Innovative Training Networks (ITN)
Call: H2020-MSCA-ITN-2017

# MultidisciplinarY training network for ATrial fibRillation monItoring, treAtment and progression

Project Nº: 766082

Start date of the project: 01/11/2017

Duration: 48 months

Project Coordinator: Luca Mainardi

# Deliverable D3.4

# D3.4: Submission of PhD thesis draft/proposal

Submission date: 31/03/2022

This project has received funding from the European Union's Horizon 2020 research and Innovation programme under the Marie Skłodowska-Curie grant agreement No 766082.

## Document Properties

| | |
|---|---|
| Document ID | D3.4 |
| Document Title | Submission of PhD thesis draft/proposal |
| Deliverable Nº | D13 |
| Editors | Valentina Corino, Luca Mainardi |
| Contributors | All |
| Lead Beneficiary | POLIMI |
| Work Package Nº | 3 |
| Work Package Title | Monitoring, progression and risk stratification |
| Nature | Report |
| Dissemination Level | Public |
| Number of pages | 22 |
| Due Date (in months) | 53 |
| Submission date | 31/03/2022 |

# Distribution List

| Organization | Name of recipients |
|---|---|
| POLIMI | Luca Mainardi, Josè Felix Rodriguez Matas, Valentina Corino |
| UMIL | Roberto Sassi |
| LU | Leif Sörnmo |
| UNIZAR | Pablo Laguna |
| UPV | Javier Saiz |
| KIT | Olaf Doessel |
| MEDTRONIC BRC | Mirko De Melis |
| MIE | Johan De Bie, Nicoletta Marzocchi |
| GRAD | Helena Fernandez |
| EMP | Francesco Onorati |
| KH | Claus Schmitt |
| HIC | Damian Sanchez-Quintana |
| SKANE | Pyotr Platonov |
| OMP | Federico Lombardi |
| ESR Representatives | Guadalupe Garcia Isla, Giorgio Luongo |

## Revision History

| Rev. No. | Date of Issue | Author(s) | Brief Description of Change |
|---|---|---|---|
| 0.8 | 18.03.2022 | Valentina Corino | First draft |
| 0.9 | 21.03.2022 | Valentina Corino, Luca Mainardi | Second draft |
| 1.0 | 31.03.2022 | Valentina Corino, Luca Mainardi, All | Final version |

# Table of contents

# 1. Summary

This document describes the status of PhD research of the ESRs belonging to WP3 and describes the status of their PhD thesis.

# 2. PhD status

Table 1 summarizes the PhD status of each ESR: starting date, current status and defense date.

| | Starting date | Thesis status | Defense date |
|---|---|---|---|
| ESR5 | 26-03-2019 | Ongoing | April 2023 * |
| ESR6 | 15-10-2018 | Ongoing | November 2022* |
| ESR7 | 01-10-2018 | Ongoing | March 2023 * |
| ESR8 | 24-09-2018 | Thesis draft | October 2022 * |
| ESR9 | 16-07-2018 | Thesis draft | June 2022* |

* expected date

# 3. ESR5: Paroxysmal Atrial Fibrillation: Continuous tracking of arrhythmia progression

ESR5: Ricardo Salinas-Martínez

## Motivation and aim

Atrial fibrillation (AF) is the most common arrhythmia found in clinical practice, and it is highly associated with stroke episodes[1]. The guidelines for the diagnosis and management of atrial fibrillation are well documented for episodes longer than 30 seconds[2]. However, little information is known about brief AF (BAF) episodes lasting less than 30 s, these episodes may evolve into longer AF episodes[2]. The progressive behavior of AF suggest that even such brief episodes could represent a risk factor for thrombus formation and stroke[3]. These observations highlight the need to improve prevention strategies, diagnostic methodologies, management, and treatment of this type of arrhythmia.

In this project, we are investigating the association between ischemic events and BAF episodes. For this purpose, we have designed a clinical study for Holter data collection[4], and we have proposed a new methodology for the automatic detection of BAF[5]. The main challenge is to detect BAF episodes in long-term ECG recordings as they might be hidden by noise or movement artifact.

## Methods

**7-day Holter Monitoring in Adult Patients with Recent IS or TIA, to Measure the Prevalence of Paroxysmal Atrial Fibrillation Including Episodes Less Than 30 Seconds: Transversal Study (MY-ATRIA).**

This observational, transversal study is intended to enroll 660 subjects diagnosed with cryptogenic ischemic stroke or transient ischemic attack in the UOC of Neurology and Metropolitan Stroke Network at the Ospedale Maggiore in Bologna. The enrollment period of the study started on Jun 16, 2021 and is expected to be active for at least one year. Subjects will be continuously monitor for 7-days with two Holter devices: H12+™ and H3+™. The first day of monitoring will be performed with the H12+™ recording two limb leads and six precordial leads with 1 kHz sampling frequency. The next six days of monitoring will be performed with the H3+™ recording two limb leads and one precordial lead with 180 Hz sampling frequency. The primary objective of the study is to compare the prevalence of paroxysmal AF (PA AF) episodes longer than 30 s and the prevalence of PA AF episodes including episodes shorter than 30 s, in adult patients with a recent ischemic event and no previous history of AF. The secondary objectives of the project are: a) To compare the prevalence of patients diagnosed with BAF after 24-hour, 72-hour, and 7-day Holter monitoring. B) To study the feasibility of using information obtained from the ECG during sinus rhythm, for example the characteristics of the P-wave, to predict the presence of PA AF and BAF.

**Detection of Brief Episodes of Atrial Fibrillation Based on Electrocardiomatrix and Convolutional Neural Network**

This work presented a new methodology for the detection of BAF using the electrocardiomatrix (ECM) transformation and convolutional neural networks (CNN). ECG segments containing 10 beats plus 2.5 s after the last detected beat and 0.5 s before the first detected beat were converted into ECM-images. The transformation is made by aligning 10 overlapping subsegments of 3.0 s length to the first beat in the subsegment. Once the subsegments are aligned, they are downsampled to: 1) 125 Hz in the interval [0, 0.5] s, 2) 50 Hz in the interval [0.5, 3.0] s. The main motivation for the two-sections downsampling is to maintain on the left side of the subsegment a high time resolution in the P-wave interval, and removing redundant information on the right side of the subsegment keeping only local rhythm patterns. The resulting downsampled subsegments are converted to an intensity one-channel image (hereafter the ECM-image). The ECM-images have dimensions of 10x219 pixels. ECM-images were used to train the CNN to classify the images between AF and non-AF. The CNN was trained using the Long-Term Atrial Fibrillation and the MIT-BIH Normal Sinus Rhythm, and tested on the MIT-BIH Atrial Fibrillation, the MIT-BIH Arrhythmia; all public databases[6]. Additionally it was also tested on the proprietary Monzino-AF database.

Sensitivity performance for BAF in all three testing databases is summarized in Figure 1. Results show episode sensitivity higher than 80.22%, 89.66%, and 97.45% for AF episodes shorter than 15 s, 30 s, and for all AF episodes, respectively. Figure 1 highlights the lead dependency of this approach. The CNN was trained with data from leads I and II facilitating AF detection when using these leads, as for the AFDB. However, when testing on other leads, performance decreases for AF episodes shorter than 120 seconds as for channel 2 in the arrhythmia database including data from leads V1, V2, V4, and V5, and for precordial leads in the Monzino-AF database.

## Main findings

Rhythm and morphological characteristics of the ECG in the transformed ECM-image can be learned by a CNN for the detection of BAF episodes. One key limitation of the study is that the CNN was trained with data from a limited number of patients. Additionally, only a small number of BAF episodes was investigated. A larger study population is needed to verify the results.

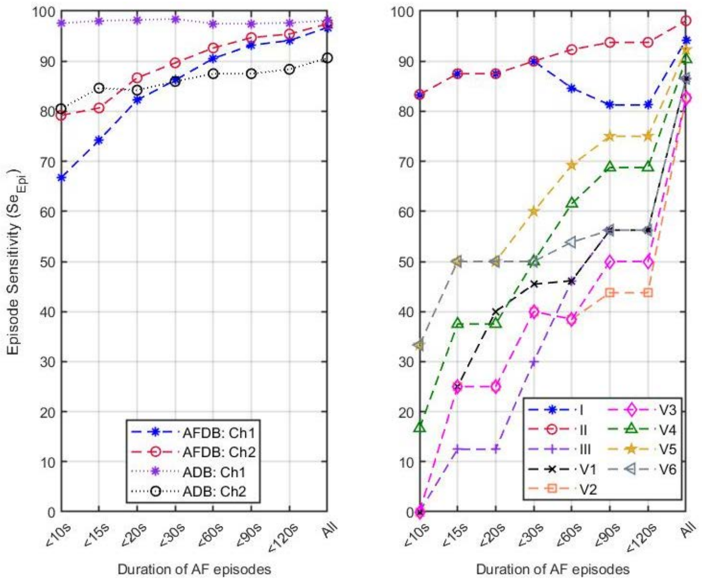


***Figure 1:*** *Episode sensitivity achieved on the episodes shorter than a particular duration present in: (left) channel 1 (Ch1) and channel 2 (Ch2) of the AFDB and Arrhythmia DB (ADB), respectively, and (right) leads I, II, III, V1, V2, V3, V4, V5, and V6 of the Monzino-AF DB.*

# References

[1] P. A. Wolf, R. D. Abbott, and W. B. Kannel, “Atrial fibrillation as an independent risk factor for stroke: the Framingham Study.,” Stroke, vol. 22, no. 8, pp. 983–988, Aug. 1991.
[2] G. Hindricks et al., “2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS),” Eur. Heart J., vol. 42, no. 5, pp. 373–498, Feb. 2021.
[3] J. S. Healey et al., “Subclinical Atrial Fibrillation and the Risk of Stroke,” N. Engl. J. Med., vol. 366, no. 2, pp. 120–129, 2012.
[4] R. Salinas-Martínez et al., “7-day Holter Monitoring in Adult Patients With Recent IS or TIA, to Measure the Prevalence of Paroxysmal Atrial Fibrillation Including Episodes Less Than 30 Seconds: Transversal Study (MY-ATRIA),” ClinicalTrials.gov. .
[5] R. Salinas-Martínez, J. de Bie, N. Marzocchi, and F. Sandberg, “Detection of Brief Episodes of Atrial Fibrillation Based on Electrocardiomatrix and Convolutional Neural Network,” Front. Physiol., vol. 12, no. August, pp. 1–16, Aug. 2021.
[6] A. L. Goldberger et al., “PhysioBank, PhysioToolkit, and PhysioNet,” Circulation, vol. 101, no. 23, Jun. 2000.

# 4. ESR6: Atrial fibrillation screening using everyday sensors and data fusion

ESR6: Hesam Halvaei

## Motivation and aim

Screening for atrial fibrillation (AF) helps to find the patients who are unaware of their disease, which by initiation of oral anticoagulation therapy, leads to a reduced risk for ischaemic stroke among those patients [1]. Therefore, AF screening is becoming increasingly common and several AF screening studies in different countries are presently ongoing, see [2] for a summary of these studies. AF Screening is nowadays done using portable devices, such as handheld ECG recorders, suitable for short-term intermittent screening, or Holters, including patches and other similar technologies, suitable for screening over an extended time when required. The signal quality of such recordings is usually poorer, compared to ECG recorded at rest in a clinical setting with expert supervision. Lower signal quality typically leads to false beat detections, which in turn may lead to falsely detected rhythm irregularity, and consequently false AF detection. While the poorer signal quality may only be observed in a small set of recordings, given the size of screening databases, it can cause a considerable number of recordings that require manual expert review. The number of recordings in the screening databases may be as high as hundreds of thousands; as an example, the Swedish StrokeStop I and II AF screening studies contain approximately 360,000 lead I ECG in total [3, 4]. Within the scope of the present doctoral thesis, the following different aspects for improved atrial fibrillation screening performance are considered: identification of transient noise to reduce false AF detection in handheld recorded ECGs, signal quality assessment of a novel electrode technology for Holter recordings, detection of short supraventricular tachycardias in handheld recorded ECGs, and AF outcome prediction.

## Methods

Transient noise is a major source of false beat detection in handheld recorded ECGs. When high sensitivity is required, such transient episodes. may cause false AF detections. In the first part of the thesis, the focus was set on the detection of such episodes [5]. Specifically, a convolutional neural network (CNN) was trained to detect transient noise, on an event-to-event basis, meaning that the events produced by a beat detector are either classified as true, a heartbeat, or as false, i.e., noise. The updated RR series is then fed to a low-complexity AF detector, optimized towards high sensitivity required for AF screening. The proposed approach was trained and validated using StrokeStop I database, containing 30-s handheld ECGs recorded in the elderly population.

Regardless of any signal quality assessment and de-noising techniques, which always carry the risk of excluding or distorting clinically important episodes, the most direct way to improve signal quality is by addressing problems at their source, i.e., directly at the electrodes performing the meausrements. In the second part of the thesis, the focus was on signal quality assessment of a novel ECG electrode with ability to reduce electrode motion artefacts [6]. For this purpose, ECG were recorded from 20 healthy subjects performing six di erent activities, i.e., sitting at rest, sitting and crossing arms, walking, walking in stairs, running, and undressing and dressing. Two types of electrodes were simultaneously used for recording using a Holter device, the novel wet electrode (Piotrode Medical AB, Stockholm, Sweden) and Ambu BlueSensor (Ambu, Copenhagen, Denmark). The assessment was done by means of detection performances (beat detection and AF detection false positive rates) and two signal quality indices (ensemble standard deviation and a time-frequency repeatability index).

## Main findings

In the first part of the thesis, by inserting the CNN before the AF detector, the number of false AF detections were reduced by 22.5% without any loss in sensitivity, see table. 1. This reduction was achieved on a subset of recordings that typically require manual review, and, therefore, the reduction directly translates to less time spent on expert review and thereby lower cost. The main limitation of the proposed approach is that the CNN is only trained using lead I handheld recorded ECGs which means that it needs to be re-trained in case other leads are to be processed.

For the second study, both detection performance and signal quality indices convey the same message; higher signal quality is achieved by the novel wet electrode (Piotrode) as subjects become increasingly active. The novel wet ECG electrode produced signals with less motion artefacts, and therefore, showing the potential to reduce the expert review burden and thereby cost associated with Holter monitoring. It should be noted that long-term properties of the new electrode technology remain to be assessed since artefact levels may vary over longer recording times. An example of signal recorded simultaneously during undressing and dressing using both electrodes are displayed in fig. 1.

The last two parts of this thesis are focused on the detection of short supraventricular tachycardias and on atrial fibrillation outcome prediction. The five-year follow-up of the StrokeStop I screening database showed a higher risk of developing AF for subjects with brief episodes of supraventricular tachycardias (SVT) in recordings five year earlier [7]. Short SVTs are defined as episodes with 5 QRS complexes appearing within 2.4 s (according to the definition of tachycardias Identification of such patients during screening provides the opportunity for extended screening and timely initiation of treatment. The challenge with detection of such episodes are accurate identification of noisy signal segments, ventricular ectopic beats and ECGs with overall fast rhythms. In the third part of the thesis, the focus is on reduction of false detections of short SVTs. In the fourth paper, ECGs features and short rhythm deviations in the screening databases StrokeStop I and II will be compared to follow-up data from the same patients with the goal to investigate the development of AF in this patient group.

Table 1 AF detection performance with and without quality control using

| | Se | FPR | PPV |
|---|---|---|---|
| **Without quality control** | | | |
| $N = 8$, $\alpha = 0.07$, $\eta = 0.55$ | $99.0 \pm 0.6\%$ | $87.5 \pm 0.7\%$ | $4.6 \pm 0.4\%$ |
| **With quality control** | | | |
| $N = 4$, $\alpha = 0.04$, $\eta = 0.65$ | $99.0 \pm 0.6\%$ | $65.0 \pm 1.4\%$ | $6.2 \pm 0.5\%$ |

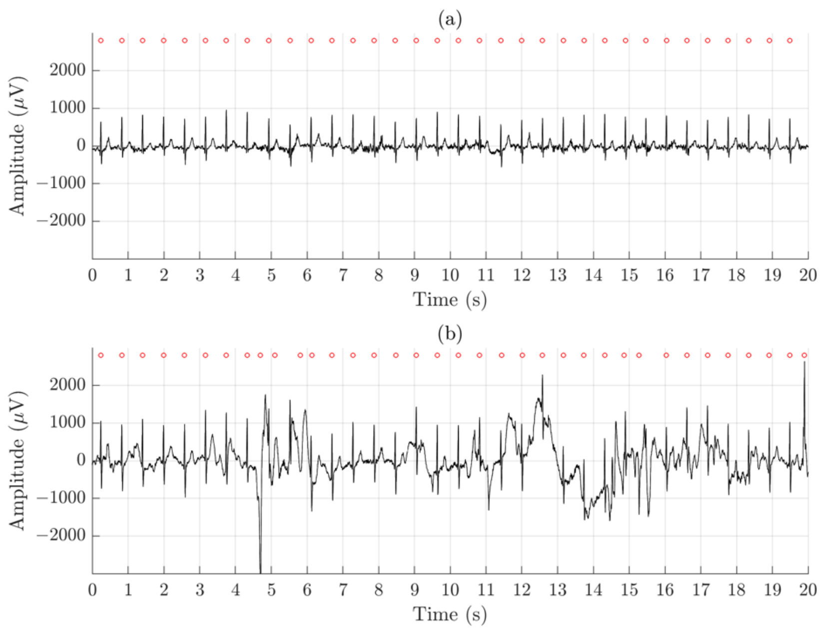


Figure 1 An example of signal recorded simultaneously during undressing and dressing using (a) the Piotrode and (b) the Ambu electrodes.

# References

[1] E. Svennberg, L. Friberg, V. Frykman, F. Al-Khalili, J. Engdahl, and M. Rosenqvist, “Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial" The Lancet, 2021.
[2] S. Khurshid, J. S. Healey, W. F. McIntyre, and S. A. Lubitz, “Population-based screening for atrial fibrillation," Circulation Research, vol. 1, no. 2020, pp. 143 - 154, 127.
[3] E. Svennberg, J. Engdahl, F. Al-Khalili, L. Friberg, V. Frykman, and M. Rosenqvist, “Mass screening for untreated atrial fibrillation: the STROKESTOP study," Circulation, vol. 131, no. 25, pp. 2176-2184, 2015.
[4] K. K. Gudmundsdottir, T. Fredriksson, E. Svennberg, F. Al-Khalili, L. Friberg, V. Frykman, Z. Hijazi, M. Rosenqvist, and J. Engdahl, “Stepwise mass screening for atrial fibrillation using N-terminal B-type natriuretic peptide: the STROKESTOP II study," EP Europace, vol. 22, no. 1, pp. 24 - 32, 2020.
[5] H. Halvaei, E. Svennberg, L. Sornmo, and M. Stridh, “Identification of transient noise t reduce false detections in screening for atrial fibrillation," Frontiers in Physiology, vol. 12, p 672, Jun 2021.
[6] H. Halvaei, L. S�ornmo, and M. Stridh, “Signal quality assessment of a novel ECG electrode for motion artifact reduction," Sensors, vol. 21, no. 16, p. 5548, Jan 2021.
[7] T. Hygrell, M. S. L. Friberg, and E. Svennberg, “Prognostic implications of supraventricular arrhythmias," The American Journal of Cardiology, vol. 151, pp. 57-63, 2021.

# 5. ESR7: Risk stratification and prediction of intervention outcome in AF using novel ECG-based markers of atrial remodelling

ESR7: Mostafa Abdollahpur

## Motivation and aim

The electrocardiogram fibrillatory waves (f-waves) characteristics in atrial fibrillation (AF) could provide important information regarding electrical activity in the atrial. The f-wave amplitude, frequency, morphology, regularity, and complexity are the main ECG-based features that have been suggested to predict AF treatment outcome. The autonomic nervous system (ANS) plays an important role in the AF initiation and maintenance [1]. Previous research has established that the f-wave frequency can change in response to changes in autonomic tone [2,3]. The individual variation in ANS induced changes is large, and we hypothesize such differences in autonomic reactivity are linked to AF progression. Hence, the purpose of the present project is to develop ECG-based markers of autonomic reactivity in AF. Specifically, we aim to quantify respiratory-induced variations in the f-wave frequency. This is challenging, since respiratory induced f-wave frequency variations are very small and may be concealed by other variations. Further, the respiration rate is generally unknown and has to be estimated from the ECG.

## Methods

Following qrst-cancellation, a harmonic f-wave model was fitted to the f-wave signal to estimate a high-resolution f-wave frequency trend and a signal quality index [4]. Considering the exclusion of segments with insufficient signal quality, the resulting frequency trend was filtered using a bandpass filter with a center frequency corresponding to the local respiration rate. Respiration rate is estimated from a surrogate respiration signal, obtained from the ECG using homomorphic filtering [5]. The magnitude of the respiratory induced f-wave frequency modulation was quantified using the envelope of the filtered frequency trend $\Delta\hat{f}(n)$. Since trend $\Delta\hat{f}(n)$ varies over time, we used its 5-minute average $\Delta\bar{f}$ to quantify the magnitude of respiratory f-wave frequency modulation. The accuracy of the estimated respiratory modulation magnitude was evaluated using simulated f-wave signals obtained by a modified version of the saw-tooth model. ECG data from clinical study involving eight patients with permanent AF and pacemaker was used to evaluate the feasibility of the proposed method [6]. The study protocol consisted of three phases; baseline rest (B), controlled respiration (CR) and controlled respiration following injection of atropine to induce full vagal blockade (PA), respectively. The ECG from these patients was recorded for a 5-minute in each phase. During phase CR and PA, the patients were asked to breathe at a fixed rate of 0.125 Hz.

## Main findings

Results from the simulation suggest that the magnitude of the respiratory induced f-wave frequency modulation can be estimated with an error of less than 0.01 Hz if the signal quality index is above 0.5. Our results from clinical data (Fig 1) show that the magnitude of respiratory f-wave frequency modulation increase with deep breathing (increased parasympathetic activity) and decrease with the vagal block (decreased parasympathetic tone). The result suggests that respiratory modulation in the f-wave frequency trend can be partly attributed to parasympathetic regulation in the atria during AF. This is supported by a recent simulation study that showed that the parasympathetic neurotransmitter acetylcholine could be an important factor in f-wave frequency modulation [7]. The findings in this report are subject to at least two limitations. First, the methodology was tested in a small group of AF patients with pacemakers. To address this limitation, a follow-up study with a population consisting of 28 participants with AF from the Swedish cardiopulmonary bioimage study (Scapis)[8] is ongoing. The ECG from these patients was recorded for 5 minutes at baseline and 1 minute during deep breathing; the patients were in AF during the recordings. A second limitation is that the band-pass filtering approach to quantify respiratory modulation does not account for changes in the respiratory pattern. To accommodate this, a subspace projection approach to quantify respiratory variation in the f-wave frequency trend is currently tested. Preliminary results suggest that the approach is feasible.

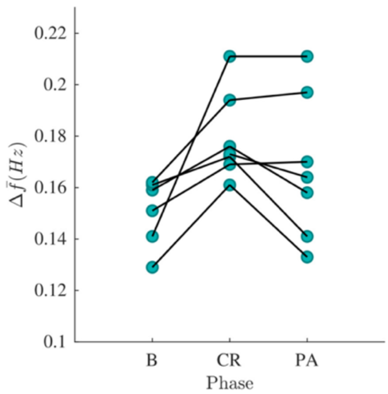


*Figure 1: $\Delta\bar{f}$ estimated from phase B, CR and PA recordings, respectively. Each curve corresponds to a patient.*

# References

[1] Fabritz L, Guasch E, Antoniades C, Bardinet I, Benninger G, Betts TR, Brand E, Breithardt G, Bucklar-Suchankova G, Camm AJ, Cartlidge D. Defining the major health modifiers causing atrial fibrillation: a roadmap to underpin personalized prevention and treatment. Nature Reviews Cardiology. 2016 Apr;13(4):230-7.

[2] Östenson S, Corino VD, Carlsson J, Platonov PG. Autonomic influence on atrial fibrillatory process: head-up and head-down tilting. Annals of Noninvasive Electrocardiology. 2017 Mar;22(2):e12405.

[3] Sandberg F, Bollmann A, Husser D, Stridh M, Sörnmo L. Circadian variation in dominant atrial fibrillation frequency in persistent atrial fibrillation. Physiological measurement. 2010 Mar 5;31(4):531.

[4] Henriksson M, Petrėnas A, Marozas V, Sandberg F, Sörnmo L. Model-based assessment of f-wave signal quality in patients with atrial fibrillation. IEEE Transactions on Biomedical Engineering. 2018 Feb 28;65(11):2600-11.

[5] Abdollahpur M, Holmqvist F, Platonov P, Sandberg F. Respiratory Induced Modulation in f-Wave Characteristics During Atrial Fibrillation. Frontiers in physiology. 2021;12:435.

[6] Holmqvist F, Stridh M, Waktare JE, Brandt J, Sörnmo L, Roijer A, Meurling CJ. Rapid fluctuations in atrial fibrillatory electrophysiology detected during controlled respiration. American Journal of Physiology-Heart and Circulatory Physiology. 2005 Aug;289(2):H754-60.

[7] Celotto C, Sánchez C, Mountris KA, Abdollahpur M, Sandberg F, Laguna P, Pucyo E. Relationship between atrial oscillatory acetylcholine release pattern and f-wave frequency modulation: a computational and experimental study. In2020 Computing in Cardiology 2020 Sep 13 (pp. 1-4). IEEE.

[8] Bergström G, Berglund G, Blomberg A, Brandberg J, Engström G, Engvall J, Eriksson M, De Faire U, Flinck A, Hansson MG, Hedblad B. The Swedish cardiopulmonary BioImage study: objectives and design. Journal of internal medicine. 2015 Dec;278(6):645-59.

# 6. ESR8: Assessment of the AF Triggers and their Role in its Progression

ESR8: Javier Saiz Vivo

## Motivation and aim

Catheter ablation, specifically pulmonary vein isolation, has become over the decades a common treatment for AF patients, especially those highly symptomatic [1] or those where anti-arrhythmic drug therapy has not been sufficient (or tolerated) for rhythm stabilization [2]. However, long-term outcomes of catheter ablation in AF reported single-procedure success rates as low as 66.6% in paroxysmal AF patients and 51.9% in non-paroxysmal AF patients [3]. Several specific rhythm outcome predictors such as APPLE (AUC 0.63) [4], SUCCESS (AUC 0.66) [5] or MB-LATER (AUC 0.62) [6] have shown relatively modest prediction capabilities. However, these predictors have the drawback of relying on conventional Holter devices to detect AF recurrence, needing image-based parameters such as LA diameter or Ejection Fraction and, in the case of MB-LATER, early AF recurrence. With the aim of assessing monitoring in a single lead subcutaneous device and its clinical utility in prediction of the effects of a specific therapy and remote therapy management, the use of common heart rate variability (HRV) derived features in conjunction with clinical data are used to predict recurrences within the first 12 months after catheter ablation in a continuously monitored patient population.

## Methods

With the aim of assessing monitoring in a single lead subcutaneous device and its clinical utility in prediction of the effects of a specific therapy and remote therapy management, the use of common heart rate variability (HRV) derived features in conjunction with clinical data are used to predict recurrences within the first 12 months after catheter ablation in a continuously monitored patient population. The study included patients from 2 cohorts: The multicenter single-arm clinical study (Reveal LINQ usability, ClinicalTrials.gov Identifier: NCT01965899) and clinical data derived from a single center with extensive experience in evaluating long-term outcome of AF ablation by means of ICM [7]. These unique databases contain patients implanted with the Reveal LINQ, an ICM with an AF detection algorithm with detection rates up to 96% [8] which continuously monitored the patients for 5.9 ± 3.8 months before catheter ablation and followed-up for more than 12 months after. For the analysis, the first beats of the last recorded AF episode and its Flashback (i.e., the timestamps of the beats preceding the AF onset, 483 ± 33 beats) were extracted. From these two signals (Flashback and last AF episode), features describing the variability and irregularity of the RR intervals were computed. In addition, clinical information such as the Age, AF type (Paroxysmal or Non-paroxysmal), Hypertension presence and Ablation type (PVI or PVI plus Extra lesions) were included in the analysis.

# Main findings

Using an ensemble classifier (with the weights optimized for maximum accuracy), an AUC value (0.85) was reached to predict successful ablation [9]. Thus, a reduced set of HRV and clinical features extracted from an insertable cardiac monitor can be used to predict AF recurrence in patients that underwent single-procedure catheter ablation. If confirmed by future studies, these findings are potentially of significant clinical relevance for several reasons: first, catheter ablation of AF substrate is a procedure with high economic and personal burden; secondly, due to the epidemic character of AF prevalence, these interventions cannot be offered (even in countries with developed health-care systems) to all patients and third, the selection of patients with higher probability of long-term elimination of AF has high priority.

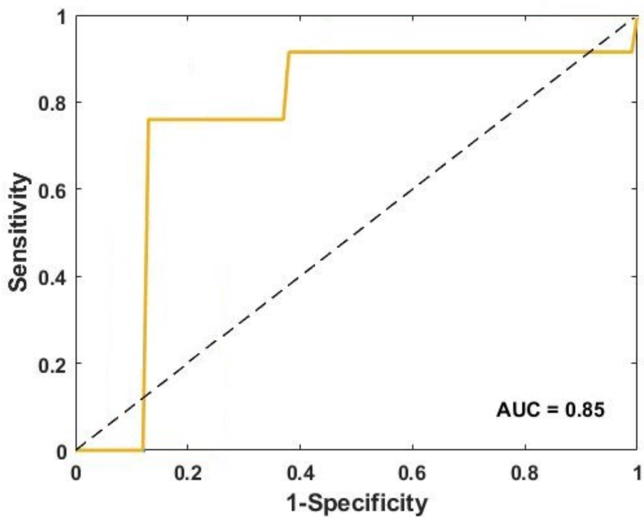


*Figure 2. Receiver Operating Characteristic (ROC) curve and the Area Under the Curve (AUC) for ensemble classifier.*

# References

[1] Arbelo E, Brugada J, Hindricks G, Maggioni AP, Tavazzi L, Vardas P, et al. The Atrial Fibrillation Ablation Pilot Study: An European Survey on Methodology and results of catheter ablation for atrial fibrillation conducted by the European Heart Rhythm Association. Eur Heart J. 2014;35(22):1466–78.

[2] Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines

for the management of atrial fibrillation developed in collaboration with EACTS The Task Force for1. Task A, Members F, Kirchhof P, Uk C, Uk DK, Uk BC, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in c. 2017;(November):2893–962.

[3] Ganesan AN, Shipp NJ, Brooks AG, Kuklik P, Lau DH, Lim HS, et al. Long-term outcomes of catheter ablation of atrial fibrillation: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2(2):603.

[4] Kornej J, Hindricks G, Shoemaker MB, Husser D, Arya A, Sommer P, et al. The APPLE score: a novel and simple score for the prediction of rhythm outcomes after catheter ablation of atrial fibrillation. Clin Res Cardiol. 2015;104(10):871–6.

[5] Jud FN, Obeid S, Duru F, Haegeli LM. A novel score in the prediction of rhythm outcome after ablation of atrial fibrillation: The SUCCESS score. Anatol J Cardiol. 2019;21(3):142–9.

[6] Potpara TS, Mujovic N, Sivasambu B, Shantsila A, Marinkovic M, Calkins H, et al. Validation of the MB-LATER score for prediction of late recurrence after catheter-ablation of atrial fibrillation. Int J Cardiol [Internet]. 2019;276:130–5. Available from: https://doi.org/10.1016/j.ijcard.2018.08.018

[7] Bou Ezzeddine H, Vachulova A, Svetlosak M, Urban L, Hlivak P, Margitfalvi P, et al. Occurrence of symptoms after catheter ablation of atrial fibrillation. Bratislava Med J. 2015;116(8):461–4.

[8] Hindricks G, Pokushalov E, Urban L, Taborsky M, Kuck KH, Lebedev D, et al. Performance of a new leadless implantable cardiac monitor in detecting and quantifying atrial fibrillation results of the XPECT trial. Circ Arrhythmia Electrophysiol. 2010;3(2):141–7.

[9] Saiz-Vivo J, Corino VDA, Hatala R, de Melis M, Mainardi LT. Heart Rate Variability and Clinical Features as Predictors of Atrial Fibrillation Recurrence After Catheter Ablation: A Pilot Study. Front Physiol. 2021;12(May):1–9.

# 7. ESR9: Atrial Tachycardia and Atrial Fibrillation Interplay Mechanism Detected by a Single Lead ECG

ESR9: Guadalupe García Isla

## Motivation and aim

Cardiac tachyarrhythmias refer to a group of pathological depolarization patterns that may occur both in the ventricles and in the atria. Although supraventricular tachyarrhythmias do not represent an explicit life-threatening risk, they are associated with high mortality and increased morbidity. Atrial tachyarrhythmias like atrial fibrillation (AF), atrial flutter (AFL) and atrial tachycardia (AT) are linked to thromboembolic events and myocardial tissue deterioration [1]. This research project aimed to develop detection techniques for different atrial tachyarrythmia in order to provide clinically relevant data for AF treatment and monitoring. In addition, it aimed to provide tools to study the relationship between premature atrial complexes (PAC), AT and AF appearance and development. Premature atrial complexes (PACs) have always been considered benign. However, several late studies link them to high risk of developing AF and stroke [2].

A detector based only on RR intervals capable of classifying other tachyarrhythmias in addition to AF could improve cardiac monitoring. In this work a new classification method based in a 2D non-linear RRI dynamics representation is presented introducing the concepts of Poincaré Images and Atlases [3], [4]. In addition, in order to study the relationship of PAC with AF episodes, we have developed a PAC and PVC detector [5].

## Methods

The Poincaré Plot is a 2D graphical representation of consecutive RR intervals. Considering the pairs of consecutive RR intervals (RRn, RRn+1) being $n \in \{1,2, \ldots , N-1\}$ with N the number of samples in the considered epoch. The Poincaré Image is a pixelated version of the traditional continuous Poincaré plot as shown in Figure 1. Three Physionet open-source databases were used. Poincaré Images were generated for the rhythms normal sinus rhythm (NSR), AF and atrial bigeminy (AB) for all signals using different Poincaré plot configurations: RR, dRR and RRdRR. The study was computed for the time windows of 20, 30, 60 and 120 s and bin sizes 5, 10, 20, 40 ms for the Poincare Images configuration RR, dRR and RRdRR.

For each rhythm, the Poincaré Images of the 80% of that rhythm's patients were used to create a reference image, a Poincaré Atlas. The remaining 20% were used as test set and classified into one of the three rhythms using normalized mutual information and 2D correlation. For classifying each Poincaré Image, NMI and 2D correlation were computed with respect to each Poincaré Atlas and classified according to the one that maximized the mentioned parameters.

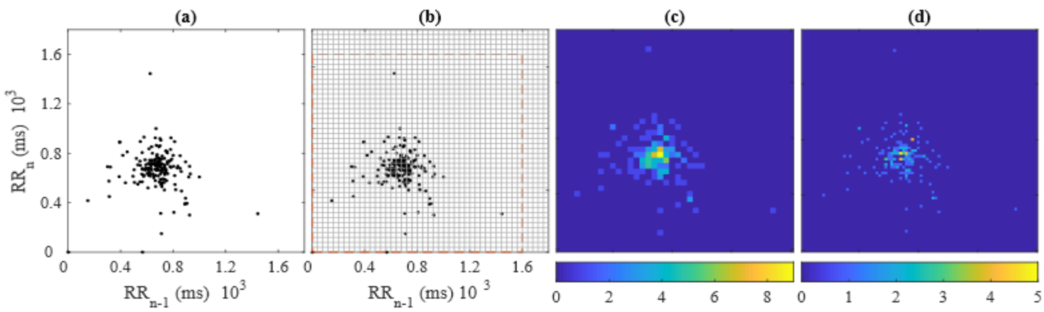


*Figure 3: Creation of Poincaré Images from Poincaré Plots. (a) Poincaré Plot obtained from a signal segment of 120 s. (b) Grid indicating the bin discretization of the Poincaré Plot. The discontinuos line accounts for the common limits applied for all Poincaré Images. (c) Poincaré Image created using a bin size of [40x40] ms. (d) Poincaré Image of bin size [20x20].*

For PAC detection two types of detectors were developed: a beat-to-beat classifier [5] and a segment detector [6]. In the first one both ECG morphology and RR intervals were used to discriminate among PAC, PVC and normal beats. In the second, only RR intervals represented in Poincaré Images were used to discriminate between ECG segments not containing any PAC or PVC and those containing at least one of such beats. While the first classifier used classic machine learning techniques, the second one used CNNs. Although the first one would provide a direct output of each individual beat class (normal, atrial or ventricular), the second one help identify regions containing such beats to reduce false positives in automatic beat classifiers (many times induced by noise altering the signal's morphology) as well as to reduce the workload if manual beat annotation is intended

## Main findings

This study poses a new approach towards cardiac tachyarrhythmia classification by transforming RRI into images. Differently than current methodologies, the proposed model can be generalized to different rhythms and, in contrast with AF-focused methods, it does not define rhythm-specific parameters and thresholds. We introduce two new versions of the Poincaré plot to which we refer as Poincaré Images and Poincaré Atlases and we explore the possibility of identifying and classifying NSR, AB and AF ECG segments.  Best performance was obtained for the combination of NMI and 2D correlation, RRdRR Poincaré Images and 40 ms bin size as shown in Table 1.

| Rhythm | Accuracy (%) | Sensitivity (%) | Specificity (%) |
|---|---|---|---|
| NSR | 88.81±3.87 | 82.07±9.18 | 95.91±3.14 |
| AF | 89.78±3.24 | 94.35±3.68 | 85.51±7.46 |
| AB | 96.08±2.25 | 88.86±12.78 | 96.10±2.25 |

*Classification results with time window 60 s and bin size 40 ms*

The developed method for PAC and PVC detection surpasses in terms of sensitivity and positive predictive value (PPV) the state-of-the-art models, reaching a sensitivity of 95.65% and 96.20% and a PPV of 13% and 58% in the long-term ST database (LTSTDB) and the supraventricular arrhythmia database (SVDB). The segment wise classifier obtained a sensitivity of 96.03%, a specificity of 98.70% and a PPV of 91.91%. The results obtained suggest this methodology could be used to reduce the ECG beat annotation workload to study PACs and other A/V implications. In addition, it could be used in combination with automatic beat classifiers to find misclassifications and obtain more reliable annotations.

# References

[1] T. V. Glotzer *et al.*, "The Relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk the trends study," *Circ. Arrhythmia Electrophysiol.*, vol. 2, no. 5, pp. 474–480, 2009.

[2] D. J. Gladstone *et al.*, "Atrial Premature Beats Predict Atrial Fibrillation in Cryptogenic Stroke: Results from the EMBRACE Trial," *Stroke*, vol. 46, no. 4, pp. 936–941, 2015.

[3] G. García-Isla, V. D. A. Corino, and L. T. Mainardi, "Cardiac Tachyarrhythmia Detection by Poincaré Plot-Based Image Analysis," in *Computing in Cardiology*, 2019.

[4] G. Garcia-Isla, V. D. A. Corino, and L. Mainardi, "Poincaré Plot image and rhythm-specific atlas for atrial bigeminy and atrial fibrillation detection," *IEEE J. Biomed. Heal. Informatics*, vol. 25, no. 4, pp. 1–1, 2020.

[5] G. García-Isla, L. Mainardi, and V. D. A. Corino, "A Detector for Premature Atrial and Ventricular Complexes," *Front. Physiol.*, vol. 12, no. June, pp. 1–11, 2021.

[6] G. García-Isla, L. Mainardi, and V. D. A. Corino, "A Poincare Image-Based Detector of ECG Segments Containing Atrial and Ventricular Beats," 2021, vol. 48, pp. 1–4.