Editorial

This issue of AMPS-QT is entirely dedicated to the introduction of a private Holter database collected over many years of clinical routine by one of the world leaders in Holter cardiology, Dr. Pierre Maison-Blanche. Dr. Maison-Blanche currently serves as a Consultant for the Assistance Publique des Hôpitaux de Paris, Hôpital Bichat, Cardiology Unit. He is a Fellow of the French Society of Cardiology. He is also an independent consultant to a number of ECG manufacturers, ECG central laboratories, Pharmaceutical companies, and he is a full Member of the Cardiac Safety Research Consortium (CSRC).

One may immediately wonder: why yet another database, and what would be the clinical and/or technical added value? The answer is simple. These continuous ECG recordings have been selected from the daily clinical routine for a specific reason (e.g. presence of one or more pathological condition, not necessarily related to heart rhythm) and extremely carefully edited with respect to both the beat annotations level (label of a single beat) and the occurrence of episodes (e.g. beginning and end of an arrhythmic event).

All the recordings included in the database have been acquired with a specific commercial platform; however, they have been subsequently converted in a public domain format and are currently available for further analysis, processing, and research.

In addition to having been a personal mentor of Fabio Badilini, Dr. Maison-Blanche is historically a close AMPS friend and collaborator and we are delighted to have now formalized his partnership with AMPS.

A Noteworthy Contribution:

Why releasing a digital Holter database on cardiac arrhythmias in 2016?

By Pierre Maison-Blanche, MD, Centre Médico Chirurgical Ambroise Paré, Paris, France

The background for our decision was three-fold

1- Non-invasive Cardiac Electrophysiology

I graduated more than 35 years ago as a medical doctor and then as a cardiologist at the University of Paris, in Lariboisière University Hospital, under the leadership of respected mentors such as François Dessertenne, Robert Slama, and above all Phillipe Coumel. In the early 80's, I was performing cardiac catheterization but became quickly fascinated by Coumel's vision of Cardiac Electrophysiology. Indeed, the 2016 digital Holter AMPS-PMB database was preceded by an analog Holter database I steadily built over years under his leadership, with the aim of investigating the spontaneous occurrence of cardiac arrhythmias.

Philippe Coumel, 1935-2004

In their obituary to Philippe Coumel published in the August 2004 Issue of the Journal of Cardiovascular Electrophysiology, Gerard Guiraudon and Etienne Aliot wrote:

He quickly appreciated the limitations of programmed electrical stimulation in investigating the factors modulating cardiac arrhythmias. He turned to Holter recording as a tool for dissecting the modifiers of the substrate, especially the autonomic nervous system. Philippe introduced the concept of the "triangle" of arrhythmogenesis, i.e. three main factors interacting to produce arrhythmia: the arrhythmogenic substrate, triggering factors, and modulating factors, with the dominant factor being the autonomic nervous system. He understood that the best time to study the triggering mechanisms was during spontaneous occurrence recorded on the Holter monitor.

Philippe Coumel vision is explained in Figure 1. Programmed electrical stimulation is a minimally invasive technique that has become extremely valuable for inducing known but infrequent arrhythmias. Stimulation of the heart at programmed intervals together with the delivery of precisely timed premature beats (Figure 1, left) allows the triggering of latent tachycardia and therefore the diagnosis of the source of arrhythmia related symptoms. Conversely, detailed analysis of observed spontaneous cardiac arrhythmias (Figure 1, right) offers a unique opportunity of investigating the actual triggering factors in a given individual.

Cardiac Electrophysiology
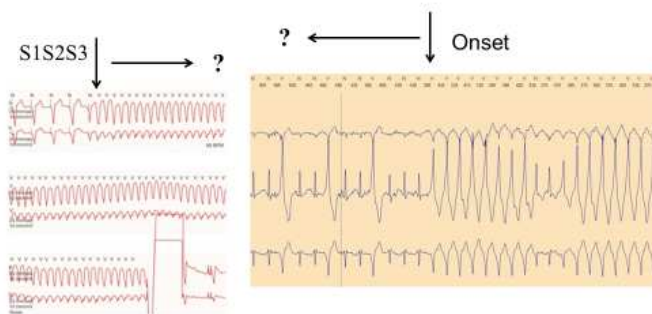## Electrical Stimulation vs Spontaneous Onset

Figure 1: Cardiac Electrophysiology Model

As far as I can remember, we have always been cautiously collecting analog tape Holter recordings in various cardiac electrical diseases. Figure 2 shows our observations in a cohort of 62 cases of ventricular
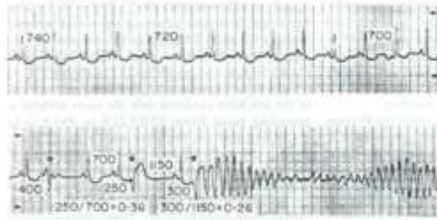
fibrillation recorded during Holter monitoring (1). Of note, in 1988, cardiac cycle lengths before the arrhythmia onset were manually measured from paper printouts. We reported that the average heart rate values before arrhythmia onsets are strikingly different between polymorphic ventricular tachycardia, monomorphic ventricular tachycardia and *Torsade de Pointes.*

Similar observations on heart rate patterns before atrial arrhythmias occurrences could be drawn from our database (2,3). Figure 3 shows the heart rate trends, together with the related ECG strips in a given individual, a few seconds before spontaneous atrial fibrillation occurrence. The RR interval lengthening is obvious, suggesting a bradycardia dependent phenomenon, and or a vagally induced arrhythmia. Our group was able to identify various modes of onset before various cardiac arrhythmias such as monomorphic ventricular tachycardia, reciprocating tachycardias and even spontaneous drug induced Torsades de Pointes (4-8) with is a very low frequency adverse event.

Figure 4 displays the initiating cardiac cycle length oscillation typical of Torsades, the so called short long short sequence, as identified from 13 cases (6). Unfortunately, our magnetic tape database became a security threat for the Hospital management since it was highly inflammable and we had to give our sorrow consent for destroying this unprecedented scientific material, lacking the budget for digitization.

Nonetheless, I was not discouraged by this poor administrative decision and with the advent of the digital ECG recording era, I decided to start the task initiated by Philippe Coumel from scratch. Fabio Badilini joined our team in 1994 and his input was decisive for the project, at various levels. It is important to know that to avoid another dramatic loss of data, we introduced a new digital standard Holter format and consequently all Holter recordings not only were collected exclusively from digital recorders, but furthermore, stored in ISHNE format (9,10).

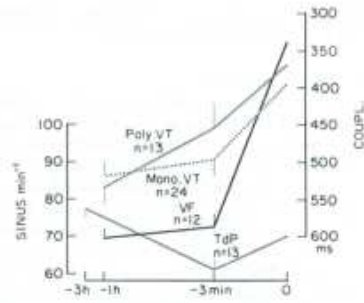# Analog Holter source annotations: manual measurements

Figure 3 Schematic representation of heart rate and CI values before SD by ventricular tachyarrhythmias. Mean and SEM are indicated. In TdP, a decrease of heart rate occurs in the three preceding hours, and the initiating CI is long. In primary VF, the heart rate is lower than in VF secondary to monomorphic or polymorphic VT, and the initiating CI is shorter.

European Heart Journal (1988) 9, 1276–1283

Respective role of sympathetic tone and of cardiac pauses in the genesis of 62 cases of ventricular fibrillation recorded during Holter monitoring

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Figure 2: Ventricular Fibrillation Database
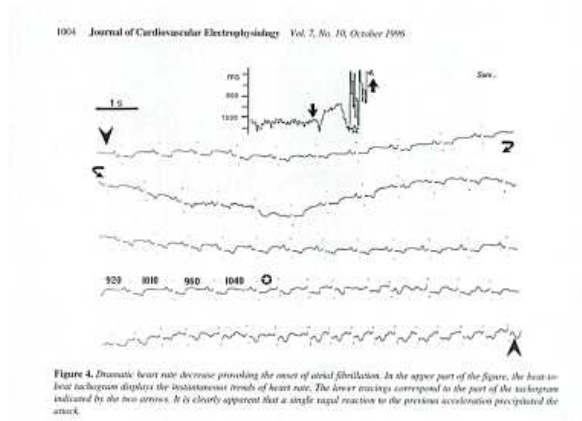
Atrial fibrillation onset

Figure 4. *Dramatic heart rate decrease preceding the onset of atrial fibrillation. In the upper part of the figure, the beat-to-beat tachogram displays the instantaneous trends of heart rate. The lower tracings correspond to the part of the tachogram indicated by the two arrows. It is clearly apparent that a single vagal reaction to the previous acceleration precipitated the attack.*

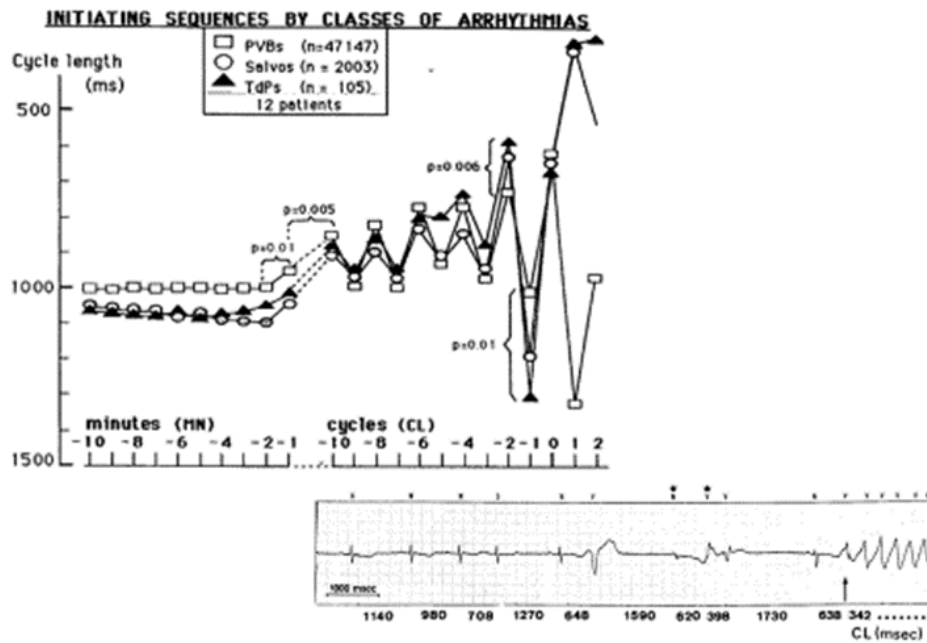*Figure 3: Atrial fibrillation onset*

INITIATING SEQUENCES BY CLASSES OF ARRHYTHMIAS

Figure 4: Initiating Sequences of Torsades de Pointes

2 - ECG Tutorials

The second purpose of this database is to provide ECG strips in digital format from a large variety of cardiac rhythm abnormalities, including depressed automaticity, cardiac conduction disorders, atrial and ventricular extrasystoles and tachycardias.

As mentioned, Robert Slama was one of my mentors and his yearly Tutorials on Cardiac Rhythms were followed by hundreds of medical students and residents. Actually, the larger auditorium in our University was not big enough and to get a seat one had to show up far in advance before the beginning of the course. Robert Slama was a wizard capable of making the most sophisticated concepts look simple. My decision to graduate as a cardiologist certainly originated from his Tutorials…

Today I still remember two lessons:

- Atrial arrhythmias with irregular atrioventricular conduction on surface ECGs. This irregular conduction corresponds to an "alternating" Wenckebach phenomenon, of a type that can be determined from what Robert Slama called

simple rules. He could demonstrate that the atrioventricular node had physiologically 3 levels of sequential block (11).

- His bundle recordings for a thorough evaluation of the capture phenomena in patients with paroxysmal re-entrant nodal tachycardia. According to whether the capture is correctly timed, delayed, or unusually premature, the inferior junction point of the re-entry circuit could be located precisely by reference to the H wave and the onset of the R wave. Again, the audience was mainly medical students but the reasoning was so incredibly simple that everyone could follow the speech to its end.

3- Long term ECG recording devices

A number of breakthrough Holter devices have recently been released, such as patches that can continuously record up to 7 days or 14 days of digital ECG, or smartphone applications that can record 30 second ECGs and send the data via internet. Longer duration of recording, up to 30 days, will soon be available and the extension of ECG monitoring duration from surface ECG recording machines (or

from implanted devices) emphasizes the need for reliable automated cardiac arrhythmia detection algorithms. The performance of a new cardiac monitor that automatically detects cardiac arrhythmias can be evaluated against our database.

Enrolment criteria and Reference Editing

The entry rules applied for inclusion in the digital database are as follows:

- There are no volunteers in this database. All recordings are collected from patients (both in- and outpatients) referred for 24-hour Holter monitoring to the Cardiology Unit by a cardiologist or a general practitioner. With documentation of symptoms being the most widely prescribed Class I indication for Holter monitoring, patients were mainly referred for documentation of palpitations or dizziness, or lipothymia, before or after initiation of therapy, or both.

- Holter recording were acquired at 200 Hz, with an amplitude resolution of 10 μV. Apart from few exception, all recordings are 2 Leads ECGs.

- Holter recordings had been anonymized with respect to all subject demographics, but birth dates and gender are kept available separately.

- For each recorded hour, the analysed time is at least 59 minutes, i.e. a maximum of 60 seconds of noisy segments per hour is allowed.

- All recordings have a minimum length of 18 hours; currently (based on 3680 recordings) the average length is approximately 21h30m.

The reference editing is performed by a single Cardiologist, Dr Pierre Maison-Blanche, using the Synescope® software from Sorin.

Holter editing is typically performed for the following findings: mean heart rate, minimum and maximum heart rates, bradycardia and tachycardia episodes, isolated premature ventricular extrasystoles, couplets, bigeminy, trigeminy, runs of three or more (V Runs), isolated premature supraventricular beats, couplets, supraventricular runs of three or more (SV Runs), cardiac pause, atrial fibrillation and other atrial arrhythmias. Ventricular Tachycardia episodes are included in the V Runs category.

The following editing tools have been used:
- Template Editing for all Categories
- Individual Beat Editing for All QRS Beats
- Inserting or Deleting QRS Beats
- Heart rate and RR interval trends Review
- Tabular Reports Review
- Scan functions
- Page Scan by Selected Events
- Sample Strip Viewing and Editing
- ST segment trends Review
- RR Interval/Ratio Histograms
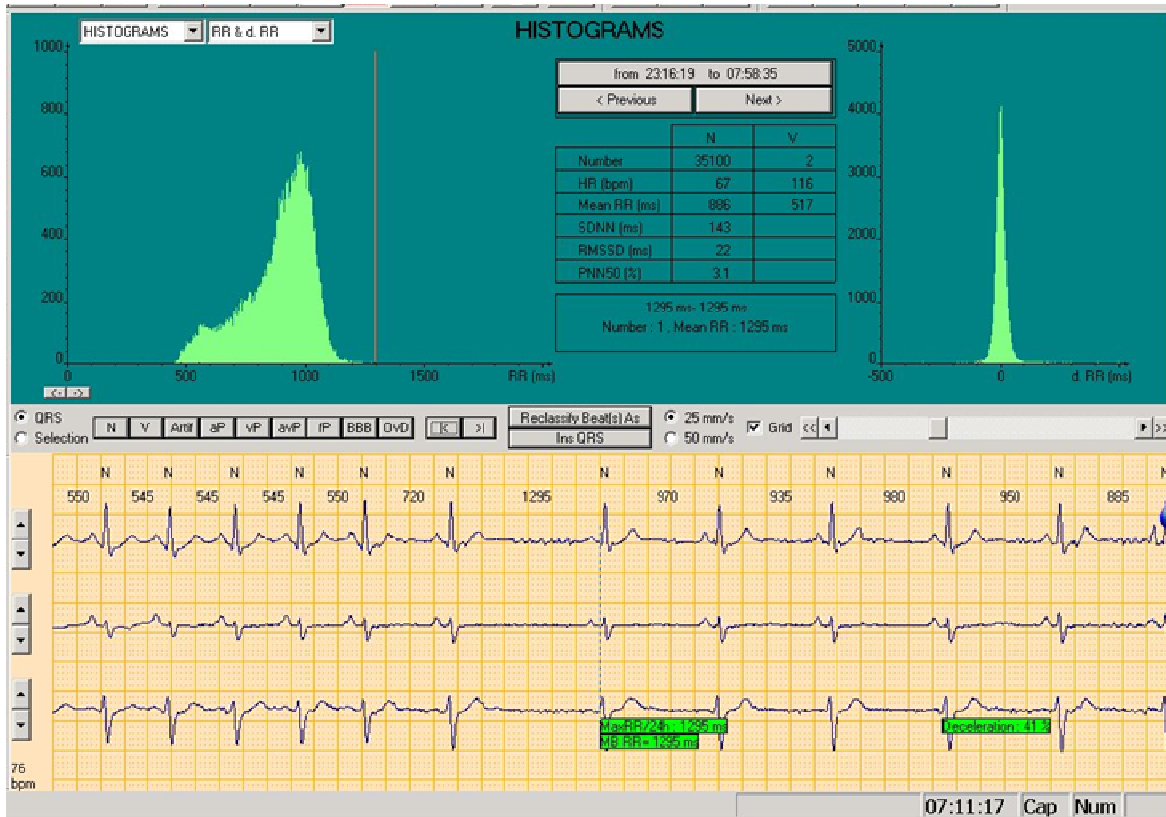- Full Disclosure Review
- Noise Region Review
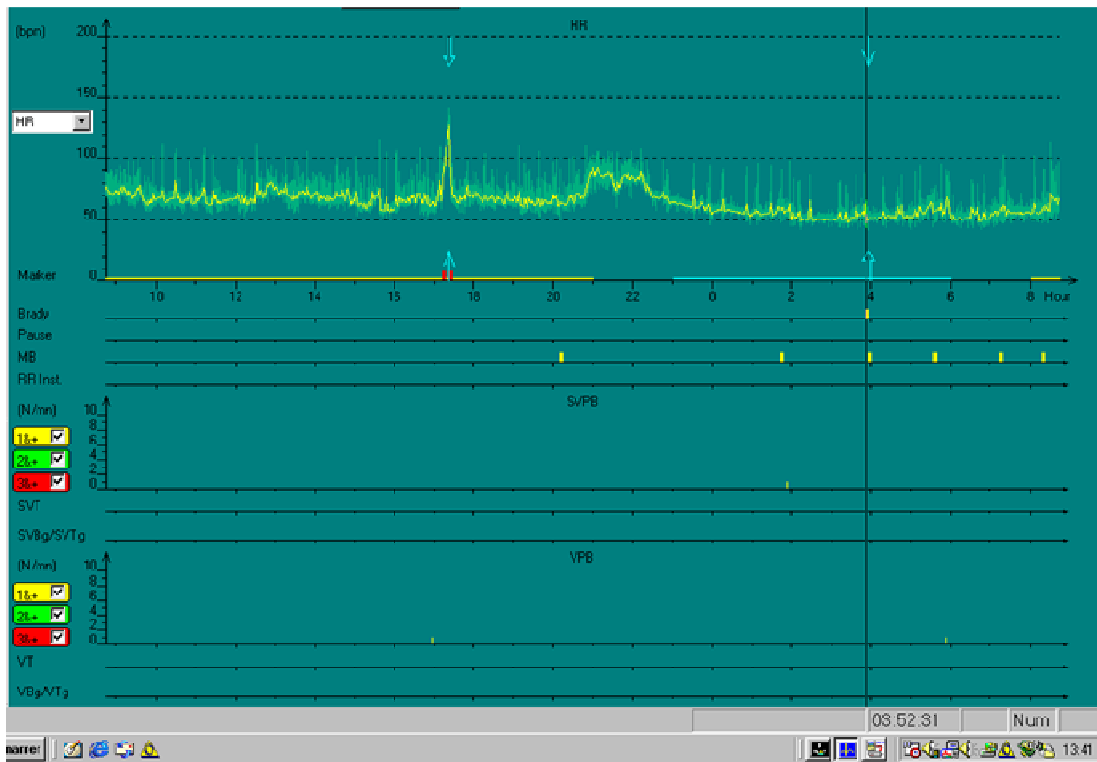
Figure 5: Histograms

Figure 6: Heart-rate Trends

All cardiac beats identified by the Holter software are grouped into templates. Editing and reclassifying these cardiac beat templates provides the quickest and easiest way to adjust the Holter analysis results.

The histogram displays either all RR intervals or all RR ratios. Editing RR histograms tails is mandatory, to delete over detections in the short RR bins, and to insert missing beats in the long RR bins (Figure 5).

In the heart rate trend (Figure 6), the horizontal axis is marked in hours, while the vertical axis is in beats per minute. Bradycardia, tachycardia and Atrial fibrillation episodes can be easily detected from the heart rate trend. Atrial fibrillation usually has a very irregular heart rate and consequently has an irregular heart rate graph.

The recordings are dived in categories depending on the predominant activity. Here are a few numbers:

NSR – Normal sinus rhythm with sporadic Supraventricular or Ventricular activity, below 240 beats	1426
Bradycardia – Sinus rhythm, including episodes of Bradycardia or Pauses (RR>2000ms)	45
PAC – Extensive and predominant Supraventricular activity, including at least 240 Supraventricular premature beats	686
Atrial TachyArrhythmias – Atrial Tachycardia, Atrial Flutter and Atrial Fibrillation	690
PVC – Extensive and predominant Ventricular activity, including at least 240 Ventricular premature beats	603
VT – Extensive Ventricular activity, with episodes of Ventricular Tachycardia (run of a minimum of 15 Ventricular beats) Including Sustained / Non sustained and Slow / Fast VT	45
AVB – Third-degree atrioventricular block, non conducted P-waves	104
Pediatric – Pediatric ECGs (age from 1 week to 14 years)	32

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Products News

Latest Releases

At the end of Q2 2016 we have released a first version of the new ViewECGWeb an HTML 5 compliant web browser component whose purpose is to both render digital ECGs and allow end user interaction with the rendered digital ECG.

Looking forward

In Q3 and Q4 2016 AMPS is planning to release:
o A new version of Fat-QT and TrialPerfect with the latest version of BRAVO algorithm, released in Q1..
o A new version of CER-S, including the following revised platforms:
  - Continuous ECG beat detection and classification
  - ECG beat editor
  - Arrhythmia detection and Arrhythmia editor
  - aECG Generator

AMPS Notebook

We announce the release of the PMB-AMPS Holter database a joint project with Dr. Pierre Maison-Blanche with the aim of launching an annotated Holter recording database, refer to the "News" section on our website www.amps-llc.com for more details.

Fabio Badilini attended the **41st ISCE Annual Conference**, held in Tucson, AZ on April 2016.
Fabio will be present at the **Computing in Cardiology** Conference that will be held in Vancouver, Canada from September 11th to 14th, 2016.