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Feasibility Assessment of Subcutaneous Radio-Telemetry Device Implantation in Cynomolgus Monkeys

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ABSTRACT

With the goal of potentially reducing the trauma caused by surgical implantation of telemetry units without negatively impacting the quality of information obtained from studies involving such implants, Altasciences investigated the feasibility and quality of data capture of two different methods of telemetry device implantation in nonhuman primates (NHPs): the standard intra-abdominal implant method vs. a less invasive subcutaneous implant method.

Four animals (2 per gender) were assigned to each group. Animals were implanted with radio-telemetry transmitters to allow for continuous capture of cardiovascular and body temperature data. All animals recovered for a minimum of 21 days prior to the beginning of monitoring. Rectal temperature and clinical pathology (hematology, coagulation, and serum chemistry) were also captured on a weekly basis.

Minimal changes in clinical pathology observed during the post-implantation phase in both groups were consistent with low-grade inflammation. The pattern and extent of the alterations were comparable across implantation sites, indicating little difference in surgical trauma between methods.

Telemetry data obtained in weeks 1 through 6 showed no marked differences in cardiovascular readings between intra-abdominal and subcutaneous implants. Blood pressure, heart rate, and ECG were all found to be within normal ranges for both groups. There was a notable difference in body temperature readings obtained between the 2 implant sites with mean temperatures recorded in the intra-abdominal implants being 1.5 to 2 degrees higher than temperatures in the subcutaneous implants during the initial 3 weeks of monitoring.

The feasibility of sustaining subcutaneous implant placement was limited by animal size, but the subcutaneous telemetry implant method appears to be a viable alternative to intra-abdominal implants in NHPs of sufficient size.

INTRODUCTION

The purpose of this study was to evaluate the feasibility and functionality of subcutaneously implanted Data Science International (DSI) PhysioTel™ Digital Implant radio-telemetry devices to measure cardiovascular function and body temperature in conscious cynomolgus monkeys. Results were compared to those obtained from standard abdominal implants.

TEST SYSTEM

- Cynomolgus monkeys - Cambodian origin
- Non-naïve status
- 2-5 years old; 2-6 kg body weight
- Screening: physical examination, clinical pathology, ECG and thorax X-rays
- Environmental conditions: individually housed

METHODS

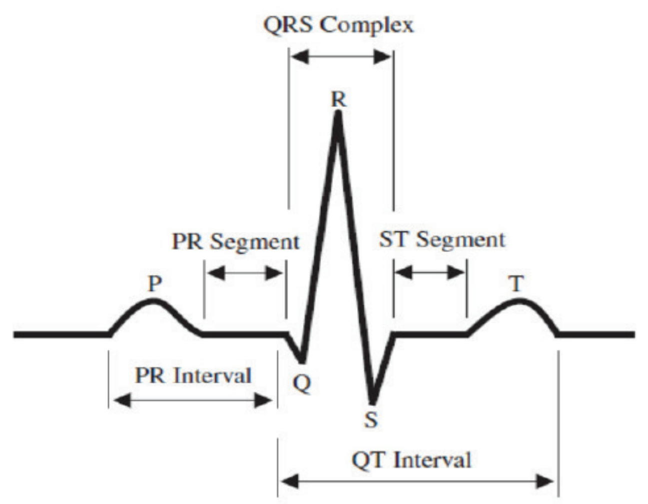
Four animals (2 per gender) were assigned to each group. All animals were implanted with a telemetry transmitter, DSI PhysioTel™ Digital series model M11, either intra-abdominally or via subcutaneous implantation, according to Testing Facility SOPs and the DSI PhysioTel™ Digital Implant Surgical Manual (Rev.03, 2015). Animals were allowed to recover from surgery for a minimum of 21 days following implantation before monitoring procedures began.

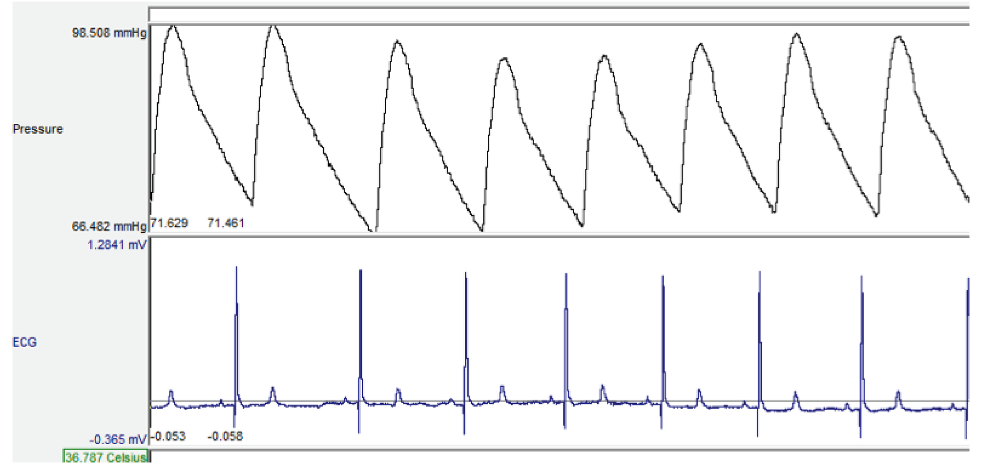
Telemetry data was collected weekly for 6 weeks (24-hr sessions each week) and consisted of the following parameters:

- ECG (RR interval, PR interval, QRS duration, QT interval and corrected QT intervals: QTcB [Bazett's])
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Mean arterial pressure (MAP)
- Heart rate
- Body temperature

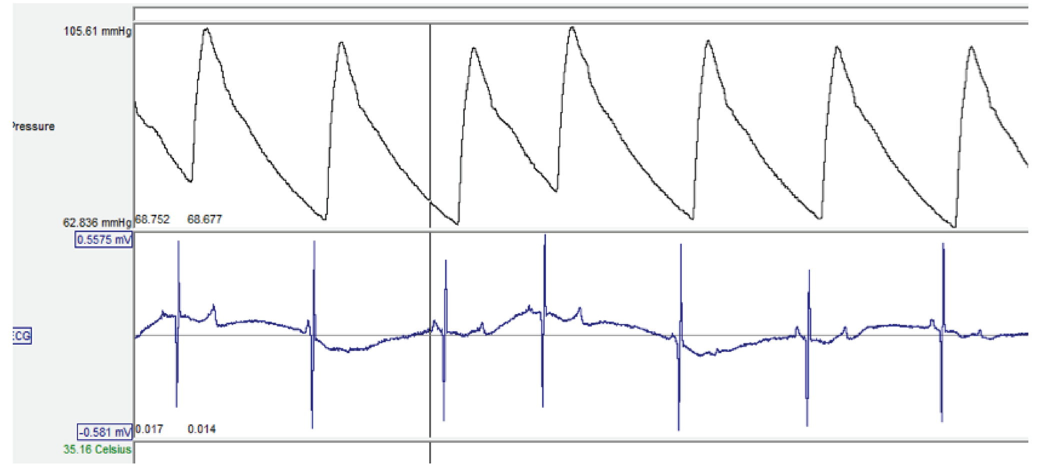
The following were also collected weekly:

- Body weight
- Rectal temperature
- Clinical pathology:
  - Hematology
  - Coagulation
  - Serum chemistry

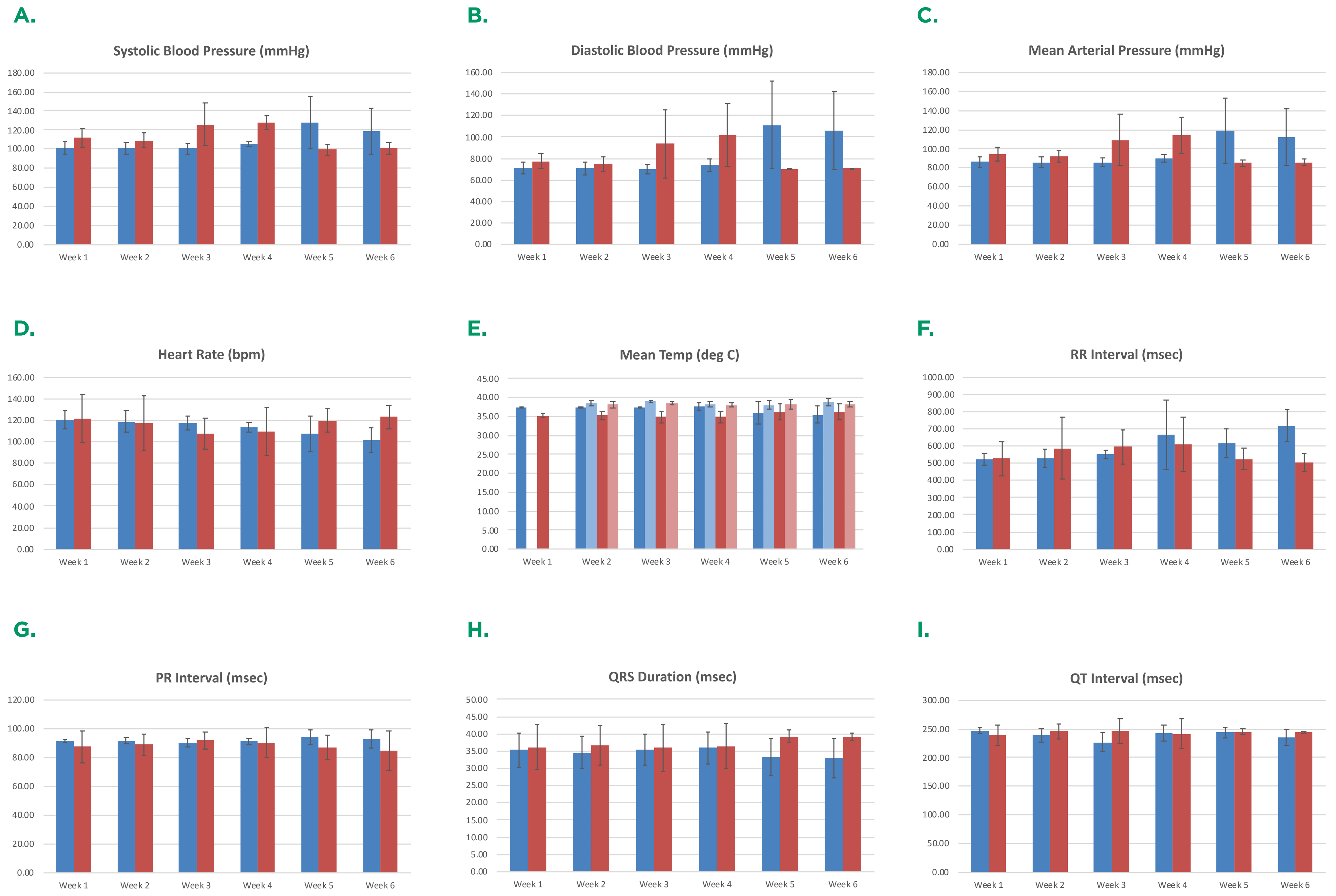




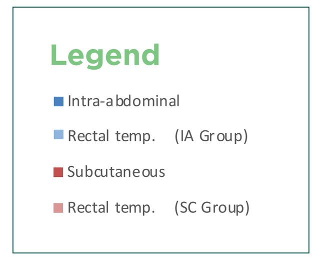
Figures 1. ECG tracing collected from an intra-abdominally placed telemetry device in a male cynomolgus monkey during week 6 of monitoring (approximately 9 weeks post-implant).



Figures 2. ECG tracing collected from a subcutaneously placed telemetry device in a male cynomolgus monkey during week 6 of monitoring (approximately 9 weeks post-implant).



Figures 3, A to I. Telemetry data parameters captured in intra-abdominally and subcutaneously placed implants and reported based on 15-minute averages (male and female values combined to calculate group mean, +/- SD) through each 24-hour weekly timepoint; a) Systolic blood pressure (SBP), b) Diastolic blood pressure (DBP), c) Mean arterial pressure (MAP), d) Heart rate (HR, derived from blood pressure), e) Body temperature, f) RR interval, g) PR interval, h) QRS duration, and i) QT interval



RESULTS

Abdominal and subcutaneous telemetry transmitter implantation caused minimal serum protein changes independent of the implantation site. Decreased albumin and A/G ratio and increased globulin occurred during the post-implantation phase, consistent with low-grade inflammation. The extent of the changes was comparable across implantation modalities, except in one female with an abdominal implant. This female had more profound serum protein alterations associated with a red lump over the implantation site, decreased red blood cell mass, and increased fibrinogen. This indicated a higher level of inflammation in this animal.

Telemetry data obtained in weeks 1 through 6 showed no marked differences in cardiovascular readings between intra-abdominal and subcutaneous implants. Blood pressure, heart rate, and ECG were all found to be within normal ranges for both groups. There was a notable difference in body temperature readings obtained between the two implant sites during the first 3 weeks of monitoring. Mean temperatures recorded in the intra-abdominal implants were 1.5 degrees lower than rectal temperatures recorded on the same day, while temperatures in the subcutaneous implants were often 3 to 4 degrees lower. There appeared to be a gradual loss of accuracy over time in intra-abdominal temperature readings after week 3.

The feasibility of sustaining subcutaneous implant placement was limited by animal size. Larger male animals (4.5-5 kg) tolerated the subcutaneous implants well; the smaller females (~3 kg) did not tolerate the implants well due to the limited subcutaneous space that would not allow the device to sit comfortably. One female was euthanized after 5 weeks of monitoring due to repeated exposure of the device.

All the electrocardiograms were qualitatively and quantitatively within normal limits (Detweiler 1989; Gauvin et al. 2009; Shah 2004). No group related abnormalities in rhythm or waveform morphology were found. The subcutaneous implant test group compared to the standard abdominal implant (Control) showed no differences between the two methods of collection. Both techniques produced some recordings with some intermittent artifact, but electrocardiograms were still considered suitable for evaluation.

CONCLUSION

Subcutaneous telemetry implants appear to be a viable alternative to intra-abdominal implants in NHPs of sufficient size, but are not ideal for smaller animals (~3 kg or less). Changes in clinical pathology parameters were consistent with low-grade inflammation secondary to abdominally or subcutaneously implanted radio-telemetry devices; the pattern and extent of the alterations were comparable across the implantation sites.

The subcutaneous implant technique provided electrocardiographic recordings that were comparable to intra-abdominally placed devices and were accurate for the analysis of any abnormalities that might have taken place.

References:

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