

# Imposed Power of Breathing Associated With Use of an Impedance Threshold Device

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**OBJECTIVE:** To measure the imposed power of breathing (imposed work of breathing per minute) associated with spontaneous breathing through an active impedance threshold device and a sham impedance threshold device. **DESIGN:** Prospective randomized blinded protocol. **SETTING:** University medical center. **PATIENTS:** Nineteen healthy, normotensive volunteers (10 males, 9 females, age range 20–56 y, mean  $\pm$  SD weight  $54.8 \pm 7.7$  kg for females,  $84 \pm 8$  kg for males). **METHODS:** The volunteers completed 2 trials of breathing through a face mask fitted with an active impedance threshold device set to open at  $-7$  cm H<sub>2</sub>O pressure, or with a sham impedance threshold device, which was identical to the active device except that it did not contain an inspiratory threshold pressure valve diaphragm. Spontaneous breathing frequency (f), tidal volume (V<sub>T</sub>), exhaled minute ventilation, inspiratory pressure, and inspiratory time were measured with a respiratory monitor, and the data were directed to a laptop computer for real-time calculation of the imposed power of breathing. **RESULTS:** There were no significant differences in heart rate, respiratory rate, tidal volume, and minute ventilation, with and without inspiratory impedance. For the sham and active impedance threshold device groups, respectively, the mean  $\pm$  SD imposed power of breathing values were  $0.92 \pm 0.63$  J/min and  $8.18 \pm 4.52$  J/min ( $p < 0.001$ ), the mean  $\pm$  SD inspiratory times were  $1.98 \pm 0.86$  s and  $2.97 \pm 1.1$  s ( $p = 0.001$ ), and the mean  $\pm$  SD inspiratory airway/mouth pressures were  $-1.1 \pm 0.6$  cm H<sub>2</sub>O and  $-11.7 \pm 2.4$  cm H<sub>2</sub>O ( $p < 0.001$ ). **CONCLUSIONS:** Breathing through an active impedance threshold device requires significantly more power than breathing through a sham device. All subjects tolerated the respiratory work load and were able to complete the study protocol. *Key words:* respiration, power of breathing, minute ventilation, inspiratory pressure, hypotension. [Respir Care 2007;52(2):177–183]

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Keith G Lurie MD is a co-inventor of the impedance threshold device and founded Advanced Circulatory Systems to develop the device.

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**Introduction**

Orthostatic hypotension and frank syncope are debilitating conditions for military personnel, astronauts returning from space, and patients who suffer from clinical autonomic dysfunction.<sup>1-3</sup> One of the challenges to effective treatment of orthostatic intolerance is maintenance of venous return and stroke volume, particularly in the presence of reduced circulatory blood volume.<sup>4-8</sup> Greater negative intrathoracic pressure can be produced by applying resistance during spontaneous inhalation<sup>9-13</sup> and has been associated with elevations in systemic arterial blood pressure and greater organ blood flows in hypovolemic, hypotensive humans, and animals.<sup>9-16</sup> Building on this concept, an inspiratory impedance threshold device was designed to generate more negative intrathoracic pressure (ie, intrapleural, intra-alveolar, and intra-airway pressures are substantially more negative each time the chest expands during the inspiratory phase of breathing).<sup>12-14,17</sup> In a recent experiment, we demonstrated that during spontaneous inhalation through an impedance threshold device, stroke volume, cardiac output, and mean arterial blood pressure increased in human subjects during a squat-stand test maneuver and is an effective countermeasure against orthostatic hypotension and intolerance.<sup>18</sup>

For the impedance threshold device to be clinically useful, the effort required for breathing through the device should not require excessive work of breathing (WOB) per minute. WOB per min is the power of breathing (POB). The objectives of this study were to measure and compare the inspiratory imposed POB (POB<sub>I</sub>) and other respiratory variables in subjects breathing through an active or a sham impedance threshold device. POB<sub>I</sub> is the imposed work load per minute on the respiratory muscles by the sham or active impedance threshold device during spontaneous inhalation.

**Methods**

**Subjects**

Nineteen healthy, normotensive, nonsmoking adults were recruited to participate in the present investigation (10 males, 9 females). Demographic data for the subjects are presented in Table 1. A complete medical history and physical examination that included a resting 12-lead electrocardiogram and clinical orthostatic examination (supine/seated/standing consecutive blood pressure measurements) were obtained with each of the potential subjects. Because of potential effects on cardiovascular function, the subjects refrained from any exercise and stimulants such as caffeine and other nonprescription drugs for 48 hours prior to testing. During an orientation period that preceded each experiment, all subjects were made familiar with the lab-

Table 1. Subject Group Demographic Data\*

	Female	Male
Age (y)	32 ± 9	36 ± 13
Height (cm)	163 ± 5	179 ± 8
Weight (kg)	54.8 ± 7.7	84.0 ± 8.0
Heart rate (beats/min)	68 ± 12	63 ± 9
Systolic blood pressure (mm Hg)	116 ± 8	127 ± 10
Diastolic blood pressure (mm Hg)	70 ± 15	68 ± 9

\*19 subjects (9 female, 10 male). Values are mean ± SD.

oratory, the protocol, and the procedures. The experimental procedures and protocols were reviewed and approved by the Human Investigative Review Board of the Kennedy Space Center for the use of human subjects. Each subject gave written informed voluntary consent to participate in the experiments.

**Protocol**

Each subject completed 2 tests:

1. During spontaneous breathing through a face mask with an impedance threshold device (Advanced Circulatory Systems, Eden Prairie, Minnesota) set with an inspiratory threshold pressure valve setting of -7 cm H<sub>2</sub>O (pressure at which the valve opens, allowing air inflow)
2. During a control session, breathing through the same face mask with a sham impedance threshold device (ie, no inspiratory threshold pressure valve)

The -7 cm H<sub>2</sub>O pressure setting was chosen, because at this impedance pressure level spontaneous breathing was shown to be tolerable and resulted in increases in arterial blood pressure, heart rate, stroke volume, and cardiac output in human subjects<sup>18</sup> and in animal models.<sup>19</sup> While subjects acclimated to breathing through the valve, peak sinusoidal flow rates varied from 0.1 L/s to 0.7 L/s. Each subject had his or her own disposable face mask. The order of treatment was selected using a computer-generated randomization list so that 9 subjects (5 males and 4 females) underwent testing with the active impedance threshold device first, and the remaining 10 subjects (5 males and 5 females) underwent testing with the sham impedance threshold device (control condition) first. Each subject, with the face mask and impedance threshold device in place, was instructed to start breathing with natural but deep breaths and to breathe continuously through the impedance threshold device for 2 min. Breathing frequency (f), tidal volume (V<sub>T</sub>), exhaled minute ventilation (V̇<sub>E</sub>), face-mask inspiratory pressure, and inspiratory time (T<sub>I</sub>) were measured with a respiratory monitor (NICO, Respi-ronics, Wallingford, Connecticut). The monitor was supplemented with a laptop computer, using specialized soft-

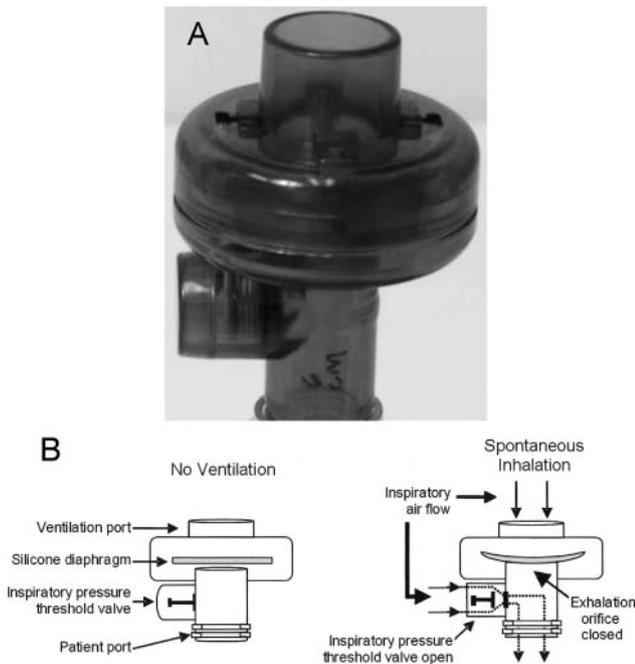


Fig. 1. A: Impedance threshold valve. B: Schematic cross-section of the impedance threshold device. During spontaneous inhalation, the silicone diaphragm on top is sucked down by the inspiratory effort, which occludes the exhalation orifice and, simultaneously, inspiratory airflow is drawn through the inspiratory pressure valve into the face mask. During exhalation (not shown), the silicone diaphragm rises and exhaled air flows out through the open exhalation valve orifice.

ware (eWOB, Convergent Engineering, Gainesville, Florida) for the real-time calculation of  $POB_T$ , based on measurements obtained from the respiratory monitor. All measurements were made over a 2-min steady-state time period after the subject had been breathing through the impedance threshold device for 5 min. An interval of at least 30 min was imposed between each test so that each experimental session was conducted over a period of less than 60 min. All subjects completed the protocol without difficulty.

### Breathing With the Impedance Threshold Device

The impedance threshold valve (Fig. 1) is composed of a valve that closes when the pressure within the thorax is less than atmospheric pressure and a second valve (termed the inspiratory threshold pressure valve) that opens at a preset negative face-mask pressure. The impedance threshold device is composed of the valve attachment to a face mask, to ensure that a seal exists between the valve and the skin of the subject's face that is sufficient to eliminate any air leakage (Fig. 2). The impedance threshold device was designed to generate a negative inspiratory threshold pressure and to therefore generate substantially more negative



Fig. 2. A subject during test measurements. The figure illustrates the impedance threshold device placement on the subjects, who were instrumented for breath-to-breath measurement of respiratory variables.

intrapleural pressure during spontaneous inhalation.<sup>9-11,17</sup> During each test, the subject was instructed to hold the impedance threshold device in place with the right hand (see Fig. 2).

Prior to the study, a plot describing the pressure-flow (resistance) characteristics of the impedance threshold device used in this study was determined under in vitro test conditions (Fig. 3). The pressure-flow plot was obtained using a *spontaneously* breathing lung model (series 1101 breathing simulator, Hans Rudolph, Kansas City, Missouri). The following programmed variables were used: respiratory system resistance 5 cm H<sub>2</sub>O/L/s, respiratory system compliance 0.08 L/cm H<sub>2</sub>O, f 10 breaths/min, and incremental peak sinusoidal inspiratory flow rates for simulating different spontaneous flow demands.

### Measurement of Respiratory Variables

A pressure/flow sensor from the aforementioned respiratory monitor, positioned between the face mask and impedance threshold device, was used to measure pressure, flow rate,  $T_I$ ,  $\dot{V}_E$ ,  $V_T$ , and f. Face-mask pressure was integrated with  $V_T$  to produce real-time pressure-volume loops, with the inspiratory portion determined to be the

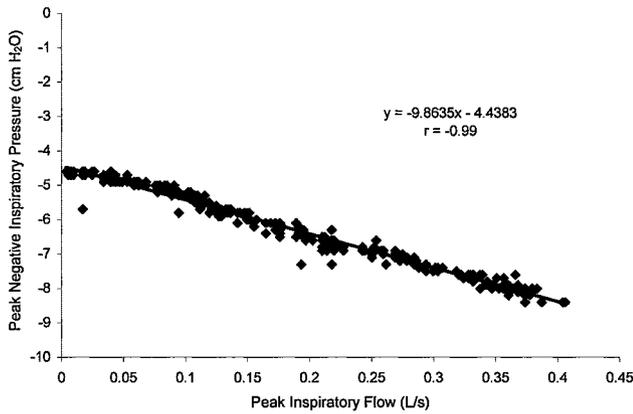


Fig. 3. Plot of the pressure-flow (resistance) characteristics of the impedance threshold device, as used in the study under in vitro test conditions of simulated *spontaneous* breathing. As simulated peak inspiratory flow rate demand increased (X axis), the pressure drop across the impedance threshold device became more negative. The slope of the line (9.86 cm H<sub>2</sub>O/L/s) relates to the imposed resistance of the impedance threshold device.

inspiratory imposed WOB per breath (WOB<sub>I</sub>). WOB<sub>I</sub> values were averaged over 1 min to calculate POB<sub>I</sub>. All data were stored on a laptop computer for subsequent off-line analysis.

**Statistical Analysis**

The data were analyzed using a standard 2-group (male, female) by 2-treatment (-7 cm H<sub>2</sub>O impedance threshold device, control) mixed model analysis of variance to determine gender differences. Alpha was set at 0.05 for statistical significance. The model was mixed in the sense that subjects were nested within groups by sex and crossed with treatments (ie, one between-subjects factor [gender] and one within-subjects factor [treatment]). All main and subsequent interaction effects were analyzed across 6 dependent effects (f, V<sub>T</sub>, V̇<sub>E</sub>, inspiratory face-mask pressure, T<sub>I</sub>, and POB<sub>I</sub>). The p values were calculated for each independent effect and reflect the probability of obtaining the observed or greater effect given only random departure from the assumption of no effects. Data are presented as mean ± SD.

**Results**

**Demographic Data**

Baseline values for age, height, weight, heart rate, and blood pressures are presented in Table 1. There were no statistically significant differences between the male and female groups for age, heart rate, or diastolic blood pressure. The mean systolic blood pressures were 127 ± 10 mm Hg and 116 ± 8 mm Hg for the males and

Table 2. Respiratory Variables While Breathing Through Active and Sham Impedance Threshold Devices

	Active Device*	Sham Device*	P
f (breaths/min)	11.6 ± 4	13.3 ± 4.5	0.62
V <sub>T</sub> (L)	1.03 ± 0.48	1.03 ± 0.49	0.71
V̇ <sub>E</sub> (L/min)	10.9 ± 4.3	12.1 ± 3.3	0.66
T <sub>I</sub> (s)	2.97 ± 1.1	1.98 ± 0.86	0.0003
PIF (L/s)	0.36 ± 0.14	0.52 ± 0.14	0.0006
Face-mask pressure (cm H <sub>2</sub> O)	-11.7 ± 2.4	-1.1 ± 0.6	< 0.001
WOB <sub>I</sub> (J/L)	0.88 ± 0.14	0.07 ± 0.04	< 0.001
POB <sub>I</sub> (J/min)	8.18 ± 4.5	0.92 ± 0.63	< 0.001

\*Values are mean ± SD.

f = frequency of spontaneous breaths

V<sub>T</sub> = tidal volume

V̇<sub>E</sub> = spontaneous minute ventilation

T<sub>I</sub> = inspiratory time

PIF = peak inspiratory flow

WOB<sub>I</sub> = inspiratory imposed resistive work of breathing per breath for the impedance threshold device

POB<sub>I</sub> = inspiratory imposed resistive power of breathing (WOB<sub>I</sub>/min) for the impedance threshold device

females, respectively (p = 0.018). Male and female groups showed the expected and well-established differences in height and weight. Values for heart rates and blood pressures were within established normal limits.

**Impedance Threshold Device and Gender Effects**

Gender did not influence the responses of heart rate (p = 0.954), f (p = 0.831), V<sub>T</sub> (p = 0.857), V̇<sub>E</sub> (p = 0.662), inspiratory pressure (p = 0.188), T<sub>I</sub> (p = 0.676), or POB<sub>I</sub> (p = 0.145) across treatment during either spontaneous breathing through the impedance threshold device or the control experimental conditions. Based on these analyses, the data were combined and analyzed with t test statistics, with a sample size of 19.

**Respiratory Effects**

Between the active device and sham groups there were no significant differences in f, V<sub>T</sub>, or V̇<sub>E</sub>. In the active device group, T<sub>I</sub>, face-mask pressure, WOB<sub>I</sub>, and POB<sub>I</sub> were significantly greater than in the sham group (Table 2). T<sub>I</sub> increased by 50%, change in face-mask pressure increased by 936%, WOB<sub>I</sub> increased by 1,157%, and POB<sub>I</sub> increased by 790%. Although face-mask pressure is governed by the inspiratory threshold pressure valve setting, it was also affected by the peak inspiratory flow rate. Higher inspiratory flow was associated with lower face-mask pressure, and vice versa. Face-mask pressure correlated inversely with inspiratory flow rate demand (r = -0.89, p < 0.001) (Fig. 4). These findings were consistent with

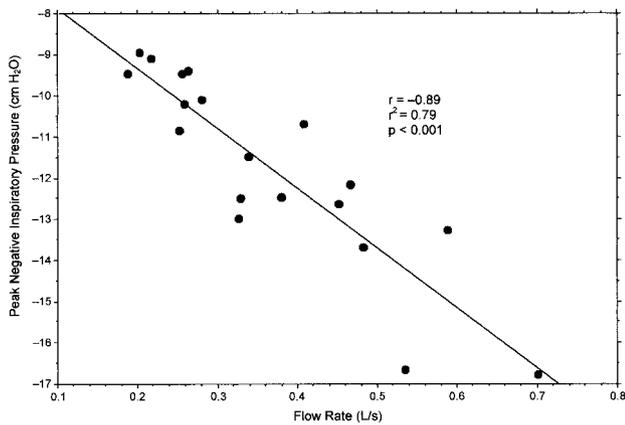


Fig. 4. Relationship between peak inspiratory flow rate demand and face-mask negative inspiratory pressure with the active impedance threshold device. Greater negative face-mask pressure is generated as peak inspiratory flow increases, and vice versa. Negative pressure generated with the impedance threshold device is dependent on both the inspiratory pressure threshold valve setting (see Fig. 1) and the peak inspiratory flow rate demand (see Fig. 3).

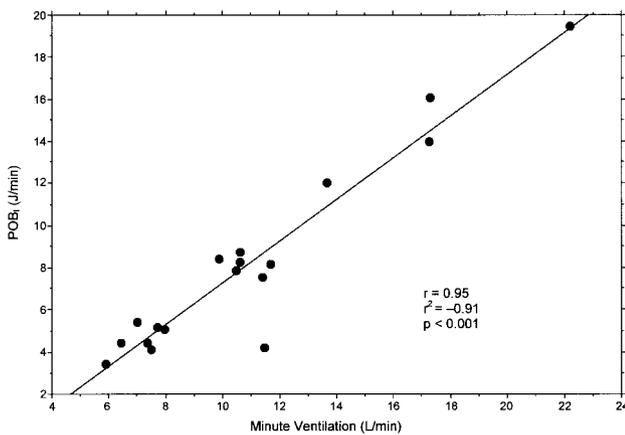


Fig. 5. Relationship between exhaled minute ventilation and imposed power of breathing ( $POB_1$ ) while breathing through the active impedance threshold device. As minute ventilation increases, the imposed power of breathing increases, and vice versa.

in vitro data that demonstrated that the impedance threshold device had an imposed resistance of nearly 10 cm H<sub>2</sub>O/L/s (see Fig. 3). The active device group had a significantly lower peak inspiratory flow than the sham group (see Table 2).  $POB_1$  correlated directly with  $\dot{V}_E$  with the active impedance threshold device ( $r = 0.95$ ,  $p < 0.001$ ) (Fig. 5).

## Discussion

This study demonstrated that  $POB_1$  with the active impedance threshold device is significantly greater than when breathing through the sham device. In addition, breathing through an active impedance threshold device is associ-

ated with significantly longer  $T_I$  and significantly more negative inspiratory pressure than the sham device, even though the subjects were instructed to breathe the same way through both the sham and active devices. However, there were no significant differences in ventilation variables such as  $f$ ,  $V_T$ , and  $\dot{V}_E$ , with and without inspiratory impedance.  $POB_1$  for the active impedance threshold device (approximately 8 J/min) represents an *additional* work load over and above the normal adult physiologic work load on the respiratory muscles (4–8 J/min).<sup>20</sup> When spontaneously inhaling through the impedance threshold device (–7 cm H<sub>2</sub>O), the total POB [physiologic POB plus  $POB_1$ ] is expected to be approximately 12–16 J/min. All the healthy volunteers in this study completed the protocol and tolerated breathing through the impedance threshold device.

Power is work per unit time (power = work per breath  $\times$   $f$ ). To put power into a frame of reference, moderate exercise that requires a  $\dot{V}_E$  of 60–80 L requires approximately 80 J/min of power.<sup>21–23</sup> In contrast, the –7 cm H<sub>2</sub>O impedance threshold device requires about 12–16 J/min of power, which should be well tolerated by most people with normal respiratory function.  $POB_1$  varied directly with  $\dot{V}_E$ , which combines the variables of  $T_I$ ,  $V_T$ , and  $f$  (see Fig. 5). Because both  $POB_1$  and  $\dot{V}_E$  share time as a common denominator, there is a direct relationship between work and volume, which suggests a predominant effect of mechanical impedance, as opposed to ventilatory pattern.

A goal of this study was to determine the work load of the impedance threshold device on the respiratory muscles. For this reason, only  $POB_1$  of the impedance threshold device was measured. Measurement of total POB (physiologic power [elastic and resistive power] plus  $POB_1$ ) was not a goal of the study. Thus, an esophageal balloon catheter, used for the measurement of esophageal pressure (indirect measurement of intrapleural pressure) and for calculating physiologic POB, was not inserted.<sup>24</sup>

In general, respiratory muscle fatigue occurs whenever energy demand (oxygen consumption and blood flow) exceeds energy supply. For the impedance threshold device to be functional, the energy required for its operation should not exceed the energy available in patients to whom it is expected to be applied, such as ill and injured patients with hypotension. It should be noted that the impedance threshold device is contraindicated in patients with pulmonary edema or congestive heart failure, because it could exacerbate those conditions.

Impedance threshold devices generate negative face-mask pressure as a result of their inspiratory threshold pressure valve setting, and, in part, due to resistance to airflow through the device. The impedance threshold device used in this study had the characteristics of a threshold load and of a resistive load. Elastic work is required to

overcome the threshold load ( $-7$  cm H<sub>2</sub>O), and resistive work is required to overcome the internal flow-resistive components of the valve (approximately 10 cm H<sub>2</sub>O/L/s) to ensure inspiratory flow (see Fig. 3). With increased inspiratory flow demand, increased negative face-mask pressure is generated (see Fig. 4). The greater the flow, the greater the negative pressure, and vice versa. Greater negative inspiratory pressure is associated with greater WOB<sub>I</sub> and POB<sub>I</sub>, and, thus, respiratory muscle loading. Care should be taken to ensure that subjects do not inhale at a high inspiratory flow ( $> 1$  L/s) so that excessively large negative pressure and intolerably high work load are not generated. We found that subjects breathing through the active device spontaneously altered their normal breathing pattern and used significantly longer T<sub>I</sub> than when breathing through the sham device. The longer T<sub>I</sub> effectively reduced inspiratory flow. Although negative face-mask pressure was much greater with the active device, even the sham device had a face-mask pressure that was less than zero, probably because there was some resistance to air-flow imposed by the pressure-relief port, even without the threshold valve in place.

The impedance threshold device is intended for use as a countermeasure for orthostasis in astronauts who return to gravity after prolonged microgravity exposure. A study of the effect of inspiratory impedance on orthostasis using the squat-stand test showed that the impedance threshold device preserved cardiac stroke volume and output during orthostatic challenge and reduced symptoms of lightheadedness and blurred vision.<sup>25</sup> It was well tolerated in this population of otherwise healthy individuals with normal respiratory function. It is also intended for use in people who suffer from chronic orthostasis and in people who suffer from acute hypovolemic hypotension.<sup>26</sup> Although work load tolerance is likely to be decreased in people who are injured and have lost blood and may have ischemia, the work load imposed by the impedance threshold device may nevertheless be tolerated because it functions to increase blood flow; however, this needs to be studied. The impedance threshold device is currently being studied with hypotensive patients suffering volume loss.

### Conclusions

The impedance threshold device with an inspiratory opening pressure of  $-7$  cm H<sub>2</sub>O has a POB<sub>I</sub> of about 8 J/min. While inhaling through this impedance threshold device, the total POB (physiologic POB plus POB<sub>I</sub>) is expected to be about 12–16 J/min. Although not specifically measured, all subjects in this study tolerated this respiratory work load well and completed the protocol.

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Two men wearing respirators and rubber gloves work at a small table  
Undated photograph  
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