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Spectral F-wave index for automatic identification of atrial fibrillation in very short electrocardiograms

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27 **Spectral F-wave index for automatic identification of atrial fibrillation in**  
28 **very short electrocardiograms**

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1        **Abstract**

2        Micro as well as clinical atrial fibrillation (AF) is associated with both F-wave occurrence and high  
3        heart-rate variability (HRV). Automatic AF identification typically relies on HRV evaluation only.  
4        However, high HRV is not AF specific and may not be reliably estimated in very short  
5        electrocardiograms (ECG). This study presents a new algorithm for automatic AF identification in very  
6        short ECG based on computation of a new spectral F-wave index (SFWI). Data consisted of short (9  
7        heartbeats) 12-lead ECG acquired from 6628 subjects divided in assessment dataset and validation  
8        dataset. Each lead was independently analyzed so that 12 values of SFWI, indicating the percentage of  
9        spectral power in the 4-10Hz band, were obtained for each ECG. Additionally, a global SFWI value was  
10       computed as the median of SFWI distribution over leads. To identify AF, a threshold on SFWI was  
11       firstly assessed on the assessment dataset, and then evaluated on the validation dataset by computation  
12       of sensitivity (SE), specificity (SP) and accuracy (AC). Results were compared with those of standard  
13       HRV-based approaches. AF identification by SFWI was already good when considering a single lead  
14       (SE: 84.6-88.8%, SP: 84.5-87.0%, AC: 84.5-87.3%), improved significantly when combining the 12  
15       leads (SE: 89.0%, SP: 87.0%, AC: 88.7%) and, overall, performed better than standard HRV-based  
16       approaches (SE: 82.2%, SP: 83.6%, AC: 83.4%). The presented algorithm is a useful tool to  
17       automatically identify AF in very short ECG, and thus has the potentiality to be applied for detection of  
18       both micro and clinical AF.

19

20        **Keywords:** Atrial Fibrillation, Fibrillatory Waves, Heart-Rate Variability, Short-Term Monitoring,  
21        Electrocardiogram.

22

## 1 **Introduction**<sup>a</sup>

2 A normal electrocardiogram (ECG) is constituted by a repetition of a typical pattern of waves  
3 representing the phases of electrical activity of the myocardium during a heartbeat: atrial depolarization  
4 (P wave), ventricular depolarization (QRS complex) and ventricular repolarization (T wave), with the  
5 QRS complex hiding atrial repolarization[1] (Figure 1A). This pattern reflects the ability of myocardial  
6 cells to synchronically depolarize and repolarize to drive a regular cardiac contraction and relaxation  
7 and thus a pseudo-periodic heart rhythm. When the myocardial cells are no longer able to depolarize  
8 synchronically, fibrillation occurs[1]; if synchronism is lost in the atrial cells, we have atrial fibrillation  
9 (AF; Figure 1B). During AF, atrial depolarization is no longer synchronized with ventricular  
10 depolarization; additionally, cardiac rhythm is irregular and characterized by high heart-rate variability  
11 (HRV). Losing of atrial synchronism is reflected by the disappearance of P waves and the appearance  
12 of a chaotic atrial depolarization patterns, signs of the summation of all independent depolarizations of  
13 atrial myocardial cells. These chaotic patterns are called fibrillatory waves (F waves),  
14 electrocardiographic waves characterized by low amplitude (0.06mV-0.35mV)[2] and high frequency  
15 (240bpm-600bpm, corresponding to 4Hz-10Hz)[2].

16 Currently, AF represents the most common form of cardiac arrhythmia[3] and can have dramatic  
17 consequences such as stroke, heart failure and other heart-related complications[3,4]. AF prevalence is  
18 estimated around 3% in adults older than 20 years, with increased values observed in subjects with other  
19 comorbidities such as obesity, diabetes mellitus, or chronic kidney disease[4–6]. According to the  
20 European Society of Cardiology (ESC)[4], one out of four middle-aged adults in Europe and in the

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**Abbreviations:** 95%CI: 95% confidence intervals; AC: accuracy; AF: atrial fibrillation; AFC: atrial fibrillation class; AUC: area under the curve; BoI: beat of interest; ECG: electrocardiogram; IQR: interquartile range; HRV: heart-rate variability; MRR: mean RR interval; NAFC: not atrial fibrillation class; NSTHRV: normalized short-term heart-rate variability; OT: optimal threshold; PSD: power spectral densities; Q1: first quartile; Q2: median value; Q3: third quartile; RBoI: residual beat of interest; ROC: receiver operating characteristic; SE: sensitivity; SFWI: spectral f-wave index; SP: specificity; STHR: short-term heart-rate variability.

1 United States will develop AF by 2030[4,7,8]. Thus, the need of further research finalized to provide  
2 tools to fight AF remains imperative.

3 According to guidelines, AF is defined as clinical if it lasts 30s or longer [3,4]. Clinical AF can  
4 be further classified based on its temporal characteristics as[9]: paroxysmal, when recurrent but  
5 spontaneously terminating within 7 days, most often within 48 hours; persistent, when recurrent but not  
6 spontaneously terminating and lasting 7 days or longer; or permanent, when established, not terminated  
7 or terminated but relapsed. Recent clinical investigations indicated AF shorter than 30s as micro AF[10];  
8 usually, micro AF is asymptomatic but is believed to be a predictor of clinical AF.

9 AF diagnosis is typically based on patient's symptoms and ECG examination. AF symptoms,  
10 which occur with high inter- and intra-subject variability, include palpitations, chest pain, dyspnea,  
11 fatigue, or lightheadedness[3]. ECG indexes of AF, usually investigated on 12-lead ECG recordings,  
12 include high HRV, P-wave absence and F-wave presence, especially in leads II, III, aVF and V1[3].  
13 Several algorithms have been presented for the automatic identification of AF by ECG processing[11–  
14 14]. Typically, automatic AF identification mainly relies on the occurrence of high HRV[15,16] even  
15 though high HRV is not AF specific but may occur in several other arrhythmias. Additionally, reliable  
16 HRV assessment requires sufficiently long ECG recordings. It has been suggested that the minimum  
17 ECG length of 30s required for clinical AF identification is mainly due to technical rather than  
18 physiological issues[15]. Indeed, 30s represent the minimum ECG length including enough heartbeats  
19 to confidently assess HRV for a reliable AF identification[16–18]. Given the non-specificity of HRV  
20 and the prognostic value of micro AF[10], availability of algorithms based on ECG features other than  
21 HRV and able to reliably identify AF from short ECG (shorter than 30s) are highly desirable.

22 In a previous pilot study [19], we investigated the possibility to define a new clinical index for  
23 AF identification from a single lead of a standard 10-second ECG, and we obtained preliminary but  
24 promising results. The major limitations of this study consisted in the study population, that included  
25 only subjects with normal sinus rhythm or atrial fibrillation (no other abnormal rhythms were  
26 considered) and in the definition of the index characterizing the entire ECG window, which made the  
27 procedure inadequate to identify transient episodes of AF. The aim of the present study was to present  
28 a new algorithm for automatic AF identification in very short ECG recordings mainly based on spectral

1 features of the F waves and able to overcome all the limitations of the previously proposed index. To  
2 this aim, the new spectral F-wave index (SFWI) was assessed and validated on 9-heartbeat ECG  
3 windows of subjects showing normal sinus rhythm, AF and other abnormal cardiac rhythms.

4

## 5 **2. Methods**

### 6 **2.1. Experimental data**

7 The experimental data consisted of 9-heartbeat windows of 12-lead (I, II, III, aVR, aVL, aVF, V1  
8 to V6; sampling frequency: 500 Hz) ECG recordings acquired from 6628 subjects (Sex: 3523 male and  
9 3105 female; Age:  $59.9 \pm 19.1$  years) in 11 different hospitals and belonging to the “China Physiological  
10 Signal Challenge in 2018 (CPSC2018)” Physionet database[20,21]. The experimental data, as all other  
11 Physionet data, had been previously randomized and anonymized and can be used without further ethical  
12 approval.

13 All experimental data were accompanied by annotations (also available in the Physionet  
14 database[22]) that indicate the occurrence of normal sinus rhythm, AF and/or other abnormal cardiac  
15 rhythms. Overall, 1183 subjects (Sex: 638 male and 545 female; Age:  $64.0 \pm 17.8$  years) presented ECG  
16 windows annotated as showing AF (of them, 943 showed only AF and 240 showed also other abnormal  
17 cardiac rhythms) and constituted the AF class (AFC); the remaining 5445 subjects (Sex: 2885 male and  
18 2560 female; Age:  $59.0 \pm 19.2$  years) presented ECG windows not affected by AF (of them, 904 showed  
19 normal sinus rhythm and 4541 showed other abnormal cardiac rhythms) and constituted the not AF class  
20 (NAFC). Specifically, the considered abnormal cardiac rhythms were first-degree atrioventricular block,  
21 left bundle branch block, premature atrial complex, premature ventricular complex, right bundle branch  
22 block, ST-segment depression and ST-segment elevation. The AFC vs NAFC classification was used as  
23 gold standard in the evaluation of the presented procedure for the automatic identification of AF.

24

### 25 **2.2. Definition and validation of the procedure for automatic identification of atrial fibrillation**

26 Briefly, the presented procedure for automatic identification of AF analyzes each single lead tracing  
27 of a 9-heartbeat ECG window independently and identifies AF occurrence thanks to the spectral F-wave  
28 index (SFWI), which indicates the percentage of spectral power in the 4-10Hz band due to the F waves.

1 In order to discriminate between ECG tracings showing and not showing AF, a threshold on SFWI is  
 2 used. The threshold is firstly assessed using a specifically constructed dataset (the assessment dataset)  
 3 and then validated on another dataset (the validation dataset). Below is reported a detailed description  
 4 of all steps involved in the definition and validation of the procedure for automatic identification of AF.  
 5 All the signal processing procedures were implemented in MATLAB.

6

### 7 **Spectral F-wave index**

8 The core of the procedure for automatic AF identification consists in the computation of the SFWI  
 9 (Figure 2) from a single lead 9-heartbeat ECG window and with its known R-peak positions (in this  
 10 study, R-peak positions were extracted using the Pan-Tompkins algorithm [23] on Lead I). Initially, the  
 11 single lead 9-heartbeat ECG window was prefiltered with a digital bidirectional (to avoid signal  
 12 distortion) bandpass 6<sup>th</sup>-order Butterworth filter with cutoff frequencies at 0.5Hz and 30Hz in order to  
 13 keep only the main ECG frequency components. R-peak positions were used to compute the 8 RR  
 14 intervals in the 9-heartbeat ECG window, which were then used to compute the mean RR interval (MRR,  
 15 ms) and the short-term HRV (STHRV, ms; defined as the standard deviation of the 8 RR intervals), as  
 16 reported in Eq. (1):

$$17 \quad \left\{ \begin{array}{l} MRR = \frac{\sum_{i=1}^8 RR_i}{8} \\ STHRV = \sqrt{\frac{\sum_{i=1}^8 (RR_i - MRR)^2}{8}} \end{array} \right. \quad (1)$$

18 Successively, SFWI was automatically set to zero in case of ECG windows characterized by very  
 19 low STHRV (i.e., STHRV less than 7.5% of MRR). Differently, the ninth heartbeat was indicated as  
 20 the Beat of Interest (BoI) and its RR interval ( $RR_{BoI}$ , ms) was used to segment all heartbeats in the ECG  
 21 window. Specifically, a heartbeat segment was identified as the tracing portion between 250ms and  
 22  $RR_{BoI} - 250$ ms before and after the heartbeat R peak, respectively. All heartbeat segments were then  
 23 correlated with the BoI segment. If the correlation coefficient of more than four heartbeats was less than  
 24 0.5, SFWI was set to zero. Otherwise, the template heartbeat was obtained as the median heartbeat  
 25 segment over the four heartbeats with the highest correlation. Eventually, the residual ECG (RBoI),  
 26 possibly containing the F wave, was obtained by subtracting the template heartbeat from the BoI



1 segment. In case of sinus rhythm, the template heartbeat would approximate all BoI components; thus,  
 2 the subtraction between BoI and template heartbeat would be practically null (no F-wave components).  
 3 Differently, in case of AF, the template heartbeat would approximate only ventricular electrical activity,  
 4 because the F-wave components, typically appearing with different phase shifts over the heartbeats,  
 5 would be cancelled by the median operation. Thus, RBoI would contains all F-wave components  
 6 because obtained by the subtraction of BoI (QRS-T waves plus F-wave components) and template  
 7 heartbeat (only QRS-T waves).

8 After computation of RBoI, both BoI segment and RBoI were filtered with a digital bidirectional  
 9 bandpass 6<sup>th</sup>-order Butterworth filter with cutoff frequencies at 4Hz and 10Hz in order to keep only the  
 10 typical F-wave frequency components (240bpm-600bpm, corresponding to 4Hz-10Hz)[2]. By  
 11 construction, the filtered BoI segment contains frequency components of all ECG waveforms in the 4-  
 12 10Hz band, whereas the filtered RBoI represents an estimate of the F wave affecting BoI, and thus a  
 13 segment of the F wave affecting the 9-heartbeat ECG tracing. Eventually, the SFWI (in %) was  
 14 computed as percentage of the power spectral densities (PSD) of the filtered RBoI with respect to the  
 15 filtered BoI segment, as reported in Eq. (2):

$$16 \quad SFWI = 100 \cdot \frac{PSD(filtered\ RBoI)}{PSD(filtered\ BoI)} \quad (2)$$

17 This procedure was recursively applied to each ECG lead independently. Consequently, 12 values  
 18 (one for each ECG lead) of SFWI were obtained for each ECG window. Additionally, a global lead-  
 19 independent SFWI was computed as the median value of the SFWI distribution over the 12 leads.

20

## 21 **Assessment and validation datasets**

22 Experimental data were randomly grouped into two datasets, each containing 9-heartbeat windows of  
 23 12-lead ECG recordings from both AFC and NAFC, specifically created to assess and validate the  
 24 threshold used by the procedure for discriminating ECG windows affected by AF from those not affected  
 25 by AF. The first dataset, called assessment dataset, contained 3315 ECG windows, 592 belonging to the  
 26 AFC (472 showing only AF and 120 showing also other abnormal cardiac rhythms), and 2723 belonging  
 27 to the NAFC (452 showing normal sinus rhythm and 2271 other abnormal cardiac rhythms).

1 Analogously, the second dataset, called validation dataset, contained 3313 ECG windows, 591  
 2 belonging to the AFC (471 showing only AF and 120 showing also other abnormal cardiac rhythms),  
 3 and 2722 belonging to the NAFC (452 showing normal sinus rhythm and 2270 other abnormal cardiac  
 4 rhythms).

5

## 6 **Comparative evaluation**

7 In order to evaluate the presented procedure for automatic identification of AF against more standard  
 8 approaches based on HRV[15,18], two HRV indexes were considered, namely the short-term HRV  
 9 (STHRV; ms) and normalized STHRV (NSTHRV; %), computed as reported in Eq. (3):

$$10 \quad \left\{ \begin{array}{l} STHRV = \sqrt{\frac{\sum_{i=1}^8 (RR_i - MRR)^2}{8}} \\ NSTHRV = 100 \cdot \frac{STHRV}{MRR} \end{array} \right. \quad (3)$$

11 Specifically, STHRV was defined as the standard deviation of the 8 RR intervals in the 9-heartbeat ECG  
 12 tracing; instead, NSTHRV was defined as 100 by STHRV over MRR.

13

## 14 **Threshold assessment and validation**

15 Quantification of the optimal threshold (OT) on SFWI, STHRV and NSTHRV for AF identification  
 16 was statistically performed by analyzing the receiver operating characteristic (ROC) obtained using the  
 17 assessment dataset. OT value was obtained in correspondence of the operating point that equals  
 18 sensitivity (SE) and specificity (SP). According to the procedure for SFWI computation, each ECG lead  
 19 is analyzed independently; consequently, 12 values of OT on SFWI were obtained (one for each ECG  
 20 lead) by using the lead-dependent SFWI distributions. Additionally, a global lead-independent threshold  
 21 was obtained as the median SFWI distribution. Eventually, OT values were validated using the  
 22 validation dataset.

23

## 24 **2.3. Statistical analysis**

25 Sex and age distributions between AFC and NAFC were compared using the  $\chi^2$  test and the t-test,  
 26 respectively.

1 Normality of SFWI, STHRV and NSTHRV distributions were evaluated with the Lilliefors  
2 test[24]. Non-normal distributions were described in terms of median value (Q2), first quartile (Q1),  
3 third quartile (Q3) and interquartile range (IQR, with  $IQR=Q3-Q1$ ), and were compared using the  
4 Wilcoxon ranksum test[25] for equal median. Statistical significance was set at 0.05.

5 Assessment of OT on the ROC curve was evaluated in terms of area under the curve (AUC) and  
6 95% confidence intervals (95% CI). Performance of the automatic procedure for AF discrimination over  
7 the various datasets when applying OT was statistically evaluated in terms of SE, SP and accuracy (AC).  
8 The statistical analysis was performed using MATLAB.

9

### 10 **3. Results**

11 Sex distribution was comparable between AFC (54% males and 46% females) and NAFC  
12 (53% males and 47% female), while subjects belonging to AFC were significantly older than subjects  
13 belonging to NAFC ( $64.0\pm 17.8$  years vs  $59.0\pm 19.2$  years;  $P<0.05$ ).

14 Table 1 reports SFWI, STHRV and NSTHRV distributions over the assessment and validation  
15 datasets. Within a dataset, median SFWI values over AFC were always statistically ( $P<0.05$ ) higher than  
16 median SFWI values over NAFC, independently from lead; moreover, SFWI IQR over AFC class was  
17 always much higher than SFWI IQR over NAFC, also independently from lead. Analogously, median  
18 STHRV and NSTHRV values over AFC were always statistically ( $P<0.05$ ) higher than median STHRV  
19 and NSTHRV values over NAFC; moreover, STHRV IQR and NSTHRV IQR over AFC class were  
20 higher than corresponding STHRV IQR and NSTHRV over NAFC. However, when comparing the two  
21 datasets, no statistically significant differences were reported between median SFWI, STHRV and  
22 NSTHRV values within a class (either AFC or NAFC).

23 Table 2 reports OT and AUC values for SFWI, STHRV and NSTHRV obtained in the assessment  
24 dataset with corresponding SE, SP and AC, as well as SE, SP and AC values obtained in the validation  
25 dataset.

26 AF identification by SFWI was already good when considering a single lead (AUC: 87.2-90.4%,  
27  $SE=SP=AC$ : 84.0-87.2% in the assessment dataset; SE: 84.6-88.8%, SP: 84.5-87.0%, AC: 84.5-87.3%  
28 in the validation dataset) and significantly improved when combining the 12 leads (AUC: 91.7%,

1 SE=SP=AC: 88.4% in the assessment dataset; SE: 89.0%, SP: 87.0%, AC: 88.7% in the validation  
2 dataset). AF identification using HRV was better when using NSTHRV (AUC: 88.9%, SE=SP=AC:  
3 83.9% in the assessment dataset; SE: 82.2%, SP: 83.6%, AC: 83.4% in the validation dataset) than when  
4 using STHR (AUC: 85.9%, SE=SP=AC: 81.3% in the assessment dataset; SE: 79.9%, SP: 81.3%, AC:  
5 81.0% in the validation dataset). Automatic AF identification by SFWI was in general better (higher SE,  
6 SP and AC) than by NSTHRV, especially but not exclusively when the 12 leads were combined. Even  
7 when AUC values were comparable, SE, SP and AC values by SFWI were higher than NSTHRV  
8 because of different ROC morphologies (Figure 3).

9

#### 10 **4. Discussion**

11 This study presented a new algorithm for automatic identification of atrial fibrillation in 9-heartbeat  
12 electrocardiographic windows based on F-wave index, that is the spectral F-wave index. It was designed  
13 to overcome all the limitations presented by our previous pilot study [19], and thus to be able to  
14 discriminate atrial fibrillation not only from normal sinus rhythm, but also from other abnormal rhythms;  
15 to be suitable for the identification of transient episodes of atrial fibrillation in possibly real time  
16 applications; and to optimize performances when more than one lead was available.

17 In order to properly identify onset and end of both clinical and micro atrial fibrillation events, the  
18 F-wave index needs to be computed for each single heartbeat. However, the proposed algorithm for  
19 spectral F-wave index computation needs some additional beats to obtain the template and to perform  
20 the QRS-T removal from the beat of interest. Thus, the procedure cannot be applied to a single beat, but  
21 rather it should be applied to an ECG window. Considering these technical requirements, we  
22 experimentally found the 9-heartbeat (8 heartbeats for template construction plus the beat of interest)  
23 ECG windows as the best trade-off between the need of having short ECG windows to allow timely  
24 identification of atrial fibrillation and the need of having long ECG window to obtain reliable templates.  
25 Clearly, time length of the 9-heartbeat ECG window may vary with heart rate; this may become an issue  
26 only in case of bradycardia with heart rates below 60bpm and ECG windows extracted from standard  
27 10-second 12-lead ECG.

1       Electrocardiographic heartbeat morphologies during sinus rhythm are the reflection of physiological  
2       electrical phenomena originating in the same cardiac site, that is the sinus node. Consequently, the  
3       deviations from a fundamental sinus morphology, including the P-QRS-T waves are very limited,  
4       especially in very short electrocardiographic windows. During atrial fibrillation, the electrical  
5       phenomena originate in triggering ectopic sites on the atria different from the sinus node. Consequently,  
6       the electrocardiographic heartbeat morphology loses its P wave and appears as the superimposition of  
7       the usual QRS-T waves plus the F wave, which is a high frequency oscillatory wave if compared to  
8       heart rate. According to our algorithm, the F wave affecting a specific heartbeat can be estimated by  
9       subtracting a fundamental heartbeat waveform, here called template, from the beat-of-interest  
10       morphology. As reported in the method section, the template is obtained as the median heartbeat over  
11       the four most correlating beats among the eight preceding ones. In case of sinus rhythm, and thus little  
12       variability, the template will have the same morphology of the beat of interest, and the resulting F wave  
13       will be practically null. Differently, in case of atrial fibrillation, the template will approximate the QRS-  
14       T waves only. Indeed, F waves typically appear with a different phase shift over the heartbeats, and the  
15       effect of the median operation will be its cancellation; as a result, F-wave estimation can be obtained by  
16       subtraction.

17       Atrial fibrillation is always associated to an increased heart-rate variability [15,18], but this criterion  
18       is not specific for atrial fibrillation. Indeed, other abnormal rhythms (such are premature atrial and  
19       ventricular beats) may also present high heart-rate variability in short ECG windows. Thus, here  
20       increased heart-rate variability was used as a necessary but not sufficient condition for the occurrence  
21       of atrial fibrillation. Additionally, in longer ECG windows (32 heartbeats or longer), increased heart-  
22       rate variability is often identified when RR-interval standard deviation overcomes 10% of mean RR-  
23       interval [26]. However, given the shortness of electrocardiographic windows considered here (9  
24       heartbeats), this condition was widened so that increased heart-rate variability was identified when RR-  
25       interval standard deviation overcame 7.5% of mean RR-interval.

26       The presented algorithm performs properly also in presence of rhythms other than sinus rhythm  
27       and atrial fibrillation. Indeed, if the rhythm is altered but sustained, the situation is analogous to that  
28       occurring in the presence of sinus rhythm, since all heartbeats in the 9-heartbeat electrocardiographic

1 window will share the same fundamental morphology, and so will do the template. Additionally, being  
2 the template computed over the four heartbeats mainly correlating with the beat of interest (and not over  
3 all the eight preceding ones), the algorithm is also robust to the occasional appearance of different  
4 heartbeat morphologies (for example, premature ventricular heartbeats occasionally occurring among  
5 sinus heartbeats). Eventually, if the beat of interest has a unique morphology within the  
6 electrocardiographic window, and thus does not correlate with at least four out of the eight preceding  
7 heartbeats, the template is forced to be equal to the beat of interest itself, so that estimated F wave (and  
8 thus the spectral F-wave index) will be null. In general, estimated F waves are confirmed as such if  
9 showing frequency components in the 4-10Hz band. Thus, percentage of the beat-of-interest power  
10 spectra due to the estimated F wave, here indicated as spectral F-wave index, will be higher in case of  
11 atrial fibrillation than in case of other rhythms.

12         The ability of the spectral F-wave index to discriminate occurrence of atrial fibrillation was  
13 assessed and evaluated in 6628 9-heartbeats 12-lead electrocardiographic windows, out of which 1183  
14 (18%) were showing atrial fibrillation and 5445 (82%) were showing sinus or other rhythms. Results  
15 (Table 1) confirmed that the spectral F-wave index is significantly higher in the case of atrial fibrillation.  
16 In addition, results indicate that the spectral F-wave index is both lead dependent (different median  
17 values of spectral F-wave index are observed among leads) and subject dependent (high value of the  
18 interquartile range of the spectral F-wave index within a lead). These findings agree with physiological  
19 observations according to which, during atrial fibrillation, the atrial electrical pathway strongly depends  
20 on triggering ectopic site location. Within a subject, this pathway will be differently represented over  
21 the leads (F-wave inter-lead variability); among subjects, differences in triggering ectopic site location  
22 will result in a different representation of the F waves on a specific lead (F-wave inter-subject  
23 variability).

24         The threshold able to discriminate values of the spectral F-wave index characterizing atrial  
25 fibrillation was quantified using the assessment dataset, which contained 3315 9-heartbeat 12-lead  
26 electrocardiographic windows, of which 592 (18%) were showing atrial fibrillation, and 2723 (82%)  
27 were showing sinus or other rhythms. The threshold was identified in correspondence of the operating  
28 point characterized by equal sensitivity and specificity. Since the spectral F-wave index is a lead-

1 dependent index, threshold determination was also lead-dependent (Table 2). In addition, a global lead-  
2 independent threshold was computed by analyzing the distribution of the median spectral F-wave index  
3 over the leads. Threshold values were then validated on a validation dataset. The validation dataset was  
4 similar to the assessment dataset (3313 9-heartbeat 12-lead electrocardiographic windows, of which 591  
5 were showing atrial fibrillation, and 2722 were showing sinus or other rhythms). Single-lead thresholds  
6 were considered to evaluate the possibility to apply the presented procedure to electrocardiographic  
7 recordings acquired using devices (such as wearable sensors) that provide a reduced number of leads  
8 (sometimes one). Although single lead identification of atrial fibrillation proved to be reliable, multiple  
9 lead identification is surely to be preferred when there is availability of multi-lead electrocardiographic  
10 recordings (Table 2).

11 Performance of the spectral F-wave index in automatically discriminating atrial fibrillation was  
12 also compared to that of indexes based on heart rate variability (Table 2). Overall, the spectral F-wave  
13 index proved to be superior mainly for two reasons. Differently from increased heart-rate variability, F-  
14 wave occurrence is specific for atrial fibrillation so that false positive detections and false negative  
15 detections of atrial fibrillation are more balanced (the receiver operating characteristic of the spectral F-  
16 wave index is more symmetrical, whereas the receiver operating characteristic of the index based on  
17 heart-rate variability is more shifted toward the right, indicating the tendency of identifying more false  
18 positive than false negative detections; Figure 3). Additionally, 9 heartbeats (and thus 8 RR intervals)  
19 are too few to reliably assess heart rate variability[15], whereas appear more appropriate to estimate F  
20 waves.

21 Eventually, the presented procedure proved to provide reliable automatic identification of atrial  
22 fibrillation from 9-heartbeat electrocardiograms. Thus, it has the potentiality to be applied to both  
23 standard 10s electrocardiographic recordings and long-term Holter electrocardiographic recordings. In  
24 the latter case, the procedure could be applied to 9-heartbeat electrocardiographic windows recursively  
25 extracted every 1 heartbeat and would provide the spectral F-wave index relating to the last heartbeat.  
26 Thus, the procedure has the potentiality to identify atrial fibrillation with a low time delay, which is  
27 estimated to be between 2.7s and 5.4s in case of heart rate comprised between 100bpm and 200bpm.  
28 This delay is acceptable for both clinical and micro-AF identification, and the procedure could be useful

1 in several clinical scenarios. For example, it could support timely diagnosis of newly emerging atrial  
2 fibrillation, also when electrocardiograms are obtained through innovative portable devices.  
3 Additionally, it could support monitoring of the pathology evolution in patients with previously  
4 diagnosed atrial fibrillation. Future works will test the potentiality of this innovative approach in real-  
5 time long-term monitoring and identification of clinical as well as micro atrial fibrillation.

6

## 7 **5. Conclusion**

8 The presented procedure based on the computation of the spectral F-wave index proved to be a  
9 useful tool to automatically identify atrial fibrillation in very short electrocardiograms and has a great  
10 potential to be applied in common clinical practice.

11

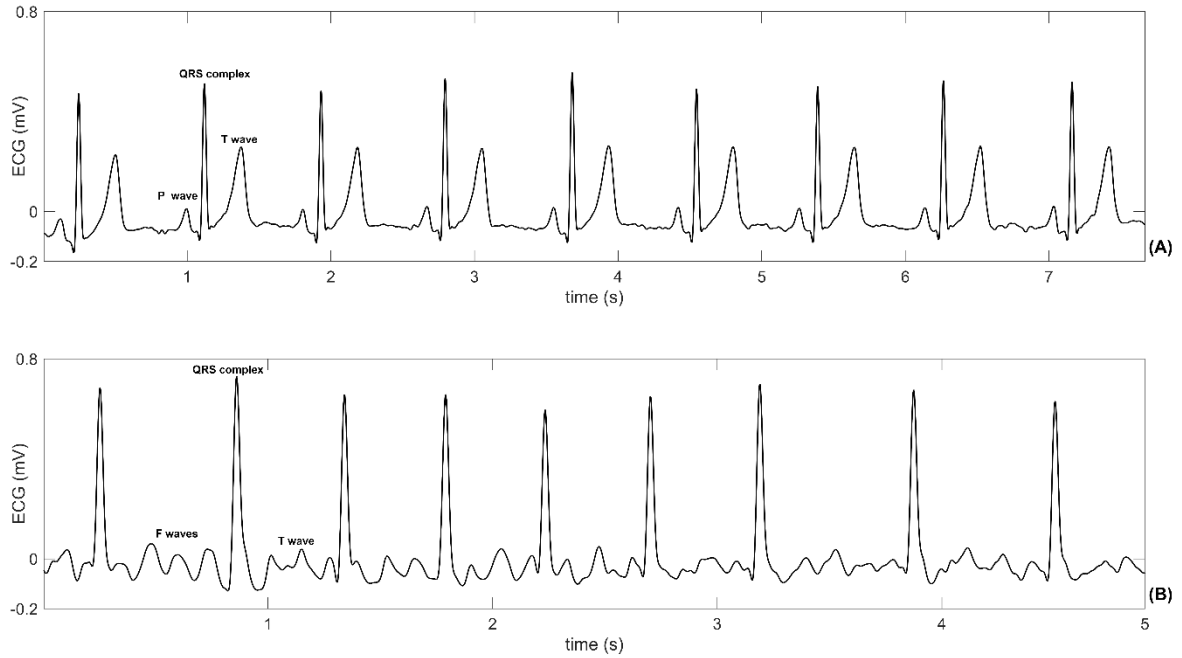


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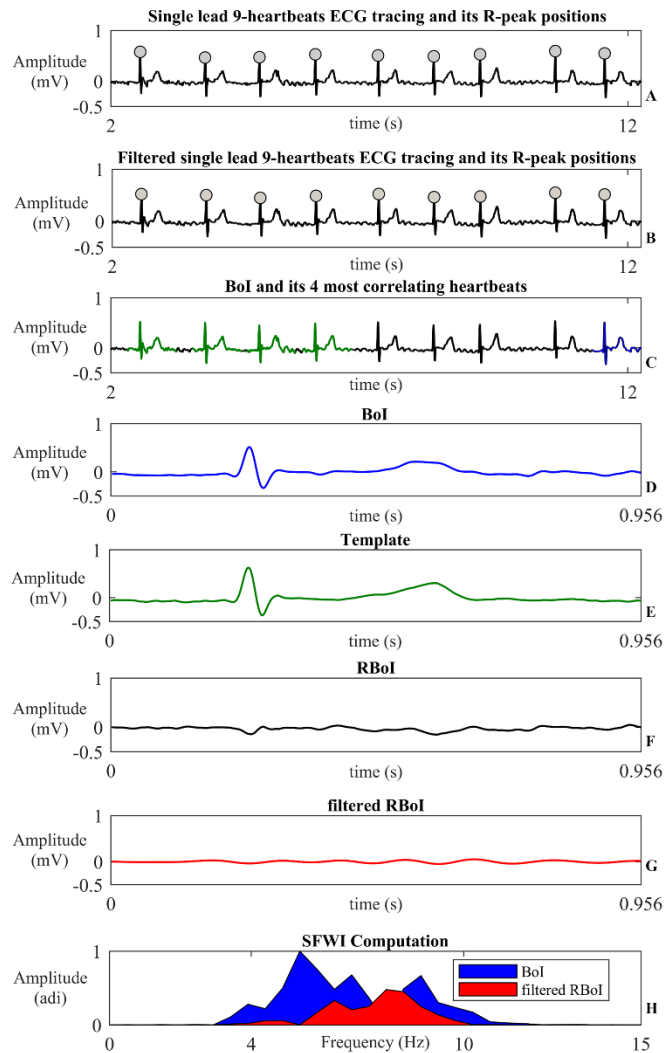
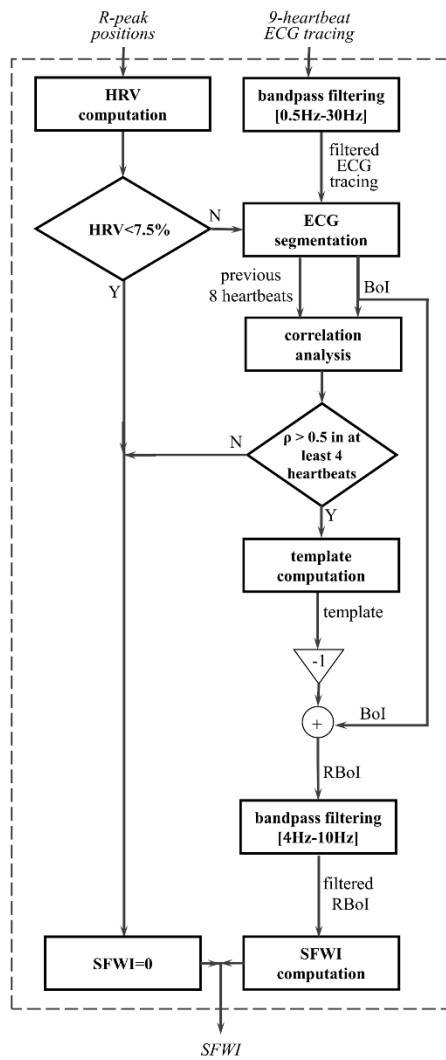
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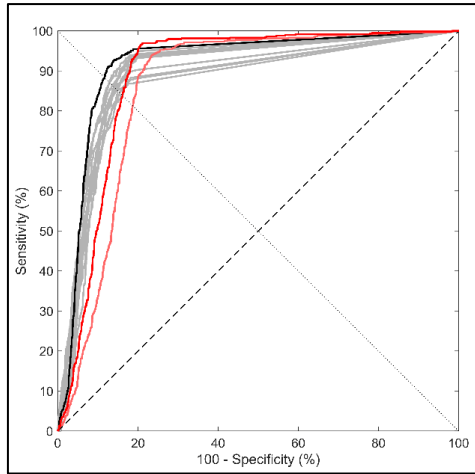
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**Figure 1.** Panel (A) shows a normal pseudo-periodic electrocardiogram (ECG; lead II of 16<sup>th</sup> recording in the CPSC2018 database) constituted by a repetition of a typical pattern of P-QRS-T waves. Panel (B) shows an ECG (lead II of 86<sup>th</sup> recording in the CPSC2018 database) affected by atrial fibrillation (AF) and thus presenting increased heart rate variability (HRV) and the F wave.



1

2 **Figure 2.** Block diagram (on the left) describing the procedure for computing the spectral F-wave index  
 3 (SFWI) from a 9-heartbeat ECG tracing. Graphical representation (on the right) of the steps for  
 4 computing spectral F-wave index (SFWI) from single lead (lead I) 9-heartbeat electrocardiogram (ECG)  
 5 tracing belonging to atrial fibrillation class (AFC) (274<sup>th</sup> recording in the CPSC2018 database).  
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**Figure 3.** Receiver operating characteristic (ROC) curves relative to lead-dependent spectral F-wave index (SFWI) distributions (gray curves), lead-independent spectral F-wave index (SFWI) distribution (black curve), short-term heart-rate variability (STHRV) distribution (light red curve) and normalized short-term heart-rate variability (NSTHRV) distribution (dark red curve).

1 **Table 1.** Spectral F-wave index (SFWI), short-term heart-rate variability (STHRV) and normalized  
2 short-term heart-rate variability (NSTHRV) distributions over the assessment and validation datasets  
3 described in terms of 50<sup>th</sup>[25<sup>th</sup>; 75<sup>th</sup>] percentiles (interquartile range).

		Assessment dataset		Validation dataset	
		AFC	NAFC	AFC	NAFC
SFWI (%)	# ECG windows	592	2723	591	2722
		3.19*	0.00	3.96*	0.00
	I	[1.22;9.75]	[0.00;0.13]	[1.32;10.62]	[0.00;0.07]
		(8.53)	(0.13)	(9.31)	(0.07)
		4.06*	0.00	5.03*	0.00
	II	[1.41;12.37]	[0.00;0.08]	[1.81;14.50]	[0.00;0.00]
		(10.96)	(0.08)	(12.69)	(0.00)
		6.65*	0.00	7.79*	0.00
	III	[1.66;19.81]	[0.00;0.00]	[2.16;22.07]	[0.00;0.00]
		(18.14)	(0.00)	(19.91)	(0.00)
		3.12*	0.00	3.55*	0.00
	aVR	[1.28;8.29]	[0.00;0.11]	[1.36;8.87]	[0.00;0.03]
		(7.01)	(0.11)	(7.50)	(0.03)
		5.06*	0.00	7.56*	0.00
	aVL	[1.64;15.15]	[0.00;0.00]	[1.67;19.34]	[0.00;0.00]
		(13.52)	(0.00)	(17.68)	(0.00)
		5.69*	0.00	6.24*	0.00
	aVF	[1.68;15.18]	[0.00;0.10]	[1.90;18.67]	[0.00;0.00]
		(13.50)	(0.10)	(16.76)	(0.00)
		4.71*	0.00	5.32*	0.00
V1	[1.39;15.56]	[0.00;0.09]	[1.37;19.60]	[0.00;0.04]	
	(14.17)	(0.09)	(18.23)	(0.04)	
	2.40*	0.00	3.10*	0.00	
V2	[0.85;7.34]	[0.00;0.08]	[0.97;9.55]	[0.00;0.05]	
	(6.49)	(0.08)	(8.58)	(0.05)	
	2.21*	0.00	2.56*	0.00	
V3	[0.90;5.55]	[0.00;0.09]	[0.96;7.12]	[0.00;0.07]	
	(4.65)	(0.09)	(6.17)	(0.07)	
	1.73*	0.00	2.05*	0.00	
V4	[0.70;4.71]	[0.00;0.07]	[0.76;6.05]	[0.00;0.04]	
	(4.01)	(0.07)	(5.29)	(0.04)	
	1.46*	0.00	1.65*	0.00	
V5	[0.57;4.47]	[0.00;0.08]	[0.66;4.85]	[0.00;0.02]	
	(3.90)	(0.08)	(4.20)	(0.02)	
	1.57*	0.00	1.44*	0.00	
V6	[0.58;4.50]	[0.00;0.08]	[0.60;3.95]	[0.00;0.00]	
	(3.92)	(0.08)	(3.35)	(0.00)	
	3.09*	0.00	3.51*	0.00	
Global	[1.62;5.92]	[0.00;0.19]	[1.67;7.33]	[0.00;0.09]	
	(4.29)	(0.19)	(5.66)	(0.09)	
STHRV (ms)	114.78*	19.27	115.48*	19.51	
	[82.96;170.35]	[10.92;45.65]	[82.78;164.44]	[10.86;44.58]	
	(87.39)	(34.73)	(81.66)	(33.73)	
NSTHRV (%)	18.95*	2.32	19.48*	2.36	
	[14.54;24.76]	[1.40;5.47]	[14.07;24.63]	[1.39;5.52]	
	(10.22)	(4.07)	(10.56)	(4.13)	

4 \*: P < 0.05, when comparing atrial fibrillation class (AFC) vs not atrial fibrillation class (NAFC) within  
5 a dataset.

1 **Table 2.** Receiver operating characteristic (ROC) analysis performance for the quantitative assessment  
 2 of thresholds and for the clinical validation.

		Assessment dataset				Validation dataset				
		OT	AUC [95%CI] (%)	SE (%)	SP (%)	AC (%)	SE (%)	SP (%)	AC (%)	
SFWI	Lead	<b>I</b>	0.56%	89.3 [87.6;91.1]	85.4	85.4	85.4	85.8	85.9	85.8
		<b>II</b>	0.63%	90.4 [88.7;92.1]	87.0	87.0	87.0	88.7	87.0	87.3
		<b>III</b>	0.55%	87.2 [85.4;89.1]	84.6	84.6	84.6	85.3	85.6	85.5
		<b>aVR</b>	0.60%	90.4 [88.7;92.1]	87.2	87.2	87.2	85.4	87.0	86.7
		<b>aVL</b>	0.49%	87.4 [85.6;89.3]	84.0	84.0	84.0	84.6	84.5	84.5
		<b>aVF</b>	0.65%	88.7 [86.9;90.5]	85.8	85.8	85.8	86.3	85.5	85.6
		<b>V1</b>	0.37%	87.6 [85.7;89.5]	85.1	85.1	85.1	84.6	85.8	85.6
		<b>V2</b>	0.42%	89.5 [87.8;91.3]	86.0	86.0	86.0	85.8	86.4	86.3
		<b>V3</b>	0.47%	90.0 [88.3;91.7]	86.5	86.5	86.5	84.9	86.7	86.4
		<b>V4</b>	0.38%	89.5 [87.8;91.3]	85.9	85.9	85.9	86.0	86.8	86.7
		<b>V5</b>	0.32%	89.3 [87.5;91.0]	85.7	85.7	85.7	85.4	85.8	85.8
		<b>V6</b>	0.31%	88.6 [86.8;90.4]	85.2	85.2	85.2	85.3	85.7	85.6
			<b>Global</b>	0.85%	91.7 [90.2;93.3]	88.4	88.4	88.4	89.0	88.7
HRV	<b>STHRV</b>	76.11ms	85.9 [83.9;87.8]	81.3	81.3	81.3	79.9	81.3	81.0	
	<b>NSTHRV</b>	12.66%	88.9 [87.2;90.7]	83.9	83.9	83.9	82.2	83.6	83.4	

3