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

K. Kearney, C. Appleby, J. Kieper, P Atterson
WIL Research, Ashland OH USA

Abstract

Telemetric evaluations are largely conducted as part of the Safety Pharmacology core battery to satisfy ICH S7A and ICH S7B requirements for assessment of changes in hemodynamic and electrocardiographic measurements, respectively. Such evaluations have allowed for the collection of conscious 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 (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 PhysioTelD70 (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 error, 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 social 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, 8-20 months, 8-12 kg
- Animals were surgically implanted with TL11M2-D70-PCT 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 PONEMAH v4.80 SP2 software
  - RMC-1 receivers (1 per animal) were connected to a data exchange matrix interfaced to the acquisition software
  - APR-1 was used to adjust for barometric pressure

Digital System:

- 4 female Beagle dogs, 29-33 months, 7-12 kg
- Animals were surgically implanted with L11 Digital transmitters
- Solid tip ECG leads were placed in a lead II configuration(one lead placed in the jugular vein and the alternate placed in the opposite lower thoracic area)
- Arterial pressure catheter placed in the femoral artery
- Animals were socially housed in pairs
- Radiotelemetry System
  - DSI PONEMAH v5.1 software
  - PhysioTel Digital Telemetry
  - TRX-1 transceivers (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 DI water) or moxifloxacin (5, 30, or 100 mg/kg) was administered by oral gavage at a dose volume of 5 mL/kg. Each animal received all doses in a latin square dose design, with at least 3-days between dosing. On each day of dosing at least 60 minutes of baseline data were collected prior to dose 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**(Figures 1 and 2)**.

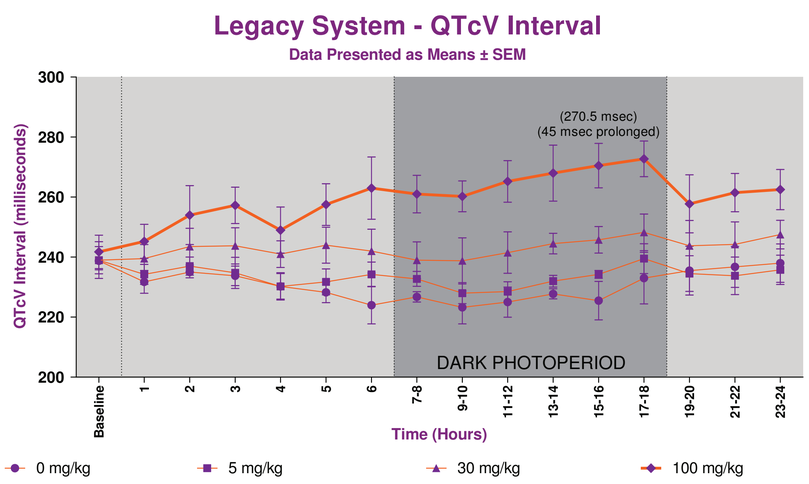

Figure 1

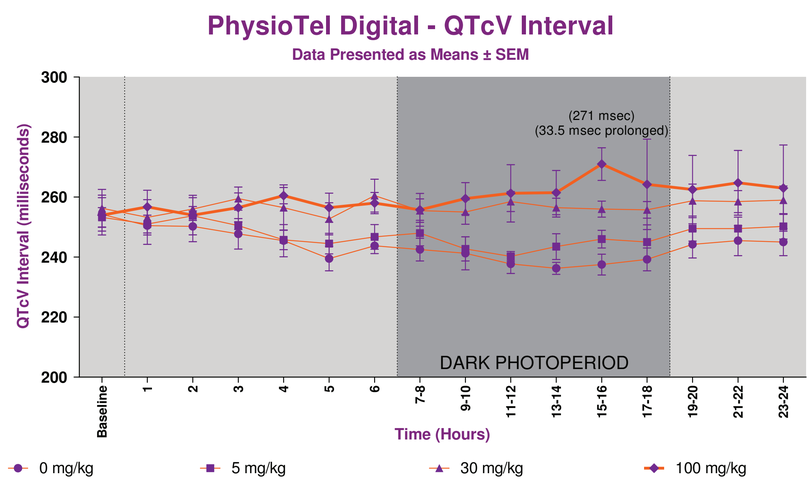

Figure 2

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).

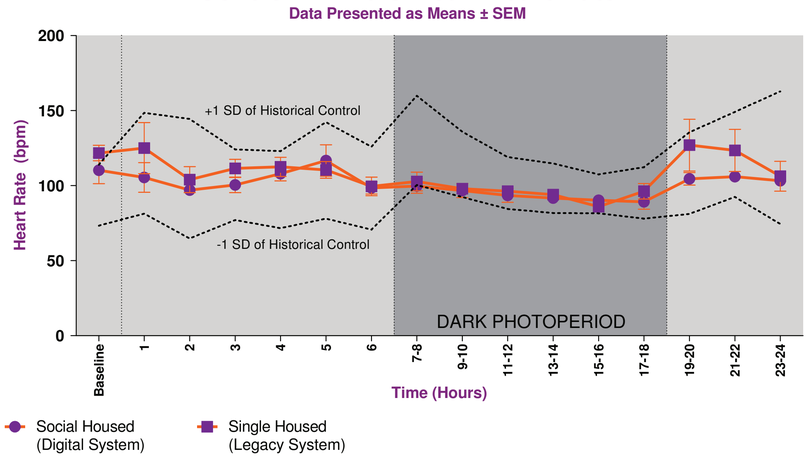

Figure 3

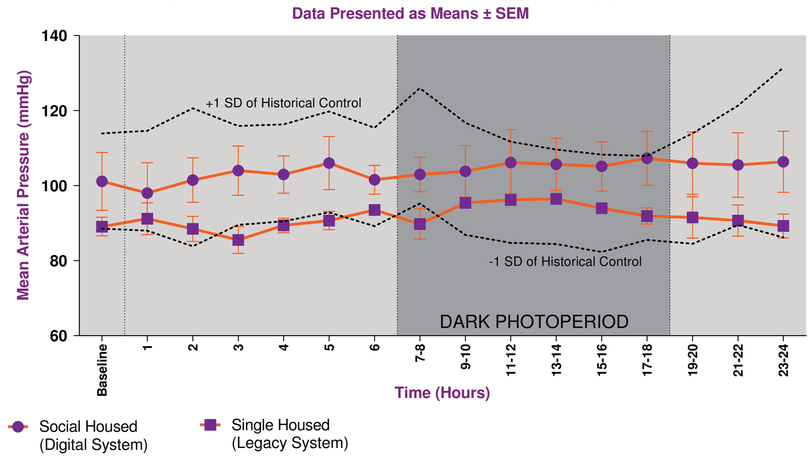

Figure 4

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 (solid tip) ECG signal **(Figure 5)**. The digital telemetry system offers advantages by way of study setup efficiencies, reduced potential for collection error, 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 compound (eg. emetic episodes) within the current study, such considerations should be taken into account when conducting telemetric evaluations with socially housed animals **(Figure 6)**.

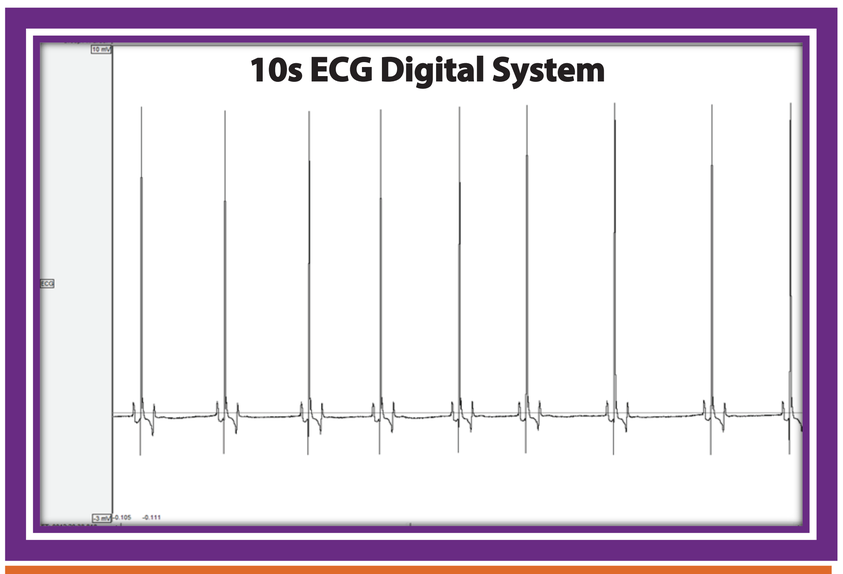

Figure 5

Advantages

- Ability to social house animals during collection*
- Significantly longer implant transmission range
- Prolonged implant battery life allows maximized utilization of implanted animals
- Bidirectional communication allows the transmitters to be turned off remotely
- Auto shut off feature for implants ensure maximization of battery life*
- Ability to configure implant channel outputs to conserve battery life
- Transmitters directly input calibration values, eliminating potential for human input error
- Mitigated risk for improper cage assignment, due to unique frequency and bidirectional communication
- Remarkably clean telemetry signals
- Windows 7, 64 bit platform allows for maximization of computer resources
  - Significantly faster processing speed (24 hours of blood pressure waveforms in <10 sec)
  - Significantly faster data saving (24 hour file in ~5 minutes)
- Ability to switch between legacy or digital platforms application configurations on a single system

Disadvantages

- Potential for vehicle control contamination during social housing with latin square design*
- Number of components can make troubleshooting difficult and cumbersome
- No means of verifying transmitter has been turned on prior to data configuration setup
- Protocol auto configuration feature is templated and cannot be customized
- Auto shut off feature for implant could cause loss of data if signal transmission falls out of range for <1 hour (ie animal sleeping in corner of cage)*.
- System is not compatible with legacy hardware
- Cannot be combined with legacy system implants on a single study, resulting in large investment for migration from legacy colony implants
- Combined cardiopulmonary implant is not available at this time

Figure 6

REFERENCES

National Research Council. *Guide for the Care and Use of Laboratory Animals*, Committee for the Update of the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, Division on Earth and Life Sciences; The National Academies Press: Washington, DC, **2011**.

ACKNOWLEDGMENTS

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