Continuous 12-lead ECG Recording in Clinical Trials

Coordination with the ECG Warehouse

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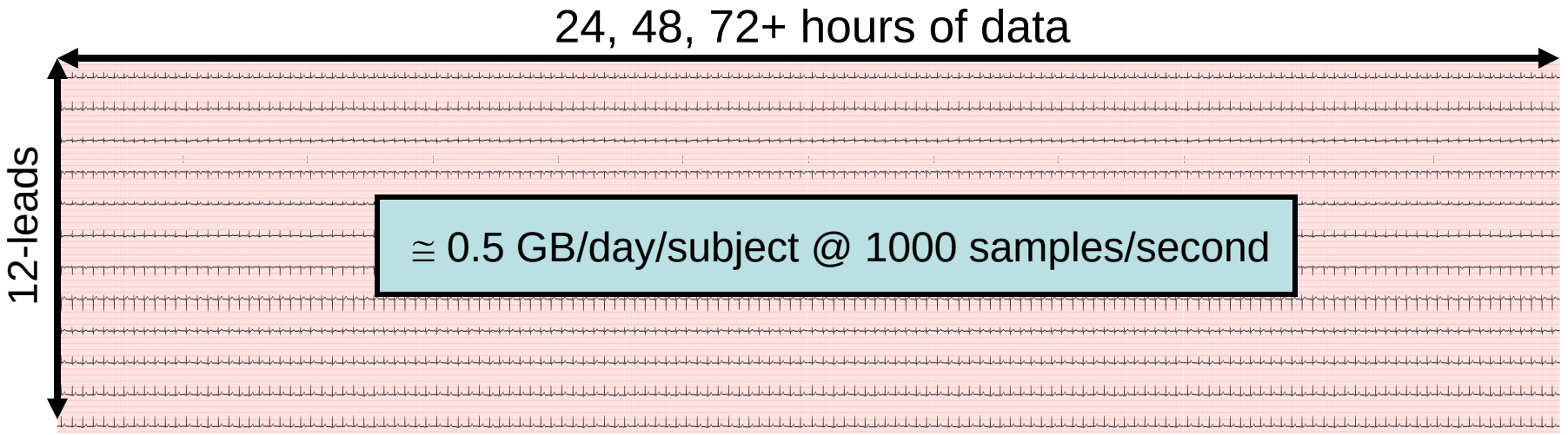
Continuous 12-lead Recording

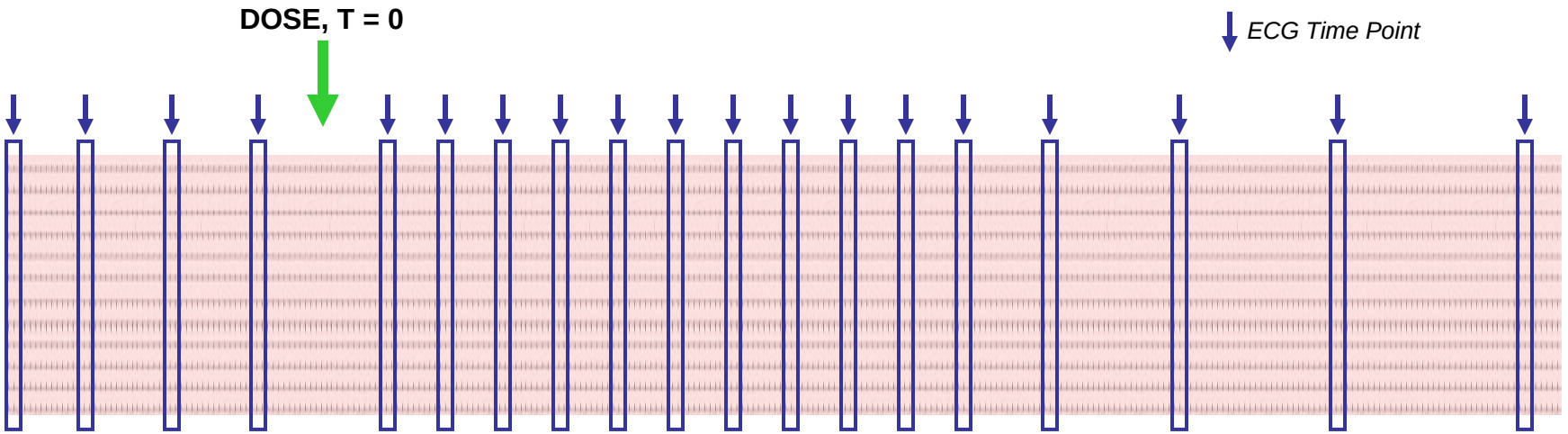
12-lead
Holter

12-lead
Telemetry



Uses in Clinical Trials Today

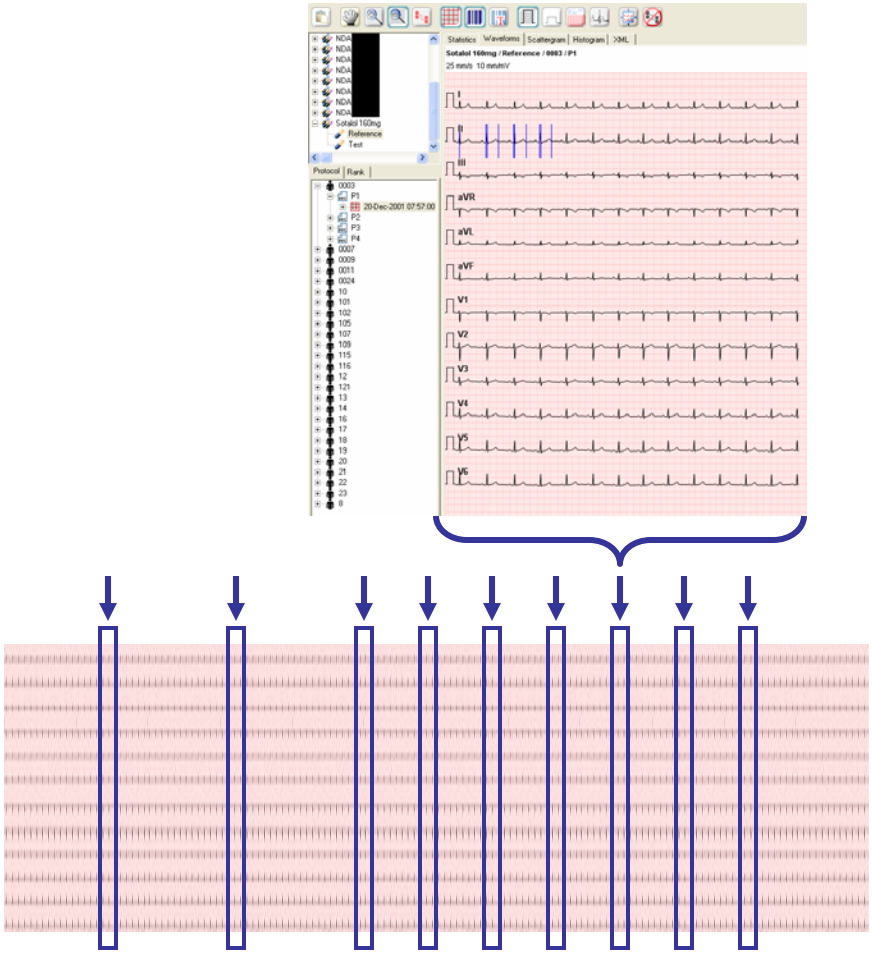
- Snapshots extracted for interval duration measurement (e.g. QT).
  - Continuous recording simplifies collection of many 12-lead ECG time points in so-called thorough-QT (TQT) trials.
  - Record everything, extract individual time points afterward for measurement.



- 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

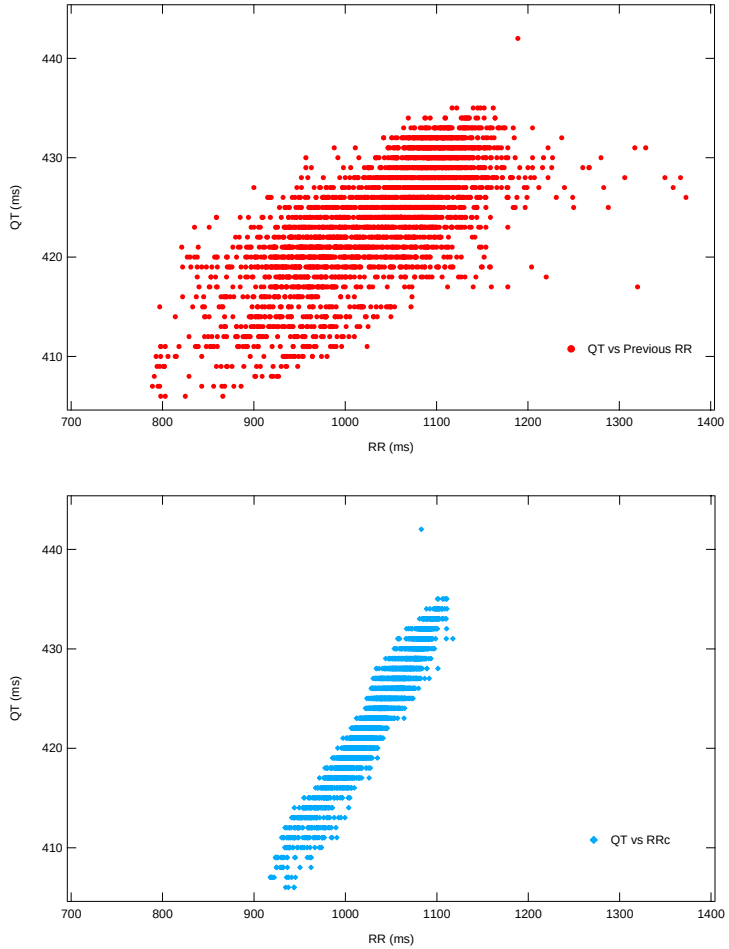
- Expanded potential for regulatory review
  - Not just reviewing the extracted ECG and annotations, but also reviewing time before and after.
  - Excellent for understanding evolution of morphology changes.

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

What is happening in between these extractions?

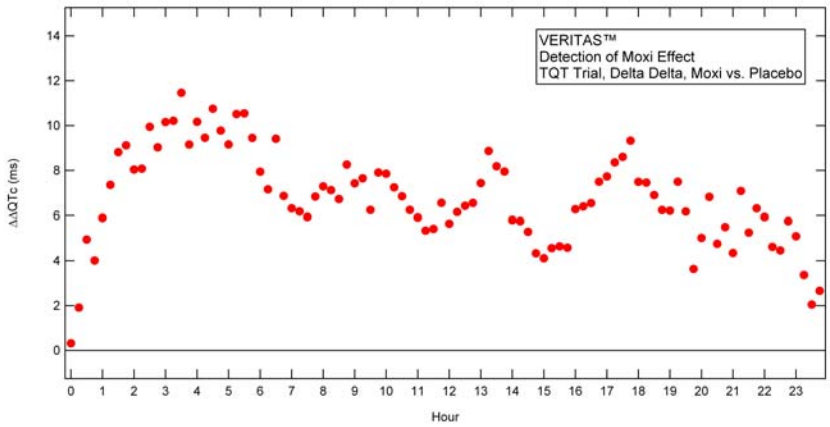
More with Continuous Records

- 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.