

A Dynamic online tool for cardiovascular and ECG data analysis

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1. Introduction

Speed is, beside quality, an important factor in a modern drug development process. In addition, refinement of data analysis can help to substantially reduce the number of animals used in a typical (cardiovascular) safety evaluation study.

Normally, the huge dataset of a telemetry study is thoroughly analyzed after the entire study. Furthermore, given the nature of these studies, statistics are performed even later. However, sometimes unwanted effects appear after the first day of administration and the question is whether these effects are significant when analyzed with statistical tools.

So, the subject of this work was to develop an online tool that can “on the fly”, during a running experiment, analyze the data and compare it with a historical dataset. With this easy-to-handle tool, one gets a visual feedback in real-time about the significance of an effect and can therefore adjust the doses or design during the onset of a study.

2. Methods

Trained dogs, minipigs and primates were equipped with radiotelemetry transmitters (ITS, DSI and TSE). Aortic pressure (AP), left ventricular pressure (LVP), ECG lead II and body temperature could be continuously monitored

Digitized telemetry signals were processed by NOTOCORD HEM software and collected from each telemetry system on a beat-by-beat basis and stored in the SEPIA database (Boehringer Ingelheim cloud). Results and visualizations were calculated in the R console of Spotfire® software (which accessed data directly from the database).



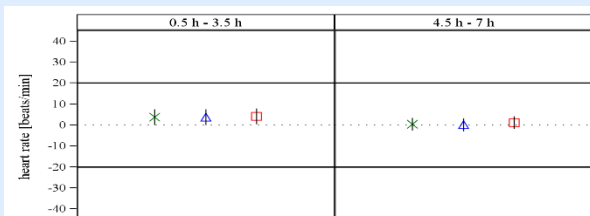
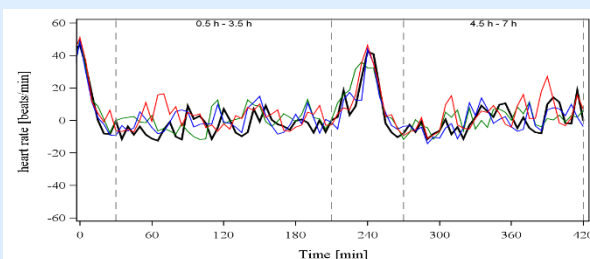
Gathering data, storing them on SEPIA database, and analyze and visualize the results.

3. Results

This online tool was shown to :

- Standardize the parameters of interest. It shows values over time for each compound dose. This time chart also dynamically specifies the minimum and maximum range of parameter in distinct time phases of the experiment.
- Calculate the AUC (Area Under the Curve) of parameters value and ANCOVA (Analyses of Covariance) calculation based on linear regression model. The graph shows estimated adjusted means with upper/lower CL for each dose in each time phase.
- Calculate QTc (Heart rate correction) which means length of QT-interval independently from rise in heart rate.

All the statistical results such as significant value, t test, p-value, standard deviation, area under the curve, etc. have been provided in different related tables for a closer look and filtered detail views on data.



4. Conclusion and Outlook

In cardiovascular safety pharmacology studies, data is typically acquired by telemetry from awake, non-anaesthetized animals. Sampling this data on a beat-by-beat basis generates huge amount of datapoints. Implementing an online visualization and statistical evaluation tool, can help to significantly speed up the process of drug safety evaluation.

Using Spotfire combines three important advantages:

- R (or Python) can be embedded in Spotfire. Complex calculation steps and all the advantages of R-Language can be used from data cleansing to complex modelling.
- It offers sophisticated state-of-the-art visualization tools.

4. References

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