Evaluation of Respiratory Inductive Plethysmography Using the EMKAbelt System in the Conscious Dog and Primate

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Huntingdon Life Sciences, Huntingdon, Cambridgeshire, UK

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Abstract
To date, respiratory measurements are typically obtained from conscious large animals using a pneumotachograph attached to a face mask. However, this method requires restraint of the animals, restricts measurements to a relatively short period of time and recordings cannot be performed during inhalation administration of test substances. Respiratory Inductive Plethysmography (RIP) is reported to provide an accurate measurement of ventilatory parameters in freely moving animals. The purpose of this study was to evaluate the data obtained from the non-invasive telemetry EMKAbelt (RIP) system to that obtained using the face mask and pneumotachograph system. Four dogs and four primates implanted with DSI™ telemetry transmitters were habituated to EMKAbelt (jacket) RIP system for 14 days. Preliminary respiratory recordings were obtained in order to evaluate the most appropriate restrained posture (standing or sitting) for calibration of the EMKAbelt System with the pneumotach/mask system. Respiratory recordings from both mask and RIP were obtained prior to and following CO2 (via a rebreath manoeuvre), doxapram (5 mg/kg i.v.) and inhaled methacholine (19.3 µg/kg over 5 min). Additionally, utilising the thoracic and abdominal EMKAbelt chest bands, the time (or angle) between the bands movement was recorded to assess phase angle as a surrogate marker for airway resistance. During all procedures, cardiovascular parameters were monitored by telemetry in order to monitor the dog’s acceptance to the jacket system and for welfare reasons following administration of the reference compounds (data not shown).

Methods
Four beagle dogs (11.6 – 15.0 kg) were dosed iv with morphine (1.0 mg/kg) (under mild restraint) with continuous post-dose respiratory recordings provided. Additional animals were dosed intravenously with doxapram (5 mg/kg i.v.) and inhaled methacholine (19.3 µg/kg over 5 min). Following a CO2 re-breath procedure, doxapram (5 mg/kg i.v.) and inhaled methacholine (19.3 µg/kg over 5 min). Additional dogs were dosed iv with morphine (1.0 mg/kg) (under mild restraint) and inhalation of methacholine (19.3 µg/kg over 5 min). Four beagle dogs (11.6 - 15.0 kg) were habituated to the RIP jacket and face mask/pneumotachograph system over a 14 day period. Respiratory recordings were obtained for EMKA IOX (v 2.5.6) telemetry EMKAbelt system and via face mask using a Flea Fluidic pneumotach and pneumograph system (v 4.9). The pneumotach was calibrated to a flush volume of 1 l and spontaneous movements were obtained from the pneumotach and EMKAbelt chest bands, with the dogs in a predetermined standing position in order to calibrate the EMKAbelt system.

Results
Following a pre-treatment recording period, respiration rate and tidal volume were monitored from both systems (standing posture) following a CO2 re-breath procedure, doxapram (5 mg/kg) i.v. and inhaled methacholine (19.3 µg/kg over 5 min). Additionally, utilising the thoracic and abdominal EMKAbelt chest bands, the time (or angle) between the bands movements was recorded in order to evaluate phase angle measurements as a possible surrogate marker for airway resistance.

Conclusion
• The study showed a high degree of correlation between the ventilatory parameters obtained from the EMKAbelt RIP system and the conventional pneumotach/mask system.
• Continuous recording of respiration rate and volume was obtained from both dog and primate throughout 20 hours recording period.
• The EMKAbelt RIP system for respiration monitoring has the potential to be used on stand-alone safety pharmacology studies or as a functional end point in toxicology studies using conscious freely moving dogs and primates.

The EMKAbelt RIP system provides a simple non-invasive method to assess for changes in lung compliance or airway resistance.