_2$ levels can increase significantly as a person exercises moderately while wearing N95 overlaid with SM and FS. Sinkule et al. showed that higher concentration in inhaled CO$_2$ while wearing SM covered N95 compared to N95-only [21]. In our six study subjects, only subject 6 did not show a TrCO$_2$ change.
Fig. 4. Effect of wearing PPE face coverings on TrCO₂ levels during moderate exercise. (A–F) Time course studies on ΔTrCO₂ without PPE (▲) and while wearing PPE-N95 overlaid with SM and FS (●) in subjects 1–6. N = 3 except for subject 5. Each plot and error bar indicates mean value and SD. (G) Comparison of differential values of ΔTrCO₂ emission rate without and with PPE obtained on the same day. There are six curves represented subject 1 (●), subject 2 (▲), subject 3 (◆), subject 4 (×), subject 5 (■), and subject 6 (∨). Each plot and error bar represents mean value and SD that were calculated with experiments performed on different days. (H) Comparison of ΔTrCO₂ emission rate between without and with PPE in each of the subjects with error bars representing SD. Mean value and SD were calculated from the values at 80–90 min in each experiment shown in (A–F). n.s. represents no significant difference. (I) Comparison of ΔTrCO₂ emission rate between without and with PPE using data from all subjects (six subjects, thirty-two experiments). Boxes, white lines, error bars, and subplots (●) indicate quartile range, median, data range, and individual experimental data, respectively.

Fig. 5. Effect of PPE face coverings breathability on TrCO₂ levels. Time course of ΔTrCO₂ emission rate with various types and overlaying patterns of PPE during 140 spm of stepping exercise: with N95 overlaid with SM and FS (●), with N95 overlaid with SM (◆), with N95 (■), with SM (▼), with FS (+), with CM (×), and without PPE (▲). Each plot and error bar indicates mean and SD calculated with data from triplicate studies.
both without and with PPE (Fig. 4F). This result may also be due to 
individual differences in tolerance to exercise. This subject particularly 
was in the habit of playing soccer, a sport with relatively high physical 
activity. It is hence possible that the subject did not reach the intensity 
threshold for TrCO\textsubscript{2} activity. It is hence possible that the subject did not reach the intensity 
was in the habit of playing soccer, a sport with relatively high physical 
performing moderate exercise. This is especially since TrCO\textsubscript{2} levels can be 
affected not only by blood CO\textsubscript{2} concentration but also by variation in 
SST, blood flow, physical condition, and skin conditions, to name a few. 
\( \Delta \text{SST} \) and \( \Delta \text{HR} \) did not differ significantly between subjects without and 
with PPE (Figs. S4I and S5I). Further, variations of physical and skin 
conditions were negated by executing control experiments (exercising 
without PPE) along with exercising while wearing PPE, on the same day. 
In principle, non-dispersive infrared (NDIR) CO\textsubscript{2} sensors can be affected by 
water vapor in gaseous samples, however, a NDIR CO\textsubscript{2} sensor that 
was used in our study compensated for water vapor interference by 
measuring the reference signal. In addition, a high correlation between 
TrCO\textsubscript{2} and arterial blood gas pCO\textsubscript{2} was measured by the same rate-based 
method in the previous study [11], although the sampler geometry was 
different. These findings suggested that the variations in TrCO\textsubscript{2} observed 
during the experiment correlate with the changes in CO\textsubscript{2} concentration 
in the body. These results are in correlation with the qualitative 
assessment on suffocation experienced during the dynamic study by 
the study subjects (Fig. S7). Note that there was a limit to the number of 
human subjects we could access during this study. In order to extend 
these findings to a general conclusion, it would be necessary to inves-
tigate with a larger sample size. Another current limiting factor is the 
fact that it is different from the actual working situation where health 
care workers have to walk around and speak.

\( \Delta \text{TrCO}_2 \) levels on different types and overlaying patterns of PPE 
(Fig. 5) correlate well with filtering performance or breathability of PPE 
[22–25]. There were two interesting observations as seen in Fig. 5: (1) 
when N95 and SM were layered, the profile of \( \Delta \text{TrCO}_2 \) was similar to 
when N95 was worn alone; (2) use of the FS alone showed a similar 
\( \Delta \text{TrCO}_2 \) profile to when PPE were not worn. The differences however 
became larger when the FS was added to SM covering N95. The first 
obsservation in the current study is consistent with the findings of a 
previous study by Roberge et al. [20] However for the second ob-
observation, computational fluid dynamics studies on airflow around 
the mask would augment the understanding in this arena. It has been shown 
that exhaled air can easily diffuse beyond the FS into the ambient air 
when the mask is not worn [26,27]. In contrast, when SM covering N95 
was worn inside FS, the mask caused a pressure loss in the exhalation 
[28–30]. As a result, exhaled air could stay in the vicinity of the masks, 
and furthermore, the FS could prevent diffusion of the exhaled breath 
to the ambient environment, which promotes re-inhalation of exhaled 
air. Note that we observed significant changes in TrCO\textsubscript{2} with bag 
breathing that mainly contributes to re-breathing (Fig. S8). Thus, there 
is a trade-off between the filter performance and breathability of a mask. 
Considering variations in TrCO\textsubscript{2} levels as in our study and earlier studies 
that have evaluated the filtering performance of masks, it is likely that 
SM would be the first choice for the general public when exercising in 
door gyms.

On the other hand, a recent study showed that commercially avail-
able powered air purifying respirator that enhance breathability could 
prevent headache related to PPE [31] induced by hemodynamic alter-
ations [32]. We are confident that our device will support the rapidly 
advancing research on filter materials [33,34] and designs [35,36] will 
lead to engineering of ergonomic masks that do not compromise on filter 
performance and breathability.

Continuous transdermal CO\textsubscript{2} monitoring using a wearable sensor 
may provide physiological insights that are of value to a number of 
medical applications and disease states [37]. Our earlier approach is 
readily amenable to a wearable format (Fig. S9) by modifying a CO\textsubscript{2} 
sensor previously designed for bioprocess monitoring [38,39].

5. Conclusions

We observed a significant effect on wearing N95 overlaid with SM 
and FS during moderate exercise/activity on TrCO\textsubscript{2} levels, but not while 
resting. There is however no significant difference in HR and SST while 
exercising with masks. Individual differences in exercising tolerance 
affect TrCO\textsubscript{2} levels during activity. Hence, having a personal TrCO\textsubscript{2} 
monitor will be a prudent solution to monitor the health of first re-
sponders in this pandemic. Given the disadvantages and limitations of 
the existing technologies, there is clearly a need for the development of 
new generation devices for rapid and accurate assessment of respiratory 
status to better guide clinical practice. Further studies are currently 
underway for a more comprehensive understanding.

CRediT authorship contribution statement

Kenta Iitani: Investigation, Visualization, Project administration, 
Formal analysis, Funding acquisition, Writing – original draft. Joel 
Tyson: Methodology, Investigation. Samyukta Rao: Investigation. Sai 
Sathish Ramamurthy: Project administration, Supervision, Writing – 
original draft. Xudong Ge: Project administration, Supervision. Govind 
Rao: Conceptualization, Project administration, Supervision, Funding 
acquisition.

Declaration of Competing Interest

None declared.

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Ethical approval

This study was approved by the Office of Research Protections and 
Compliance, University of Maryland Baltimore County.

Supplementary materials

Supplementary material associated with this article can be found, in 
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