Non invasive blood pressure monitoring in ambulatory beagle dogs
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Introduction
The integration of safety pharmacology endpoints into early toxicology studies brings scientific, practical and ethical benefits, and there has been increasing interest in such approaches. In this context, the recording techniques must be non-invasive, and it is currently possible to record ECG, respiration and behavior in freely moving non-rodent models by non-invasive external telemetry associated with video recording. However, one of the main physiological signals missing until now has been Arterial Blood Pressure (ABP), for which a surgical approach is required. The aim of the present study was to evaluate the feasibility and efficacy of a novel technique for Non-Invasive Blood Pressure (NIBP) recording by telemetry in dogs, using the oscillometric cuff method developed by EMKA Technologies.

Two male and two female beagle dogs were used in the study.

Preparation of the animals
1) For external telemetry recording (EMKA Technologies system)
On each day of treatment, ECG electrodes were stuck on the thorax of each animal using adhesive patches, and connected to multi-derivative electrodes (Fig. 1). A dedicated cuff was placed around the base of the tail, the area was shaved beforehand to permit better contact with the caudal artery. A jacket was used to carry the external telemetry equipment and keep the electrode in place (Fig. 2).

2) For internal telemetry recording (Data Sciences International (DSI) system)
Before inclusion in the study, the animals were surgically implanted with telemetry devices (Type TLI11M2-D70-PCT).
On each day of treatment the animals were placed in individual cages equipped with DSI receivers.

Study design
Before the first day of treatment, the animals were habituated for at least 24 hours to wearing the jacket.
The animals received successive treatments with the vehicle (5% methylcellullose aqueous solution), and the reference item, prazosin, at the dose-level of 0.1 mg/kg, by oral administration (gavage) under a dosage-volume of 5 mL/kg.
The internal and external telemetry systems were used to continuously record, in parallel, cardiovascular signals from 1 hour before dosing until 12 hours afterwards. The tail cuff was inflated/deflated at intervals of 2 minutes.

Recording and analysis systems
1) For external telemetry (ExtT)
ECG and ABP signals were recorded using IOX software, and analyzed using ECG-Auto software.
2) For internal telemetry (IntT)
ECG and arterial pressure were recorded through DSI Open-ART and Notocord HEM (Notocord System, France) and analyzed with EMKA proprietary detection algorithm (shown in green) through the XY plot points; finally, systolic, mean and diastolic values are estimated from the fitted curve. During the study, approximately 75% of the inflation/deflation cycles recorded were of sufficient quality for analysis.

Results
Part 1: Quality and analysis of the signal obtained with the NIBP system
The raw ABP signal measured during a cycle of tail cuff inflation/deflation is presented in Fig. 3a. The signal is processed using an EMKA proprietary detection algorithm in order to extract values for systolic, diastolic and mean arterial blood pressure from each cycle, according to the following sequence: the signal is filtered and a shape recognition algorithm excludes invalid pressure pulses; then, valid pressure pulses produce an XY plot of pulse amplitude versus average cuff pressure (Fig. 3b). Fitting techniques allow the best curve to be obtained (shown in green) through the XY plot points; finally, systolic, mean and diastolic values are estimated from the fitted curve. During the study, approximately 75% of the inflation/deflation cycles recorded were of sufficient quality for analysis.

The values of ABP signals recorded with the non-invasive system and with the implanted catheter were slightly different, but the variations were consistent (Fig. 4).
The lower values obtained with NIBP were probably due to the fact that pressure was measured in the caudal artery for NIBP and in the descending aorta for the implanted catheter.
The expected effects of prazosin on ABP were reported with both recording systems: marked decreases in systolic arterial pressure (-22% with IntT and -16% with ExtT) and in mean arterial pressure (-19% with IntT and -22% with ExtT) were noted during the first hours after dose administration (Fig. 5). No effects were observed on diastolic arterial pressure.

Conclusion
Using this oscillometric cuff method for non-invasive blood pressure monitoring in freely moving dogs, we were able to obtain signals of good quality, and 60 to 90% of recorded cycles produced reliable data.

Cross validation against data obtained from implanted telemetric sensors demonstrated a good correlation between the two methods.
Expected changes on systolic, diastolic and mean blood pressure were demonstrated after administration of the reference drug prazosin. In conclusion, this study demonstrates that NIBP measured by external telemetry is an appropriate alternative method for recording ABP over long periods in dogs without the need for surgery.