# Performance of the LRRI Real-time Rabbit Plethysmography System

## E.B. Barr, S.M. Storch, T. Brasil

Lovelace Respiratory Research Institute, Albuquerque, NM

## Abstract

Background: Select agent studies using rabbits typically determine dose delivered to the animal by measuring chamber concentration of the aerosolized agent and estimating respiratory minute volume (MV) of the animal using Gayton's MV formula, cc/min = 2.1 (weight, g)²/³. Lovelace Respiratory Research Institute (LRRI) employs a system that measures actual inhaled volume using real-time whole-body plethysmography. The LRRI rabbit plethysmography system is designed to contain an unanesthetized rabbit in a uniquely designed chamber for nose-only exposures. The plethysmograph system is composed of the plethysmograph chamber, screen pneumotachograph, pressure transducer, Busco Max II pneumopipette, and BioSystem XA for Windows software.

Methods: The plethysmograph chamber is calibrated prior to each use by injecting 20-30 mL of air into the sealed chamber. A pressure drop is generated across a series of fine mesh screens (pneumotachograph) that are connected to the chamber. The pressure drop is detected by a transducer and a signal is sent to a pneumopipette. The BioSystems XA software correlates the signal to flow rate. The rabbit is placed in the chamber and movement of air caused by the rise and fall of the thoracic cavity is detected by the pneumotachograph and frequency (F), tidal volume (TV), and MV are calculated by the software. The chamber is connected to a nose-only exposure system after which select agent aerosol is delivered. Concentration of the agent in the generator suspension is calculated to deliver the target inhaled dose in a predetermined inhalation volume.

Results: 104 rabbits weighing between 2.6 and 4.1 kg were exposed to a select agent dose determined by chamber aerosol concentration and a target total inhaled volume of 19 L or 20 L. Average F was 181 ± 73 bpm, TV was 11 ± 5 mL, and average MV was 1707 ± 723 mL/min.

Conclusions: The LRRI rabbit plethysmography system demonstrates that inhaled volume can be quantified accurately. Results show that the F, TV, and MV of similar weight animals can differ significantly.

## Introduction (Continued)

Nose-only fast flow rate to chambers

### Methods

- Two whole-body plethysmography chambers are incorporated in the LRRI rabbit exposure system (Figure 1).
- Prior to placing rabbits in the plethysmograph chambers, each chamber is calibrated by injecting a 20-30 mL bolus of air into the sealed chamber. The BioSystems XA software correlates the signal to the flow rate.
- Concentration of the agent in the generator suspension is calculated to deliver the target inhaled dose in a predetermined inhalation volume (I.E., 5 L) or a set time (I.E., 10-20 min).
- The rabbits are placed in the chambers prior to exposure and each chamber is connected to the nose-only exposure system. The operator verifies that the BioSystems XA software is displaying signals from each chamber (Figure 4).

### Results

- 104 rabbits weighing between 2.6 and 4.1 kg were exposed to a select agent dose determined by chamber aerosol concentration and total inhaled volume as measured by real-time plethysmography.
- MV measurements ranged from 280 to 3608 mL/min.
- F measurements ranged from 47 to 400 bpm.
- TV measurements ranged from 1 to 28 mL.

### Discussion

- Using the Gayton and Bide equations, MV estimates for the 104 rabbits in these studies range from 773-1072 mL/min and 1086-1543 mL/min, respectively (Figure 5).
- Both Gayton and Bide estimates are much lower over much longer real-time plethysmography.
- Gayton and Bide estimates are up to 74% lower than plethysmography.
- Plethysmography indicates much more variability in MV than the Gayton and Bide equations (Figure 6).

### Conclusions

- Results show that the F, TV, and MV of similar weight animals can differ significantly.
- Overall, the Gayton and Bide equations underestimate MV and do not account for individual animal differences and variability.
- The LRRI rabbit plethysmography system demonstrates that inhaled volume can be quantified accurately. This is a critical parameter in accurately estimating the dose to individual animals.

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