Continuous 12-lead ECG Recording in Clinical Trials

Coordination with the ECG Warehouse

Justin L. Mortara, Ph.D.
Vice President, Mortara Instrument
Continuous 12-lead Recording

12-lead Holter

12-lead Telemetry

24, 48, 72+ hours of data

\[ \approx 0.5 \text{ GB/day/subject} @ 1000 \text{ samples/second} \]
Uses in Clinical Trials Today

- Snapshots extracted for interval duration measurement (e.g. QT).
  - Continuous recording simplifies collection of many 12-lead ECG time points in so-called thorough-QT (TQT) trials.
  - Record everything, extract individual time points afterward for measurement.

- NDA submission includes TQT trial.
  - Extracted ECGs from TQT trial uploaded to ECG Warehouse.
  - FDA can review ECG waveforms and annotations once loaded into Warehouse.
ECG Warehouse

• Motivation for ECG Warehouse
  – Facilitate regulatory review of ECG studies.
  – Enable research into alternate repolarization measures using rich digital data repository.

• Status Today
  – Over 150 Studies accessible for FDA review
  – Nearly 2 million ECGs and quickly growing….this is fastest growing digital ECG repository in the world.
  – CSRC is developing mechanisms for select data from this repository to be used for research purposes.

Accumulated ECG snapshots
More with Continuous Records

- Expanded potential for regulatory review
  - Not just reviewing the extracted ECG and annotations, but also reviewing time before and after.
  - Excellent for understanding evolution of morphology changes.

*Flattening of T-wave from hour 1 to hour 3.*

*What is happening in between these extractions?*
More with Continuous Records

- Improve QTc determination.
  - Historical approach is to use prior RR in QT normalization.
  - Utilize continuous record for bin-method (method of Coumel) or alternate determination of RR (RRc pictured at right)
- Reduce variability, reduce need for additional subjects, reduce cost of study.
  - Cannot be achieved with simple snapshot ECGs.
More with Continuous Records

- Apply automatic algorithms to entire continuous recording.
  - Increase statistical power by making the ECG algorithm do “all” the work.
  - Detection of positive control well reproduced using these methods.
- In a 24 hour recording there are over 8,600, 10-second snapshot ECGs to be analyzed and typically over 100,000 beats to be annotated.
  - Excellent venue for algorithm automation.
  - If this becomes common, what should be submitted to ECG Warehouse?
Conclusions

• Use of continuous recordings is already widespread.
• Much more can yet be done to leverage the continuous aspect of the recorded data.
• Creating a warehouse of continuous recordings can further both regulatory and research possibilities.