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.

Editorial

It is no news to no one that there is a good amount of garbage published on the Internet, virtually on any subject, and including cardiac safety. But it is possible however, to find interesting and useful information reminding us how much nowadays we are used to rely on computers, and the dangers that may result from it.

We would like to start this first issue of 2010 by submitting to your attention this little pearl found browsing around: "Don't rely on the ECG computer-generated interpretation! It's only as accurate as the human who programmed the machine!"

We find this statement very true, not only when related to patient diagnosis, but also in the context of clinical trials/studies for new drugs. Our belief is that, at the current state of the art, there is really no safe way to completely eliminate human expert review from the process.

What can be done with the current technology, however, is to support human reviewers with tools that, benefitting of the expertise accumulated after many years and millions of interpreted ECGs, can help to narrow the focus of the reviewers to the subset of ECGs that no machine can safely interpret, thus maximizing the amount of automated processing that can be safely employed. This is exactly the philosophy behind FAT-QT, the new tool released by AMPS last February, which represents a major step forward, allowing experts and stakeholders working on the clinical trials to focus where they need to. This issue's article is dedicated to the technology behind it, so enjoy!

AMPS Views on:

FAT-QT: The fully automated solution for T-QT studies.

In January 2010 we have released Fat-QT, the latest new tool in the AMPS portfolio.

Fat-QT includes parts of the automatic annotation capabilities of CalECG, but also the scoring quality metrics of the FDAEcg Suite. With these two distinct facets, Fat-QT can be used to fully-automatically measure ECGs from different manufacturers (identically to CalECG) and then automatically classify them according to quality-based pre-configured categories.

Based on quality of the ECG data, it is therefore possible to correctly configure a study in order to have a large percent of ECGs automatically measured and confirmed (and thus ready to be submitted to the FDA ECG Warehouse), and a smaller percent of ECGs that will undergo the standard human-driven over-read process.

This approach can drastically reduce human intervention to confirm good quality ECGs, on which the CalECG automated algorithm is known to be accurate. The manual review will be limited to low-quality ECGs, typically ECGs with noise, large baseline-wonders, other artifacts or clinically relevant abnormalities that would decrease the likelihood of a correct automated measure.

This will result in a much faster annotation process, and a drastically reduced turnaround time from received ECGs to final annotations.

As with the majority of AMPS tools, Fat-QT exposes an Application Programming Interface (API) so that it can be easily integrated into any platform. Fat-QT is also now embedded in TrialPerfect, the AMPS ECGs management system, that together with CalECG provides a complete solution for clinical trials. In this setting, the ECGs imported into TrialPerfect are automatically fed to Fat-QT for automatic annotation (following the specified ECG measuring protocol) and classification, following the scoring metric rules chosen for each specific study.

Depending on the ECG category, ECGs will be automatically confirmed or they will be queued for Cardiologist review.

As stated above, based on quality of the ECG data, it is possible to build classification strategies for the automatic ECG classification.
The classification strategies can include one or more metrics and thanks to specific thresholds will place each ECG into two ore more ECG categories (or buckets), sorted by quality.

The list of available quality metrics include:

- All Frequencies noise
  amount of noise in all frequency components, computed on unfiltered ECG. This can be computed on any individual lead (I, II, III, … V6) or on all leads at once (All Leads).
- High Frequency noise
  amount of high frequency noise (above 40 Hz), computed on unfiltered ECG. It can be computed on any individual lead (I, II, III, … V6) or on all leads at once (All Leads).
- Low Frequency noise
  amount of low frequency noise (baseline wondering). It can be computed on a single lead (I, II, III, … V6) or on all leads at once (All Leads).
- High Frequency Noise Around Toff on RepBeat Annotations
  amount of high frequency noise (above 40 Hz) around T-wave offset calipers, it is computed around (+/- 50 ms) all Toff annotations on all individual leads of Representative Beats, based on High frequency-pass filtered ECG.
- High Frequency Noise Around Toff on Rhythm Annotations
  amount of high frequency noise (above 40 Hz) around T-wave offset calipers, it is computed around (+/- 50 ms) all Toff annotations on Rhythm data, based on High frequency-pass filtered ECG.
- Low Frequency Noise Around Toff on Rhythm Annotations
  amount of low frequency noise (baseline wondering) around T-wave offset calipers, it is computed around (+/- 50 ms) all Toff annotations on Rhythm data, based on baseline wondering between Qonset and Toffset calipers.
- Derived Measurements
  - QT: QT interval computed by the algorithm.
    the Global QT generated by AMPS on Representative Beats (superimposed) is used.
  - QTcB: QT interval computed by the algorithm, corrected with "Global RR" using Bazett's formula
    the Global QT generated by AMPS on Representative Beats (superimposed) is used.
  - QTcF: QT interval computed by the algorithm, corrected with "Global RR" using Fredericia's formula
    the Global QT generated by AMPS on Representative Beats (superimposed) is used.
- Protocol Agreement: percentage of successfully measured annotations specified in the ECG protocol.
- R-wave Amplitude
  amplitude of the R-wave, measured on the specified lead (I, II, III, … V6) of Representative Beats (from AMPS algorithm).
- T-wave Amplitude
  amplitude of the T-wave computed on the specified lead (I, II, III, … V6) of Representative Beats (from AMPS algorithm).
- Rhythm
  - Heart Rate
    HR from AMPS algorithm, automatically computed on all leads.
  - QRS Regularity
    the percentage of normal QRS complexes detected by the automatic algorithm versus artifacts and abnormal beats.
- T-wave complexity
  number of zero crossing of the first derivative of the T wave, automatically computed, assessed on the specified lead (I, II, III, … V6) of Representative Beats.

In order to generate a specific classification session, Fat-QT users need first to select the quality metric(s) to use and second, based on the numbers of classes to generate, the threshold levels for the selected metric(s).

An example of classification strategy based on T-wave amplitude on lead II and using/generating three categories could be as follows:
ECGs with T-wave amplitude below 75 μV would be linked to category 3 (labeled as BAD, or worst quality); ECGs with T-wave amplitude between 75 and 150 μV would be linked to category 2 (labeled as AVERAGE) and finally ECGs with T-wave amplitude above 150 μV would be linked to category 1 (labeled as GOOD ECGs). ECGs with negative T-wave on lead II would fall in the BAD-labeled category.

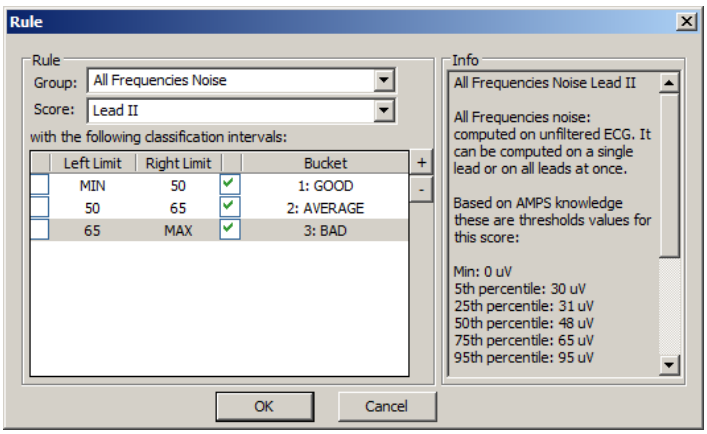
One of the strength of Fat-QT is the possibility of combining more quality metrics, applying the worst category priority approach (i.e. an ECG will be categorized to the worst case scenario, when using all the metrics individually). For example one could combine T-wave amplitude and "All Frequencies noise on lead II" as following:

- T-wave amplitude below 75 μV → category 3 (BAD),
- T-wave amplitude between 75-150 μV → category 2 (AVERAGE,)
- T-wave amplitude above 150 μV → category 1 (GOOD),

AND
- Noise below 48 µV → category 1 (GOOD),
- Noise between 48-65 µV → category 2 (AVERAGE),
- All Freq noise above 65 µV → category 3 (BAD)

For example, an ECG presenting T-wave amplitude and All Frequencies noise on lead II respectively equal to 250 µV and 55 µV will be linked to the 2-AVERAGE quality category, although the T-wave amplitude alone would have linked it to the 1-GOOD quality ECG category.

It has to be noted that for all the quality metrics that are not clinical, such as the various noise assessments, Fat-QT provides percentiles values based on the AMPS in-house ECG repository, as shown in the figure below. This population includes ECGs from Thorough QT studies, as well as clinical ECGs and automatic holter extractions generated by Antares, and contains about 500,000 ECGs.



In the example above, of a combined classification based on T-wave amplitude and noise, it is clear that the noise level used in the thresholds were not randomly selected, but were derived from the AMPS analysis.
The classification based on All Frequencies noise, could be re-written as:
- All Freq noise below 50th percentile → 1-GOOD category,
- All Freq noise between 50th - 75th percentiles → 2-AVERAGE,
- All Freq noise above 75th percentile → 3-BAD

In the figures here below there are two examples of ECGs with similar T-wave amplitude on lead II, 643 and 700 µV respectively, but different All Frequency noise on lead II (46 and 74 µV, respectively). This causes the first ECG to be classified as GOOD, while the second falls into the BAD category.

It has to be clear that most likely there will be different classification strategies, depending on the study type. We don't expect a single classification strategy per study, but if, for example, there are two different studies, one on supine subjects and the other on subjects exercising, most likely there will be the need to define different classification strategies.
Although it is the newborn of the family, thanks to its versatility (think about all the possible configuration combinations) Fat-QT has a huge potential and is already promising a brilliant future.

Products News

Latest Releases

In February AMPS has released major updates of the following tools:

- Antares v.2.5.x: automatic generation of Representative Beats of the extracted 10 s, 12-leads snapshot, using our automatic algorithm.
- CalECG v.3: totally redesigned graphical interface, with new display on ECG signal in predefined format, such as 3 X 4, 6 X 2. Enhanced automatic algorithm for annotation measurements with abnormal beat classification. If desired CalECG v.3 will also include a diagnostic algorithm, embedded in the tool thanks to the cooperation with Glasgow University.
- TrialPerfect v.2: enhanced ECG management, new role definitions, fully compatibility with CalECG v.3 and Fat-QT .
- Fat-QT v.1 has also been officially released in February. The highlights of this new product are described in the section "AMPS View on" of the current issue.

Looking forward

In May AMPS is planning to release a major update of:

- FDAEcg Suite v.2: enhanced graphical interface, with advanced scoring display, new scoring metrics and optimized ECG management.

AMPS Notebook

The paper "The Time Course of New T-Wave ECG Descriptors Following Single and Double-Dose Administration of Sotalol in Healthy Subjects" authored by Dr. Extramiana and for which both Fabio Badilini and Martino Vaglio are coauthors has just been published on the January issue of the Annals of Noninvasive Electrocardiology.
A copy of this contribution, as well as the whole list of papers published by the AMPS team, can be found on the AMPS web site under the "Useful Documents /Publication" page.
AMPS will be present at the 35th Annual Scientific Session of the International Society for Computerized Electrocardiology held in Albuquerque, NM at the end of April where Dr. Fabio Badilini will be co-chairing a session.

AMPS people

We continue our round of staff introductions with Gianpietro Spagna.
Gianpietro, as many of the members of the AMPS team, started his Engineering studies in Italy at the Polytechnic University of Milan where he obtained his Master Thesis degree in 2005.

Gianpietro Spagna, BS

He joined AMPS in 2005 and since then became the leading developer of both WinAtrec and Antares products. Gianpietro is also an expert in image editing/processing and he is currently also leading the ECGScan project.

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