



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.

Editorial

Several of our readers are probably familiar with the history of AMPS, how it was born, and how it developed, but we thought that it would be worth it to provide a brief summary, with an historical perspective, highlighting the beginnings and the milestones that in the last 14 years have become our trademark. The best candidate to write this summary was easily identified in Gian Franco Treccani, AMPS President since its inception. Gian Franco's short biography was published in the 13th issue of AMPS-QT and so our readers are already familiar with his career highlights. After an outstanding academic path started in Italy, continued in France, and concluded in the United States he has spent many successful years in the industry, holding managerial functions in several multinational corporations, and he has played a pivotal role in the birth of AMPS. It is therefore also thanks to him that AMPS is nowadays a consolidated reality.

A Note from the President

Gian Franco Treccani, President, AMPS llc.

The encounter between a brilliant man and a business man: if I had to say in a couple of words how AMPS was born.

It was the year 2000, when, in Paris, I received a call from an old friend, asking me to meet his son Fabio, a young biomedical engineer that, at the time, was working with Coumel at Laribiosière Hospital. It's difficult to forget the feeling I had, facing a person that, behind a gentle and simple attitude, was hiding talent and knowledge that, I soon realized, could easily develop in a successful business venture.

And time proved us right. Fourteen years later, AMPS is a successful business, globally recognized. A dynamic

Company able to interpret and often foresee market needs, offering state of the art Software in the cardiovascular arena.

In the past years, Fabio's work has been recognized by the academic and professional world. These recognitions and particularly the Commissioner's Special FDA Citation in 2003 and the Honorary Fellowship of the American College of Cardiology in 2009, represent a further guarantee of the quality and value of AMPS work.

As President, I am particularly proud of the relationships we have developed in these past years: relationships with our customers and partners, with whom the initial commercial dealings have developed in friendship and support; relationships with our young engineers, a highly qualified motivated team, that gives the best of their effort individually and successfully as a group; relationships with the academic and regulatory institutions whose interest has made AMPS a dream target for many young professionals that aspire to learn and play a major role in our market sector.

Looking back from when we started, I can't be but well satisfied of the results achieved, especially for the contribution that AMPS has given to the grand mosaic of the cardiovascular scientific research, providing several useful and precious building blocks, as it was recently recognized by a renown figure of the world we are active within.

In the last fourteen years we have been through substantial and to some extent unbelievable changes. Back in 2000 most of ECGs from clinical trials were based on paper technology and were manually measured, sometimes on-screen and in some cases directly on paper using magnifying lens or similar gear. ECG acquisition was in most cases based on non-diagnostic ECG machines which

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recorded non-simultaneously subset of leads and, even worse, used lossy transmission protocols (e.g. trans-telephonic signal transmission through acoustic coupling).

Today, virtually all ECG core labs use state of the art technology, spanning from hi-resolution ECG charts to Holter and more and more frequently telemetry systems that make the ECG from early phase clinical trials an hi-tech reality. In the near future, we reasonably expect to see the advent of even more advanced technologies, such as the use of implantable ECG recording devices.

On the software side we have also witnessed giant steps forward, and we proudly believe to have been one of the catalysts of these changes. Today, the analysis of the 10-seconds ECG within the context of clinical trials has become a highly-automated process and while the QT interval remain a primary outcome many more sophisticated parameters, such as the assessment of drug-induced morphological changes, are reliably measured. The momentum is now on the analysis and assessment of continuous ECG data (whether it is from Holter, a telemetry or any alternative form of acquisition) under the guidelines of regulatory bodies and in particular the FDA who recently “extended” the ECG warehouse to host continuous data. With reasonable timeframes we expect to be moving away from the so-called extraction paradigm (where “our” Antares has been massively used) toward a more dynamical approach that will look in depth both stationary (stable heart rate) but also transient, and maybe even more interesting data.

AMPS has still much to say and much to do and it is ready to take all the stimulating challenges to give new answers to the needs of our partners with products that, we are certain, will get interest and surprise.

Products News

Latest Releases

In Q1 2014 we have released:

- The first official version of AMPS CER-S (Continuous ECG Recordings Suite) including the first two platforms: the aECG Generator (Pollux) and Continuous ECG Viewer.

The major features of CER-S include:

- Continuous recordings annotation capabilities
- Continuous recordings aECG generator
- Ergonomic Viewer of Continuous recording

Looking forward

In Q2/Q3 of 2014 AMPS is planning to release:

- The second version of CER-S including the two following platforms:
 - continuous ECG beat detection and classification
 - ECG beat editor
 - beat-to-beat continuous ECG solution

AMPS Recommends

We recommend an important manuscript from Dr. Paul Kligfield appeared on line last summer and published on paper on the February 2014 issue of the American Heart Journal (1). In this article, co-authored by representatives of major industry manufacturers and by our Chief Scientist Fabio Badilini, standard ECG measurements (RR, PR, QRS and QT intervals) from four computer-based algorithms have been cross compared over recordings from the CSRS repository which included 400 normal subjects (200 at baseline and 200 during peak moxifloxacin effect) and 200 LQTS patients from the French registry (2).

To minimize potential biases related to the different technical implementation of the different algorithms (briefly but nicely overviewed in a dedicated Appendix of the paper), “global” measurements rather than single-lead findings of the analysis were considered. QT intervals were not corrected for heart rate because the same tracings were used by all participants. The total population was separated by sex and also by normal, moxifloxacin, and LQTS groups for analysis.

Results indicated small but significant differences between the methods, differences which were least in normal subjects and greatest in patients with abnormal ECGs (as represented by the LQTS group). Nevertheless, all algorithms clearly and similarly assessed differences in measurements between men and women and identified progressively increasing QT measurements in normal subject, in subjects taking moxifloxacin, and in patients with LQTS.

From our perspective, and more specifically for the context of clinical trials, the results of this study confirm that automated measurements can be reliably used for the analysis or baseline ECGs and in the presence of mild alterations produced by moxifloxacin. However, care must be taken to use the same algorithm consistently to avoid small but significant biases related to the technical implementation differences that necessarily characterize each single method.

[1] Kligfield P, Badilini F, Rowlandson I, Xue J, Clark E, Devine B, Macfarlane P, DeBie J, Mortara D, Babaeizadeh S, Gregg R, Helfenbein E, Green C. **Comparison of automated measurements of ECG intervals and durations by computer-based algorithms of digital electrocardiographs.** *Am Heart J* 2014;167(2): 150-159.

[2] Donger C, Denjoy I, Berthet M, Neyroud N, Cruaud C, Bennaceur M, Chivoret G, Schwartz K, Coumel P, Guicheney P. **KVLQT1 C-terminal missense mutation causes a forme fruste long-QT syndrome.** *Circulation* 1997 Nov 4;96(9):2778-81.

AMPS Notebook

Fabio Badilini will be chairing a session on Telemedicine at the 8th **Conference of the European Study Group on Cardiovascular Oscillations (ESGCO 2014)**. This year's conference will be held in Trento, Italy, in the beauty of the Dolomites mountains, from May 25th to 28th, 2014.

Fabio will also be attending the 39th **ISCE Conference**, the meeting he chaired last year, that will be held in Atlantic Beach, FL from April 26th to 30th, 2014.

On March 19th, Gianfranco Toninelli received his Master degree in Electrical Engineering at Brescia University, presenting a thesis on "ECG Quality Assessment Using Data Mining", supervised by Prof. Alfonso Gerevini. The picture below was taken right after Gianfranco's dissertation.

AMPS proudly congratulates Gianfranco for this important achievement.



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Use the right ECG tools!**

CalECG	Measure ECG intervals quickly, precisely, and automatically
TrialPerfect	The safe and powerful back-end solution for an error-free trial
ECGScan	Convert paper ECGs into XML for FDA submission
FDAEcg Suite	View, validate, and score ECGs before the FDA submission
Antares	Extract meaningful ECG strips from Holter traces
FAT-QT	Measure automatically thousands of ECG in minutes

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