



AMPS-QT

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AMPS-QT is a quarterly journal dedicated to all the people and organizations involved in the world of cardiac safety. Published by AMPS LLC, it covers all aspects of methodology and software technology related to clinical trials and Thorough QT studies.

Happy 10th Birthday AMPS-QT!!

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Editorial

When we wrote the first editorial, 10 years ago, we wanted to make sure from the beginning that our main purpose for the AMPS-QT was not to become another scientific journal, competing with all the existing authoritative publications in the field of cardiac safety.

Rather our focus was to offer a series of articles contributed by important and influential people in the community. We sought those active in the field of clinical trials and Thorough QT studies (TQT) and willing to share their views and ideas.

In addition, we wanted AMPS-QT to become a useful communication tool for our existing and future AMPS customers and a means for them to learn periodically about AMPS' new methods and software tools.

As we look back, after 40 issues, we can proudly say that AMPS-QT went "above and beyond" for our readership. And our thanks go to the contributions made by many of our readers! We thank all of you for making this quarterly a great success and for your continued attention and support! Let's keep up the good work, for the next decade. We welcome contributions and ideas for articles as well as comments. Please send them to: AMPS-QT@amps-llc.com.

Noteworthy Contributions

In the 39 previous issues, AMPS-QT has hosted over 30 external contributions from exceptional members in the Pharmaceutical industry, ECG Corelabs, CROs, and Hospitals and University faculty. Each contribution presented interesting topics in many different aspects of Electrocardiology. Some contributions covered specific research projects from the authors, whereas others were more focused on ECG analysis in general. In addition to external contributions, in some issues of the bulletin, AMPS presented their own view on important topics of the day.

Remarkably, in early issues (it was only 2009...), AMPS introduced two topics that are still extremely up to date: "Continuous Holter in clinical trials" and "ECG Biomarkers". Indeed, these areas of development led to specific products now available as part of AMPS licensable product solutions.

Initially we focused on the development of automated "ECG biomarkers" obtained by modeling the ECG repolarization segment with parameterized functions named Gaussian Mesa Function [1,2]. This modeling leads to a set of surrogate parameters that quantify various features of the repolarization component, including parameters of duration

(JT and QT internals), amplitude and morphology. All these measurements are now part of AMPS **BRAVO** algorithm and can be used within *CalECG*, *Fat-QT* and *FDAEcg Suite*.

In 2013 we began the development of **CER-S** platform, namely the AMPS suite of software tools for the analysis of Continuous ECG Recordings. Initially, the software addressed the management of Holter recordings for the submission to the FDA Warehouse, in FDA aECG HL7 format. Then we moved to the development of **ABILE**, an algorithm aimed at ECG beat detection and classification, and at the assessment of cardiac atrial and ventricular arrhythmias. We increased our efforts to make **ABILE** extremely flexible, thus fully compatible with ECG records from multiple public (and private) data formats. Additionally, it is adept at data based on any number of leads, covering a sampling rate range from 100 to 1000 Hz, and capable to seamlessly operate on ECG recordings with lengths from 5 minutes to 30 days.

CER-S has been one of the primary development activities at AMPS of the last few years. As previously reported in AMPS-QT, over the past years we have released several versions, with progressive algorithm update and enhancements of the user interface. In addition to standard arrhythmia analysis, **CER-S** also includes the capability of measuring ECG intervals such as PR, QRS, QT, JT_p, TpTe plus it provides ST displacement and heart rate variability analyses. Together with **CER-S**, AMPS continues to support **WinAtrec**, the software solution developed more than 15 years ago in collaboration with the Lariboisiere Hospital in Paris. **WinAtrec** includes the Holter-binning approach and all the rate-related averaging techniques used to assess the dynamic behavior of repolarization [3] and the circadian patterns of Brugada syndrome [4, 5].

We have published a few contributions which cover the importance of ECG quality and focus on the optimization of ECG collection, towards exclusively acquisition of digital electrocardiograms with more sophisticated digital ECG equipment. Other articles were on the development of algorithms for ECG analysis software with the addition of signal quality checks and metrics to make the "highly" automated dream a reality.

FDAEcg Suite, our platform solution to manage all aspects of ECG quality, was released 10 years ago. This software package offers validation of resting ECGs in FDA aECG HL7 format, and allows successful uploads to the FDA Warehouse. In addition, the **FDAEcg Suite** includes ECG metrics to evaluate ECG quality in heterogeneous fashion,

including quality metrics, such as, noise level (in various frequency bands), heart-rate, T-wave amplitude and complexity (to assess presence of notches), and many other scoring functions. These features have been helpful for years to Corelabs to identify problematic sites or dysfunctional equipment while the trials were ongoing and promptly resolve the issues.

Fat-QT, originally released in 2011, is designed for the optimization of the ECG flow in TQT studies, based on ECG quality metrics available in **FDAECg Suite**. The basic principle is that *good quality* ECGs where the measuring algorithm correctly measures the expected annotations will be measured fully automatically. On the other hand, *low quality* ECGs (with for example: high noise level, low-amplitude T-wave, biphasic T-wave, or with presence of notches) will be measured automatically, *but a cardiology review will be requested*. Then, whenever editing is performed by the cardiologist on a specific ECG, all the ECGs from the same subject will be prompted to the cardiologist for review, to limit editing bias.

There are three historical AMPS software products that were already available 10 years ago (before the launch of AMPS-QT bulletin) and that are still largely used today are **CalECG**, **Antares** and **ECGScan**.

CalECG (now at version 4 generation), is the most popular among AMPS software solutions. In the Pharmaceutical arena, the majority of Corelabs and CROs use today's **CalECG** and its embedded **BRAVO** algorithm to annotate resting ECGs or Holter ECG extractions acquired during clinical Trials. Thanks to a sophisticated and comprehensive program interface, **CalECG** can be used as a standalone application or embedded into a larger platform manager.

As early phase clinical trials remain based on the concept of timepoints, **Antares**, is the AMPS solution in wide use to obtain automatically noise-free and stable heart-rate ECG extractions at the given study protocol timepoints.

What was perhaps unexpected back in 2009 was the large need still in 2018 for digitization of paper ECGs. With the large production and easy availability of high-quality digital ECG devices, we believed that paper ECGs would soon disappear, while **ECGScan**, AMPS software for the digitization of ECG waveforms from scanned paper ECGs, is still largely used, not only in research and academic environment, but also on pharma studies, mainly in oncology field.

Apart from **CER-S**, latest software releases from AMPS include **ViewECG Web**, a JavaScript library designed for fully-customizable display of digital ECGs viewed by an HTML5 web browser. This new solution leverages the ease of the Internet to deliver a display of ECGs, customizing the layout and enabling the end-user to interact with the rendered digital ECG. The Viewer supports the display of both 10s Rhythm strip and Representative Beats and ECG annotations from input ECG file or passed through the APIs. Thanks to this interface, ECG layout, paper speed, number of leads and zooming can be fully customized.

A special Thanks to all the contributors!!!

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- [2] Dubois R, et al. A Machine Learning Approach for LQT1 vs LQT2 Discrimination. IEEE CinC 2012; 39:437-440.
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- [4] Extramiana F, et al. Quantitative assessment of ST segment elevation in Brugada patients. Heart Rhythm 2006; 3:1175-1181.
- [5] Extramiana F, et al. Type 1 electrocardiographic burden is increased in symptomatic patients with Brugada syndrome. J Electrocardiol 2010; 43:408-414.

- Arrhythmia detection and Arrhythmia editor
- ECG Beat Measure, for measuring averaged time-templates ECG complexes, including ST-displacement assessment.
- Report generation.

AMPS Notebook

The Board of Directors of AMPS LLC is pleased to announce the appointment of Dr. Fabio Badilini, as the new President, effectively January 1st, 2019. Fabio's appointment is a clear reflection of the board confidence in his ability to lead the company to even greater success in the future. Fabio retains his role as Chief Scientist continuing to be the leader of the AMPS R&D department. The Board is delighted to welcome Fabio to his new expanded role and looks forward working with him.

Franco Treccani, AMPS Founder, Partner, and former President, has been awarded a lifetime AMPS Fellowship as reward for his pivotal role in the founding of the company and his two-decade service.

Products News

Looking forward

In 2019Q1 we are going to release a new version of **CER-S** (v. 3.2.0), including the following revised platforms:

- Continuous ECG beat detection and classification, including the fully renewed **ABILE** algorithm, with new long analysis capability, up to 30 days.
- ECG beat editor



The members of the AMPS team from when AMPS-QT was launched 10 years ago.
On the cover page: view of the castle of Montichiari, Italy, the location of AMPS R&D Department.