Comparative Analysis of Data Sciences
International PhysioTel™ D70 and PhysioTel™ Digital Telemetry Platforms

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Abstract
Telemetric evaluations are largely conducted as part of the Safety Pharmacology core battery to satisfyICH S7A and ICH S7B requirements for assessment of changes in hemodynamic and electrocardiographic measurements, respectively. Such evaluations have allowed for the collection of consistent ambulatory data from unanesthetized animal models. However, historically, acquisition limitations have precluded social housing of animals during the telemetric evaluation period due to signal interference.

Technological advances in implantable telemetry devices and supporting hardware now offer benefits of greater signal quality, greater durations of implantation (due to upgraded battery usage and device construction), with the added capacity to offer group housing during the collection period.

The current study was conducted to assess the enhancements offered by the PhysioTel Digital (platform). Telemetric data were compared between moxifloxacin-treated animals using each telemetry platform. Both system evaluations were completed using a latin square cross-over dose design. Single-housed animals were used for the evaluation of the PhysioTel D70 (legacy) transmitter, while socially housed animals were used during the evaluation of the digital system.

While both systems demonstrated equivalent changes in the potential for delayed ventricular repolarization (QTcV >270 msec; up to ~45 msec from control at 15-16 hrs post dose), the digital telemetry system offers advantages by way of study setup efficiencies, reduced potential for collection errors, and extended implant battery life, all while satisfying expectations for group housing of social animals. Under the current study condition, no meaningful differences in cardiovascular parameters were noted between individually and socially housed animals. While no contamination issues were observed as a result of the social housing paradigm, considerations should be made to limit potential for contamination between treatment groups, and contamination of control, when evaluating socially housed animals.

Introduction
Changes in regulatory expectations now require socialization of animals as a refinement to animal welfare (National Research Council, 2011). Collecting meaningful cardiovascular and ECG endpoints were previously unable to accommodate social housing during periods of data collection due to technology limitations, resulting from signal interference. Technological advances in implantable telemetry devices and supporting hardware now offer benefits of greater signal quality, greater durations of implantation (due to upgraded battery usage and device construction), with the added capacity to offer group housing during the collection period.

Methods

Legacy System:
- 4 female Beagle dogs, 6-20 months, 6-12 kg
- Animals were surgically implanted with尾巴111G/7D/P/T-CTR transmitters
- ECG leads placed subcutaneously in a lead II configuration (one lead placed on the upper clavicle and the alternate lead placed in the opposite lower thoracic area)
- Arterial pressure catheter placed in the femoral artery
- Animals were single housed

Radiotelemetry System:
- DSi PONERA4 40-60 SP2 software
- BIC-1 receivers (1 per animal) were connected to a data exchange matrix interfaced to the acquisition software
- APR-I was used to adjust for barometric pressure

Digital System:
- 4 female Beagle dogs, 20-35 months, 7-12 kg
- Animals were surgically implanted with tail111 Digital transmitters
- Total 6 lead ECG leads were placed in a lead II configuration (one lead placed in the jugular vein and the alternate lead placed in the opposite lower thoracic area)
- Arterial catheter pressure placed in femoral artery
- Animals were socially housed in pairs
- Radiotelemetry System:
  - DSi PONERA4 40-60 SP2 software
  - PhysioTel Digital Telemetry
  - TRX-1 transmitters (1 per social group) were connected to communication link (CLC) interfaced to the acquisition software
  - APR was coupled to the ethernet to serial converter (E2S-1) to adjust for barometric pressure

Study Design

Female Beagle dogs received a single dose of vehicle (0.5% methylcellulose in DDW water) or moxifloxacin (10, 50, or 100 mg/kg) administered by oral gavage at a dose volume of 5-6 mL/kg. Each animal received all doses in a latin square design, with at least 3-days between dosing. On each day of dosing at least 60 minutes of baseline data were collected prior to dosing administration. Following administration of vehicle or test article, telemetry data were collected continuously for approximately 24 hours. Data from the legacy system (single-housed animals) were analyzed and compared to data collected from the digital system (socially housed animals).

Results

Despite the use of different subsets of animals for the assessment of each system, nearly identical measures of QTcV (each >270 msec; up to 45 msec greater than control) were observed following administration of 100 mg/kg moxifloxacin (at 15-16 hours post-dosing), thereby demonstrating concordance between the legacy and digital systems for the expected response to moxifloxacin as delayed ventricular repolarization (Figure 1 and 2).

Under the conditions of each study, no meaningful differences in heart rate (Figure 3) or blood pressure (Figure 4) were observed between single and socially housed animals. Heart rate and blood pressure were generally consistent with the normal variance of WIL Research Historical Control data (±1 standard deviation).

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Results, continued.

Data acquired from each system were of high quality with minimal noise throughout the data collection period. Although slightly less ambient noise was observed in the digital link/EKG signal (Figure 5), the digital telemetry system offers advantages by way of study setup efficiencies, reduced potential for collection errors, and extended implant battery life, all while satisfying expectations for group housing of social animals. While there were no observed clinical observations which would increase the potential for cross-contamination of test compounds (eg. emetic episodes) within the current study, such considerations should be taken into account when conducting telemetric evaluations with socially housed animals (Figure 6).

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REFERENCES