CASE STUDY

a division of Harvard Bioscience, Inc.

The Next Generation Digital Cardiopulmonary Large Animal Implant

Introduction

Charles River Laboratories (CRL) is a long-time user of Data Sciences International's (DSI) implantable telemetry, and currently use the D70-PCTR implant in their large animal safety pharmacology studies. In 2019, DSI introduced the L11R device for the PhysioTel™ Digital platform as a replacement to the D70-PCTR. The objective of this study was to benchmark and validate the respiratory signal data from the L11R to signals collected from current industry standards.

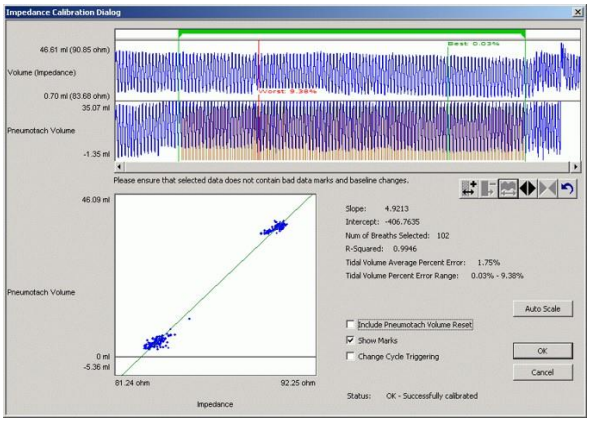
The Background

Safety pharmacology is a branch within drug development that assesses the potential adverse pharmacodynamic effects of a compound within and above the therapeutic range on physiological functions. Monitoring and evaluating the safety of a compound on the central nervous system, the cardiovascular system and the respiratory system are all required and mandated by the ICH guideline S7A. In 2010, DSI released a first-of-its-kind large animal cardiopulmonary implantable telemetry device, the D70-PCTR. This allowed researchers to simultaneously collect cardiovascular and respiratory endpoints in conscious, unrestrained subjects, while decreasing the number of animals and resources needed (Kearney et al, 2010). To keep pace with technology advancements, the L11R was introduced for the PhysioTel™ Digital platform.

The Study

Four cynomolgus monkeys were instrumented with L11R implants. To obtain respiratory signals, the excitation and sensing leads were placed cranial and caudal to the 7th rib, in the intercostal muscles. The device utilizes electrical impedance to derive lung volume. Calibration of these signals was done through calculating respiratory flow by measuring differential pressure across a pneumotach screen (Figure 1). All subjects were acclimated to the chair restraint, head dome and collection process over 5 days prior to the study. For cardiovascular signals, electrocardiogram (ECG) electrodes were placed on the diaphragm and superior vena cava for ECG measurement, and systemic blood pressure was collected through the femoral artery. The researchers used a cross-over study design with Doxapram (a respiratory stimulant), Dexmedetomidine (a respiratory depressant) and saline as the vehicles.

Figure 1: Impedance calibration dialog example when calibrating against a pneumotach



The Results

Respiratory and cardiovascular signals were collected during baseline and dosing using DSI's Ponemah v5.3 acquisition and analysis software. The results from the study demonstrates physiological changes to both Doxapram and Dexmedetomidine (Figures 2,3) and expected responses when compared to previously published non-human primate (NHP) literature (Authier et al, 2010; Kearney et al, 2010).

Figure 2: Heart Rate and Minute Volume

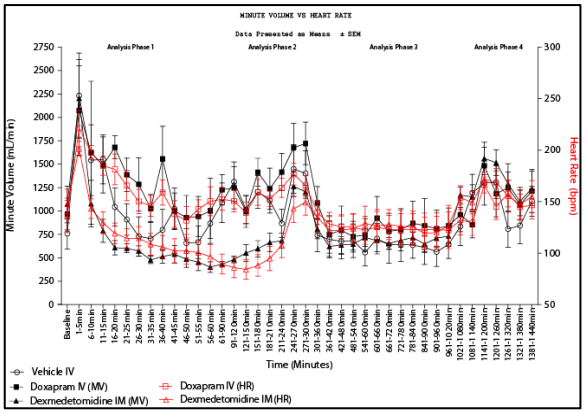
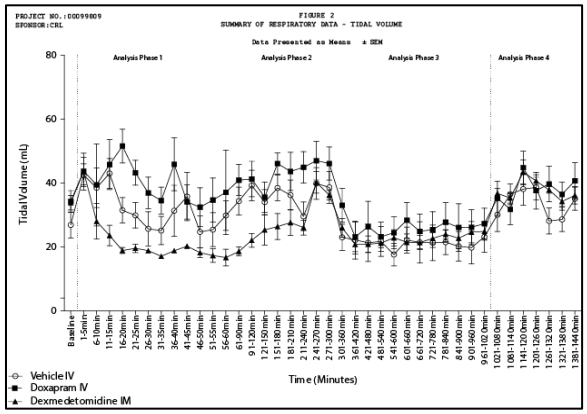


Figure 3: Tidal Volume



The Successes

This study enabled CRL the ability to compare results of the L11R to their experience with the D70-PCTR. The L11R provided expected response in NHPs compared to published literature and accurately detected pharmacological respiratory responses for both stimulant and depressant vehicles. In addition, the PhysioTel™ Digital platform offered the following advantages:

- Equal to and/or superior function
  - Surgical approach was identical, aside from the device body and antenna placement
  - Smaller device body allowed for placement on one side of the incision instead of crossing the incision
  - Increased battery life of up to 125 days
  - Improved signal quality resulting in cleaner and more analyzable data

- PhysioTel™ Digital platform
  - Social housing allowed for data to be collected from all animals without crosstalk
  - Ongoing signal transmission when removing the animal for dosing

DSI

Data Sciences International (DSI) offers complete systems that sense, transmit, acquire, and report physiologic data. In order to create a more robust study design, scientists rely on DSI technology to study specific targets as well as obtain a holistic view; allowing them to look at side effects that are upstream or downstream of the main pathology.

The DSI team ensures that researchers are equipped and prepared from the first minute of their study to the last; because your research is everything.

References:

Authier, S., Haefner, P., Fournier, S., Troncy, E., & Moon, L. B. (2010). Combined cardiopulmonary assessments with implantable telemetry device in conscious freely moving cynomolgus monkeys. *Journal of pharmacological and toxicological methods*, *62*(1), 6-11.

Kearney, K., Metea, M., Gleason, T., Edwards, T., & Atterson, P. (2010). Evaluation of respiratory function in freely moving Beagle dogs using implanted impedance technology. *Journal of Pharmacological and Toxicological Methods, 62*(2), 119-126.