

# Non-Invasive Telemetry for Monitoring ECG in Singly and Group Housed Dogs – The Effect of Moxifloxacin

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## Introduction

Assessment of electrocardiogram (ECG) is commonplace in dog toxicology studies. However, the standard 'snap-shot' technique has significant limitations that impact data quality and hazard identification. To overcome these limitations we evaluated a non-invasive telemetry system for ECG acquisition in freely moving singly and group housed dogs treated with moxifloxacin a fluoroquinolone antibiotic known to cause QT prolongation (Chen *et al* 2005).

## Objectives

- Evaluate the ability of a non-invasive telemetry monitoring system (EMKA IOX and EMKA ECG Auto) for detecting and quantifying changes in ECG parameters in response to moxifloxacin administration in conscious freely moving dogs.
- Identify the time period required for dogs to acclimatise to the jackets and collars required for non-invasive telemetry monitoring.
- Assess the quality of the ECG data collected by comparing the signals acquired and the response detected to data collected from an internalised telemetry device.
- Determine if animals can be group housed when using a non-invasive telemetry system.

## Methods

Male (n=3) and female (n=3) beagle dogs, were acclimatised (over 3 days) to the jackets required for non-invasive telemetry monitoring. On test days animals were prepared with ECG leads and jackets (Fig.1) and were given single oral doses of vehicle or moxifloxacin at 30 mg/kg, when either singly or group housed. Heart rate and Lead II ECG signals (Fig.2) were continuously monitored for 2 hours predose and for 22 hours following dosing. ECG signals were recorded at 1000Hz sampling rate by EMKA IOX and analysed by EMKA ECG Auto. The following parameters were reported: (RR, PR, QRS, QT and QTc corrected according to Van de Waters formula). Group mean and standard error of the mean (SEM) are reported for all numerical data, each data point is the mean over a 30 minute collection period. Clinical observations, food consumption and body weights were also recorded.

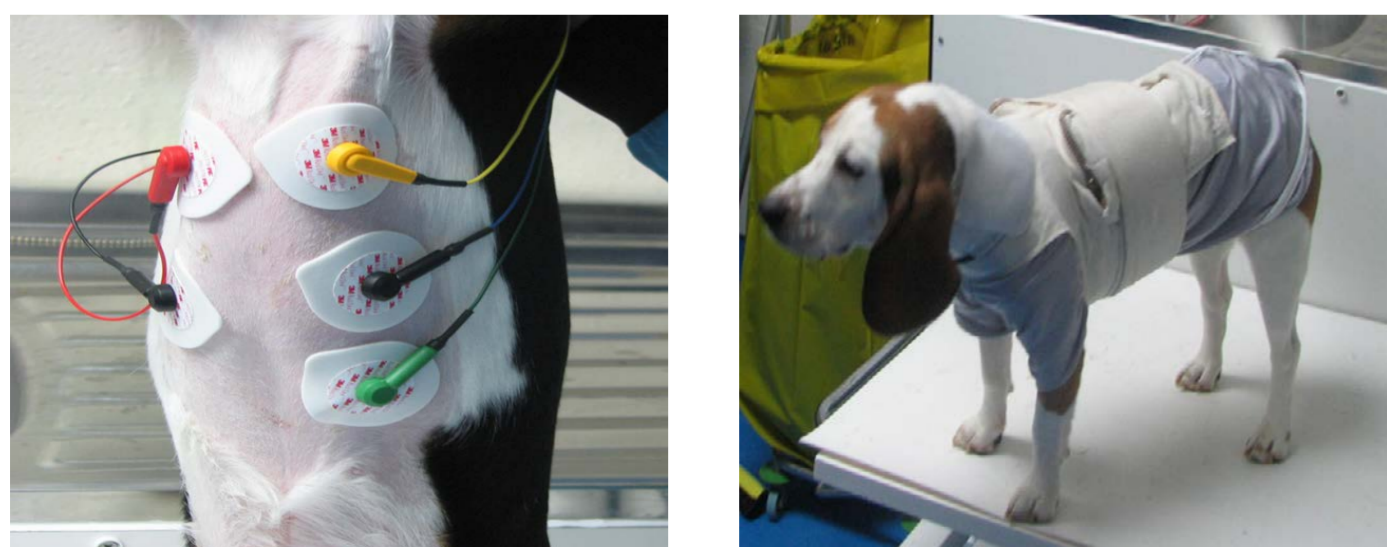


Figure 1 Position of ECG Electrodes and the jacket and collar required for the EMKA Non-Invasive Telemetry System

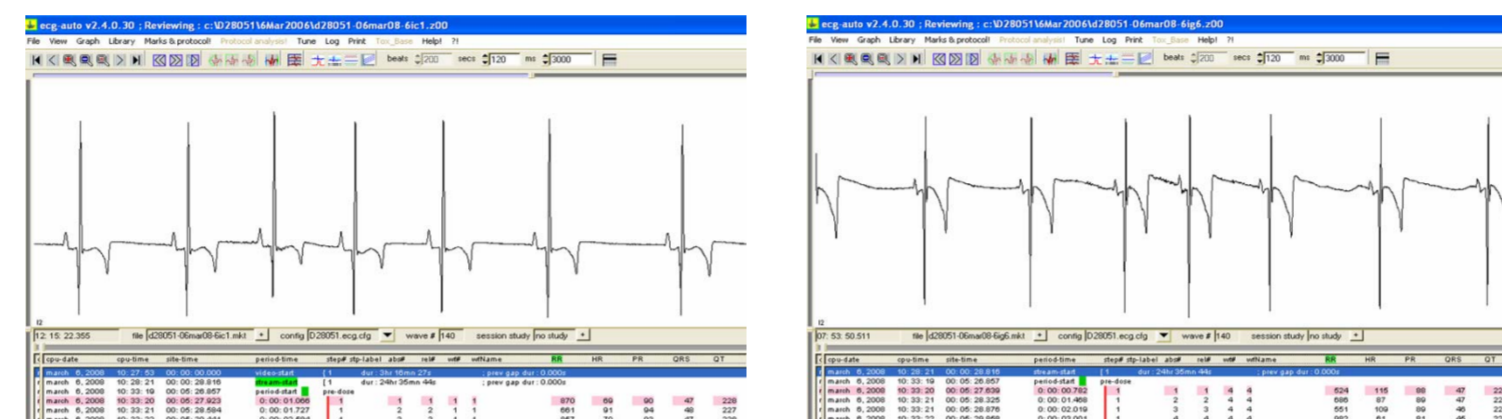


Figure 2 Examples of the ECG Signals Acquired Using the EMKA IOX System and Analysed using EMKA ECG Auto

## Results

- Singly housed (all animals) and group housed (5 out of 6 animals) were successfully acclimated within the 3 day period.
- A reduction in food consumption (20 – 35 %) was observed following administration of moxifloxacin at 30 mg/kg.
- No treatment related changes were noted in clinical signs or body weight.
- Dosing with moxifloxacin at 30 mg/kg produced a reduction (10 - 11 msec) in PR interval at 30 mins to 10 hrs post dosing (Fig.3).
- Moxifloxacin at 30 mg/kg resulted in a sustained prolongation of QT and QTc interval (18 - 22 msec) from 0.5 hrs to 20 and 22 hrs post dosing, respectively.

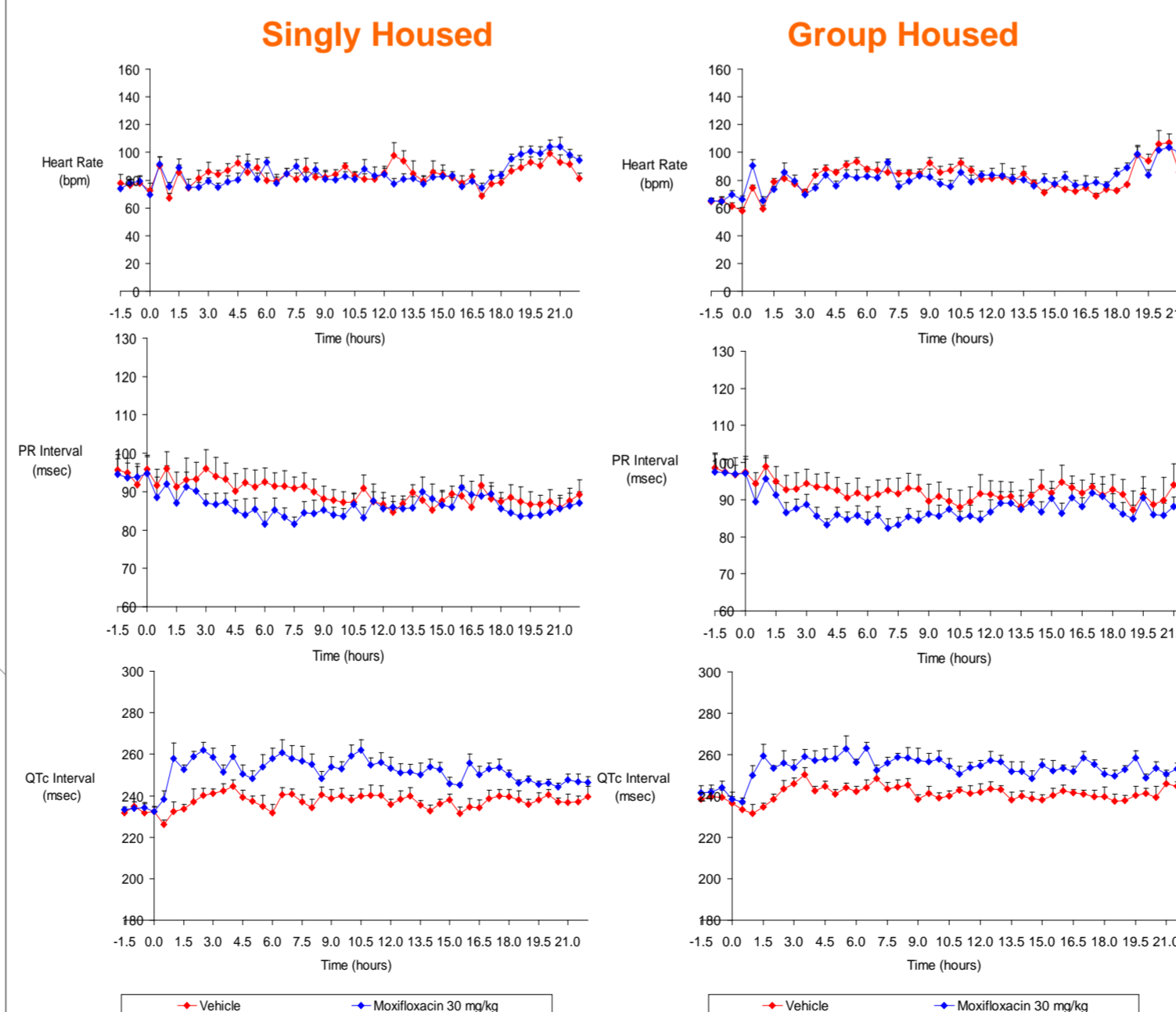


Figure 3 Heart Rate, PR Interval and QTc Interval Following Treatment with Moxifloxacin at 30 mg/kg in Singly and Group Housed Animals (n=6).

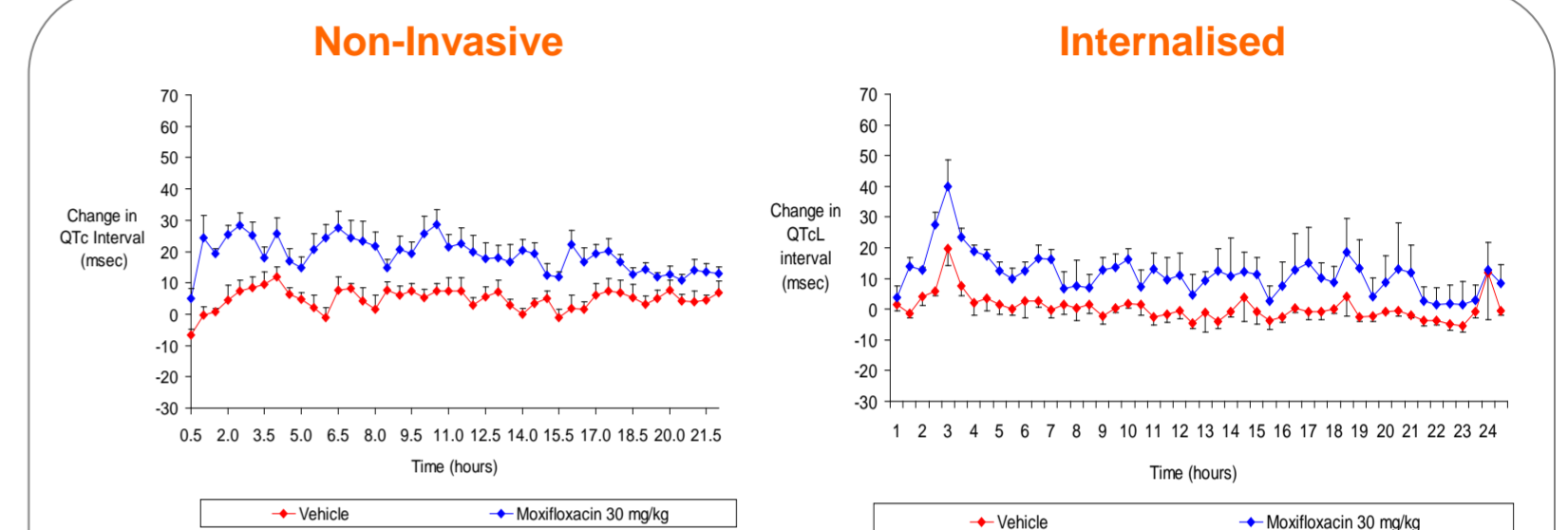


Figure 4 Comparison of the Change in QTc Interval Observed with Non-Invasive (n=6) and Internalised (n=4) Telemetry Systems (DSI).

Heart Rate using Conventional Recording	Predose Heart Rate from Singly Housed Animals	Predose Heart Rate from Group Housed Animals
Approx. 110 bpm	Approx. 75 bpm	Approx. 65 bpm

Table 1 Comparison of the Predose Heart Rate Values Observed with Non-Invasive and the Standard 'Snap Shot' Sling Restrained Technique for Measuring ECG

## Discussion

- The QT prolongation observed in response to moxifloxacin in this study is similar in magnitude and duration to the effect observed when using internalized telemetry in a previous Safety Pharmacology study and the effects reported in the literature (Chen *et al* 2005, Mittelstadt & Hart, 2005), (Fig.4).
- The pre-dose heart rates obtained from animals using non-invasive telemetry were lower (65 to 75 bpm) compared to the average heart rates obtained from the current method used to monitor ECG in toxicology studies (110 bpm) (Tab.1).
- A non-invasive telemetry monitoring system can be successfully used to detect and quantify changes in ECG parameters in response to treatment in conscious freely moving dogs, when both singly and group housed.
- Acclimatisation of dogs to the jackets and collars required for non-invasive ECG recording can be achieved in 3 days.

## References

- Chen *et al* (2005). QT prolongation and pro-arrhythmia by Moxifloxacin: concordance of preclinical models in relation to clinical outcome. *B.J.P.* 146, 792-799
- Mittelstadt & Hart (2005). Effects of moxifloxacin on QT interval in conscious dogs. *J. vet. Pharmacol. Therap.* 28, 253-256.