A Physiologic Research to Assess the Effect of an Inline Filter during Cardiopulmonary Exercise Testing (CPET): A Healthy Volunteer Study

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Objectives

1. Assess the Effects of an In-Line Filter on the Physiologic Responses during CardioPulmonary Exercise Testing (CPET) and the Aerosol Particle Size Distribution in the Environment.

2. Hypothesis: An in-line filter will have minimal effects (< 5% effect) on minute ventilation (VE), oxygen uptake (VO2), carbon dioxide output (VCO2), and heart rate (HR) during CPET. The placement of filter will significantly reduce the particle concentrations generated by subjects during CPET.

Background

The arrival of the COVID-19 pandemic (SARS-CoV-2) has dramatically changed the landscape of healthcare, including clinical care and research trials (Zhu, Zhang et al. 2020). The initial response of health care systems and research institutions was to cease all activity and turn all efforts towards the pandemic response (Christian, Sprung et al. 2014). However, as levels of infection in the local community begin to recede, institutions are considering ways to restore normal clinical care and research trials (Faghy, Sylvester et al. 2020).

Physiologic testing (Pulmonary Function Testing - PFT) and (Cardiopulmonary Exercise Testing – CPET) is an important component of clinical care (Wasserman, Hansen et al. 2012), however both are aerosol generating procedures (AGPs) (https://www.advocatehealth.com/covid-19-info/_assets/documents/aerosol-generating-procedures.pdf),

and thus may pose a risk to patients, and clinical staff (Tran, Cimon et al. 2012). PFT AGPs are mitigated by using an inline filter during breathing trials, however, this is not standard practice with CPET. For example, European respiratory society (ERS) does not recommend the utilization of HEPA filter during CPET, due to the concerns of creating the resistance for breathing.

Therefore, the issue that requires investigation is the effect of the in-line filter on the gas exchange measurements, as these are the ultimate 'product' of the CPET testing. If these values are severely affected (> 5%) by an inline filter, then other mitigation strategies may need to be considered.

Further, we need to establish the effects of the in-line filter on several of the common CPET hardware/software platforms in use throughout the world (e.g Medical Graphics Corporation, Vyair Vmax, Cosmed, etc), specifically on the important measured variables (V_E, VO_2, VCO_2 and HR). We also want to evaluate the effects of the filter on reducing particle concentrations that are generated by subjects during CPET, as well as the time that is required to clean the room air.

Acquiring this data and publishing it in the near future would be important to safely return to practice and also to support our CPET colleagues throughout the world.

Methods

1. Inclusion and Exclusion Criteria

Inclusions:

- Ages 18-65, Male or Female

- Normal exercise tolerance without dyspnea or clinically important limitation of exercise tolerance.

Exclusions:

- Complicated heart or lung disease
- Pregnancy
- Complex arrhythmias
- Severe Anemia
- Uncontrolled Diabetes, hypertension, or untreated thyroid disease
- Has any of the following symptoms in the last 21 days: sore throat, cough, chills, body aches for unknown reasons, shortness of breath for unknown reasons, loss of smell, loss of taste, fever at or greater than 100 degrees Fahrenheit.
- COVID-19 test positive within 21 days.
- Any Disease that the PI feels will markedly increase the risk of CPET testing

2. **Sample size:** 10 subjects
3. **Subject recruitment:**

Advertisement will be posted in the public area at Rush University Medical Center, including fitness center, healthy subjects including employee or patients/family in Rush University Medical Center will be recruited.

4. **Study Timelines**

- *The duration of an individual subject's participation in the study.*

  This requires two visits over two days for an hour or less on each visit. Two increment work rate CPET studies with one performed on each day taking no

more than 45 minutes. With a one-hour break for cleaning and room air exchange between subjects.

- *The duration anticipated to enroll all study subjects.*

  3 weeks (to prescreen and set up testing schedule)

- *The estimated date for the investigators to complete this study (complete primary analyses)*

  August 2020

5. Study outcome

- Primary: Determine the effect of the in-line filter (< 5% effect or > 5% effect) on minute ventilation ($\dot{V}_E$), oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), and heart rate (HR) during CPET. Effect of in line filter on oxygen pulse, ventilatory equivalents, end tidal O_2 and CO_2. Sensation of dyspnea by the subject (Borg Score).
- Secondary: Effect of in line filter on aerosol particle concentrations inside the test room during CPET testing to determine if wait time between patients can be calculated

6. Termination criteria:

Standard termination criteria for CPET during testing are BP > 240/120, serious arrhythmias, chest pain, oxygen desaturation and severe dyspnea.

7. Procedures Involved*

- **study design.**

  The subject will spend two visits one hour each day (~ 1 hour) in the PFT lab and will have two separate CPET (Vyair Vmax, Vyaire medical, Mettawa, IL)

tests performed by registered pulmonary function technologists. One day the test will be performed with the inline filter during CPET, and the second day the CPET will be performed without a filter. During the test, electrocardiogram (ECG) electrodes will be attached to participants as well as a mask, and their heart rate will be measured for 10 minutes at rest, and then they will ride bicycle for 20 minutes at different levels of intensity. The work rate increment will be the same for both tests. All gas exchange and aerosol particle concentrations measures will be compared with Bland Altman analysis and paired t-testing.

- **Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks.**

  The standard CPET (Wasserman 2012) includes real time monitoring of the 12 lead EKG, pulse oximetry, gas exchange variables, physician assessment, and symptom query.

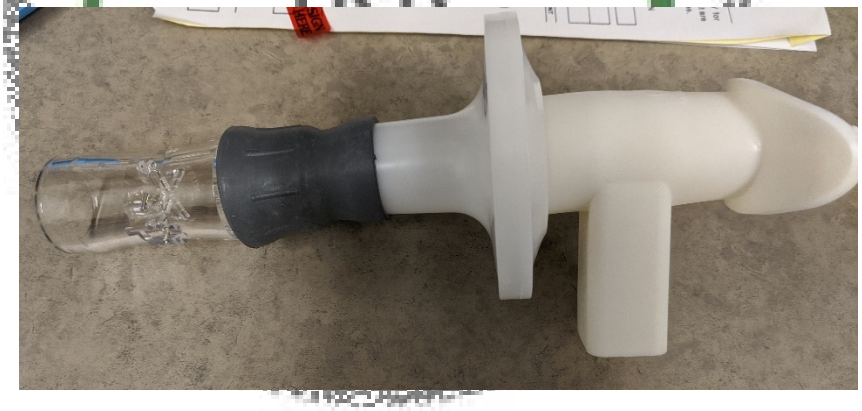
- **Procedures performed to lessen the probability or magnitude of risks.**
  - *All drugs and devices used in the research and the purpose of their use, and their regulatory approval status.*

    No drugs. The device is an inline filter (MicroGard™ II PFT Filter).

    MicroGard™ II PFT Filter

Proposed filter to be used (current standard of care with PFTs)

MicroGard™ II PFT Filter in line with Mouthpiece and Flow Sensor



** Picture shows the Pitot flow sensor, and adapter, the Microgard Filter, and a standard mouthpiece.

- The relevant characteristics of this filter are:

  Inspiratory Resistance: 0.45 cm/H_2O/L/S

  Expiratory Resistance: 0.45 cm/H_2O/L/S

  Filter Efficiency: Bacteria>99.98%

Virus filtering efficiency > 99.92%

Dead Space = 53ml

The filter is for single patient and single occasion use only.

8. Data Management* and Confidentiality

- **Describe the data analysis plan, including any statistical procedures.**

Data from each subject will be compared with a Bland Altman Analysis (*https://www.jstor.org/stable/2987937?seq=1*) and paired T-Testing using the non-filter data for minute ventilation (V_E), oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), and heart rate (HR) during a work rate increment CPET, comparison of the non-filter to the filter data will be analyzed. Mean and standard deviation of the measurements will be presented. Statistical importance will be assigned at $P \leq 0.05$.

- **Describe the steps that will be taken secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.**

No identification will be collected. The electronic data will be stored on the Redcap, which is a secure network with appropriate institutional security, and password protection.