Inclusion of Blood Pressure Measurements in Canine Toxicology Studies

Validation of a non-invasive telemetry method
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Introduction
The current gold standard for cardiovascular safety evaluation of new drugs in safety pharmacology studies in large animals is the use of invasive implanted transmitters. However these studies are generally designed to evaluate acute effects of compounds so a method of evaluating repeated dosing over longer periods of time is needed. While the use of non-invasive external telemetry is becoming a new standard for ECG recordings, simple options for blood pressure assessment are still to be defined.

Current Method
Currently, the method used to measure blood pressure in our sub-chronic and chronic toxicology studies is an invasive ear catheter. This method has many disadvantages, firstly it is invasive and the animals have to be restrained in order for the catheter to be inserted. This process is stressful for the animals which may affect the quality and accuracy of the data recorded. Also using this method you can only get a snapshot result of about 30 seconds and it can only be repeated twice a day, once a week due to recovery of the ear artery.

NIBP System
Recent advances in technology have led to a new way of measuring non-invasive blood pressure using high-definition oscillometry.

Advantages
- The blood pressure device designed by EMKA technologies uses indirect oscillometric tail cuff measurements and the well-established principle of blood flow occlusion of the medial coccygeal artery to measure blood pressure in the freely moving dog.
- No continuous trace available limiting correlation with ECG findings.

Disadvantages
- However due to the nature of the jackets and tail cuffs the dogs require training so they become accustomed to wearing the jacket and cuffs.
- Blood pressure recordings up to 24 hours which gives a better idea of any effects the compound may be having over time.

How does it work?
The dogs are equipped with surface ECG electrodes and a jacket which is used to carry the external telemetry equipment. A blood pressure cuff as seen in the picture below is placed around the base of the tail (shaved beforehand to ensure better contact with the artery) and left for the duration of recording (up to 24hrs). The signal is picked up by an aerial in the pen and the data is automatically uploaded onto the computer.

Validating our new technology
To begin with we have already assessed the acceptance of the jacket and cuff, characterised the length and duration required to jacket train and determined the optimal positioning of the cuff along the tail artery.

The second phase of the study validation will investigate the number and frequency of tail cuff inflations required to get a successful and accurate blood pressure measurement, and comparing baseline signal with the DSI implanted telemetry system.

As the third phase will involve a cross validation of the EMKA non-invasive blood pressure system with the DSI implanted system to detect changes in blood pressure in response to various compounds and may help the reduction of animal use and study cost.

Study Validation Plans
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The third phase will involve a cross validation of the EMKA non-invasive blood pressure system with the DSI implanted system to detect changes in blood pressure in response to reference compounds known to cause hypertension or hypotension.

Future Work
Once validated, the NIBP system will be incorporated into toxicity studies as an addition to the current 24 hour ECG recordings. As an extension to this study non-invasive respiratory assessment in conscious free-moving dogs using EMKA respiration belts will be investigated.

References