0081

Epicardial (EPI) and intravascular (IV) electrocardiogram (ECG) signal characteristics in cynomolgus monkeys: A comprehensive one-year review

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Intrathoracic epicardial lead arrays have been employed to optimize ECG signal quality in relation to alternative skin surface or subcutaneous lead arrangements. In addition to enhancing the certainty of outcomes on qualitative and quantitative ECG analyses, an additional benefit is realized in the comparative longevity of the high-fidelity signal, which typically outlasts the effective functional (battery) life of the transmitter device. Recent efforts have focused on characterization of a telemetry unit with intravascular lead configuration which has potential to simplify surgical protocols in comparison to the intrathoracic procedure normally associated with epicardial lead placement. This study was designed to evaluate qualitative and quantitative aspects of ECG signal characteristics in the cynomolgus monkey, derived from either an EPI ($n = 5$) or IV ($n = 5$) lead array, with specific comparisons of 1) estimates of raw signal quality, variability, and amenability to qualitative and quantitative integration, 2) variability in quantitative, derived ECG intervals, 3) relative durability of device configurations *in vivo*. Raw signal quality was consistently lower for IV relative to EPI, however, this difference did not translate to any change in the variability estimates for quantitative interval determinations, nor any issue with qualitative rhythm (arrhythmia) analyses. Ultimately, a similar number of library waveform entries were required for EPI and IV lead-based signals for a given proportion of successful signal integration.

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0082

New surface ECG analysis technique reduces variability and increases data density

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Existing commercialized analysis algorithms typically used in safety pharmacology (SP) and toxicology employ template matching techniques that originated in the 1980's. Originally developed for ECG recordings from a hospital environment or other situations where the ECGs are relatively noise free, they have since been widely adopted for ambulatory ECGs. In the presence of noise these techniques have difficulty achieving a template match and exhibit unpredictable template switching that can result in high interval measurement variability. A new technology, referred to as Multi-Domain Signal Processing (MDSP) addresses these shortcomings. In this study, we evaluated the performance of an interval (i.e. PR, QRS, QT, RR) measurement algorithm (MDSPi) based upon this technology. One and two-lead jacketed NHP and dog surface ECG recordings (e.g. DSI JET, emka) were analyzed using MDSPi to obtain 60 second mean and SD and compared to those from commercially available products. Results show that: a) MDSPi and existing algorithms provide equivalent parameter values for relatively noise-free recording segments but differ when noise is present, b) MDSPi measurements on 24-hour surface recordings exhibit 2 to 4 times less variability, c) MDSPi can use information from multiple leads to improve the accuracy of results and better handle noise in recordings, and d) MDSPi achieves significantly higher data density (analyzes >85% of beats). The demonstrated reduction in measurement variability and high data density provided by MDSPi may result in greater sensitivity in detecting drug-induced changes and may facilitate more frequent inclusion of SP-endpoints in toxicology studies.

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0083

Telemetry used to determine efficacy of intravenous plazomicin against inhaled tularemia in cynomolgus macaques (CM)

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Telemetry has been utilized to assess febrile status for infectious agents such as *Francisella tularensis*, a potential bioweapon. Abdominally implanted telemetry probes continuously monitored body temperature (BT), respiration rate (RR), and heart rate (HR). Baseline BT data were utilized to determine febrile status (+2 °C above baseline BT for ≥4 h). Plazomicin [a novel aminoglycoside] was assessed for efficacy in a CM model of lethal pneumonic tularemia. In two separate studies, a total of 52 CMs were treated with placebo or intravenous plazomicin: 25 mg/kg/day for 5, 7 or 10 days (Study 1) or 6.25, 12.5 or 25 mg/kg/day for 10 days (Study 2). Plazomicin doses were chosen to correspond with projected human exposures at doses of 2.5, 5 or 10 mg/kg/day. Treatment was initiated within 12 h and delayed treatment within 24–36 h after fever onset as determined by telemetry. All animals became ill (febrile with tachycardia; and unstable circadian pattern for BT, HR and RR) 31 to 77 h post-infection. All placebo animals died of pneumonic tularemia 5–10 days post exposure. No plazomicin-treated CM died from tularemia. BT, HR and RR of surviving plazomicin-treated animals returned to baseline levels approximately 2–7 days into therapy; except the 6.25 mg/kg/day group where BT and HR remained slightly elevated for up to 30 days. Continuous telemetry monitoring of BT and HR was essential in determining time to initiate treatment as well as characterizing fever onset, treatment and recovery. This study was funded in whole with federal funds from BARDA, Contract No. HHS0100201000046C.

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0084

Cardiovascular effects in three known compounds using the HD-S11 telemetry transmitter: Proof of concept

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This study was conducted to evaluate the cardiovascular effects of a well-characterized β-adrenergic agonist (isoproterenol; ISO), antagonist (propranolol; PRO), and L-type calcium channel blocker (verapamil;