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Velocity characteristics of atrial fibrillation sources determined by electrographic flow mapping before and after catheter ablation☆

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ABSTRACT

Background: Electrographic-Flow-(EGF)-Mapping is a novel method to identify Atrial Fibrillation (AF) drivers. Sources of excitation during AF can be characterized and monitored.
Objective: The aim of this study was to evaluate the correlation between velocity of EGF around a respective AF source and its spatial variability (SV) and stability (SST).
Methods: 25 patients with AF were included in this study (persistent: n = 24, long-standing persistent: n = 1; mean age 70 ± 8.3 years, male: n = 17). Focal impulse and Rotor-Mapping (FIRM) was performed in addition to pulmonary vein isolation. One-minute epochs of unipolar electrograms recorded via a 64-pole basket catheter in both atria were re-analyzed with EGF-Mapping. SST was calculated as the percentage of time in which a source was detected.
Results: AF sources identified with EGF-Mapping show a wide range of SV during 1 min covering between 0.12% and 38% of the recorded basket-catheter surface. The 12 atria where the sources showed highest temporal stability (TS; between 34% and 97% of 1 min recorded) and those 12 with the lowest TS (between 11 and 20%) differed significantly in their velocities (17.8 el/s vs 12.2 el/s; $p < 0.01$). In 11 atria ablation caused an average decrease of TS by 47% and of velocity by 27% while SV more than doubled.
Conclusion: Less stable AF-sources with high spatial variability showed reduced excitation propagation velocity while stable AF sources displayed a high average velocity in their vicinity. Importantly, catheter ablation reduced stability of sources and velocity suggesting a role of these parameters in guidance of ablation.
Condensed abstract: Electrographic Flow (EGF)-Mapping is a novel method to identify Atrial Fibrillation (AF) drivers based on modeling of an electrical potential surface and subsequent flow analysis. Sources of excitation during AF can be characterized and monitored. The aim of this study was to evaluate the correlation between velocity of EGF around a respective AF source and its spatial variability and stability. Less stable AF sources with high spatial variability showed reduced excitation propagation velocity while very stable AF sources displayed a high average velocity in their vicinity. Catheter ablation reduced stability of sources and velocity.

1. Introduction

Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia worldwide and is associated with a significant health burden [1–4]. Catheter ablation of pulmonary veins (PV) has been established as a therapeutic option for patients with symptomatic drug-refractory paroxysmal AF and results in high clinical success [5]. However, the treatment of persistent and long-standing persistent AF is still challenging. A large number of patients present with recurrence of atrial tachyarrhythmia during mid- and long-term follow up [6,7]. To achieve higher success rates different ablation strategies have been reported, usual targeting additional AF sources [8–12]. The initial results of focal impulse and rotor (FIRM) mapping for guiding catheter ablation of AF have been promising [9,11]. Though several data exist, there remains no conclusive evidence for the efficacy of AF driver ablation [13]. However, AF driver ablation is promising although randomized controlled data are awaited [14]. Current available systems for AF driver identification still have some limitations such as limited

Abbreviations list: AF, Atrial fibrillation; FI, Focal impulse; EGF, Electrographic flow; FIRM, Focal impulse and Rotor-Mapping; PVI, Pulmonary vein isolation; SR, Sinus rhythm; STT, Stability; TS, Temporal Stability; SV, Spatial Variability; INR, International normalized ratio; ACT, Activated clotting time; LA, Left atrium; RA, Right atrium.

☆ All authors takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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spatial resolution and difficulties in discriminating between centrifugal (potentially active) and centripetal (potentially passive) rotors. Electrographical flow (EGF) mapping represents a novel technology. EGF allows creating a full spatial and temporal reconstruction of electrographic potentials derived from endocardial unipolar electrogram data collected with a 64-pole basket catheter. This novel method allows to identify AF drivers based on subsequent flow analysis and sources of excitation during AF can be characterized and monitored [15,16]. However, the mechanisms of focal impulses and rotors have not yet been fully understood.

Therefore, the aim of this study was to evaluate the correlation between velocity of EGF around a respective AF source and its spatial variability and stability.

2. Methods

In this study 25 consecutive patients with persistent (n = 24) or long-standing persistent (n = 1) symptomatic, drug refractory AF who underwent AF ablation including pulmonary vein isolation (PVI) and focal impulse and rotor mapping (FIRM) at the Charité, Universitätsmedizin Berlin, Berlin, Germany were included. FIRM was performed in addition to PVI using radiofrequency in conjunction with a 3D-mapping-system (EnsiteVelocity™; St. Jude Medical). One-minute epochs of unipolar electrograms recorded via a 64-pole basket catheter (FIRMap® 50–70 mm, Abbott) in the right or left atrium were exported from the EP-recording-system (LABSYSTEM™ Pro v2.4a EP Recording System; Boston Scientific, Boston, USA) and re-analyzed with Electrographic Flow (EGF) Mapping. Patients with previous PVI and intra-atrial thrombus were excluded from the study. The same applies for patients who presented sinus rhythm (SR) at the beginning of the procedure and AF was not inducible. For the induction of AF a standardized protocol at the beginning of the procedure was used. An analysis regarding centrifugal (potentially active) and centripetal (potentially passive) nature of AF sources of the same study population was published previously [16]. This study conforms to the guiding principles of Helsinki of 2014 and was approved by the ethics committee of the Charité, Universitätsmedizin Berlin (EA4/111/16).

2.1. Patient management and ablation procedure

Pre- post- and periinterventional management has been described previously [16]. In brief, a transesophageal echocardiography was performed prior to the procedure to exclude atrial thrombi. The ablation procedure was carried out under deep sedation with propofol, fentanyl and midazolam. If patients presented in sinus rhythm at the beginning of the procedure, AF was induced with programmed atrial stimulation using a standardized protocol. After femoral venous punctures, a diagnostic catheter was placed in the coronary sinus and one in the inferior caval vein as a reference catheter (Supreme 5F, St. Jude Medical) in the first 10 patients and an external reference electrode (RhythmView® Reference Electrode, Fa. Abbott, USA) was used in the subsequent 12 patients. When the activated clotting time was (ACT) over 300 s, the 64-pole basket-catheter was introduced (FIRMap® 50–70 mm, Abbott). The 64-pole basket catheter was used for rotor identification in the right and left atrium. FIRM mapping was performed using the RhythmView® System Version 5 (Abbott, USA). The electrical data from the 64-pole basket-catheter were stored in the electrophysiological recording system (LABSYSTEM™ Pro v2.4a EP Recording System; Boston Scientific, Boston, USA) and 1 min samples were exported and transferred to the RhythmView® System Version 5 (Abbott, USA) via USB stick. In the regions where a rotor was detected via FIRM, rotor ablation was performed using the irrigated 3.5 mm tip TactiCath™ Quartz contact force ablation catheter (Tactisys™; St. Jude Medical) with contact force measurement guidance. Ablation was performed until no further AF drivers were identified by RhythmView®. At the end of the procedure, electrical cardioversion was necessary in 21 patients. In one patient, AF terminated during the procedure. No termination during active RF ablation occurred in any patient. Continuous telemonitoring was performed for 24 h after the procedure. A pericardial effusion was excluded by transthoracic echocardiography after the procedure and on the day after the procedure.

2.2. Electrographic flow mapping

Electrographic Flow (EGF) mapping (AblamapTM, Ablacon Inc. Wheat Ridge, CO, USA) is a novel method that allows detailed characterization and long-term monitoring of the behavior of AF sources in human atria [15,16]. The method of EGF has been published previously [15,16]. In brief, EGF represents a full spatial and temporal reconstruction of electrographic potentials and their flow derived from endocardial unipolar electrogram data collected with a 64-pole basket catheter. In two-second EGF maps, excitation sources appear as quadripoint centers where the four colors indicating flow direction (red = left, black = right, green = down and blue = up) adjoin and where the arrows indicating excitation velocity originate in all directions. Each EGF Map is automatically analyzed with respect to centrifugal (potentially active) sources of EGF, source characteristics (rotational or focal Impulse) and centripetal (potentially passive) rotors. The velocity measurements using the basket catheter are to be seen as a relative measure and may be less accurate than exact activation maps as obtained by individual diagnostic catheters. EGF based velocities are still much more powerful than individual activation measurements to measure the velocity profile in a whole atrium and the average velocity and velocity profile in the wider surroundings around a localized source. EGF velocity has originally been calibrated by determining conduction velocity directly measured from the basket catheter data.

2.3. Statistical analysis

Baseline and procedural data were summarized as means and standard deviations or medians and interquartile range for continuous data. Categorical data were presented as absolute frequencies and proportions. Source stability (temporal) was calculated as the percentage of time in which a source was detected. Yes or No of detection was decided based on the typical detection rate found for a source. Source spatial variability refers to the percentage of the total detection surface in which 80% of the detected sources are located during 1 min. Velocity of the leading source was calculated in a 2×2 electrode area taking into account only the vector component, which is in parallel with the catheter splines to be independent on the variable spline distance. Velocity is calculated in mean electrode distances per second averaged over 2 s of the most relevant time segment of the respective source.

3. Results

In all patients, circumferential PVI was performed successfully and no major complications occurred in any of the patients. Baseline characteristics are displayed in Table 1.

Fourty-four AF sources were found in 50 atria of 25 patients with FIRM-mapping out of which 40 were verified with EGF-mapping. Out of this 40 EGF-mapping verified sources, 26 were located at the left atrium and 14 at the right atrium. AF sources identified with EGF have shown a wide range of spatial variability during 1 min covering between 0.12% and 38% of the recorded basket catheter surface. At the same time variability of the velocity of excitation propagation between 6.3 electrode distances up to >25 electrode distances per second was found in the area around an AF source. A correlation of these two parameters was performed. The 12 atria where the sources showed highest temporal stability (between 97 and 34% of a minute recorded) and those 12 with the lowest temporal stability (between 11 and 20%) differed significantly in their velocities (17.8 el/s vs 12.2 el/s; p = 0.004). If sources were targeted by ablation this generally affected their velocity and their temporal and spatial stability. In 11 atria ablation caused an average decrease of temporal stability by 47% and of velocity by 27% while spatial variability more than doubled suggesting a role of these parameters in guidance of ablation (Table 2).

Thirteen of the 44 identified AF sources were identified as stable sources. Eleven of these 13 stable sources underwent ablation. Temporal stability of the ablated stable sources decreased to 53 ± 9% of their value pre-ablation (see examples below). Velocity in the surroundings of the source that has been ablated decreased to 73 ± 11% while spatial variability increased to 222 ± 38% of their value pre ablation. It is important to understand that centrifugal (potentially active) sources

Table 1
Baseline characteristics.

Number of Patients, n	25
Male, n (%)	17 (68)
Age, years (mean, SD)	70.0 ± 8,3
BMI (mean, SD)	26,7 ± 3,9
LVEF, % (mean, SD)	59,9 ± 6,4
Persistent AF, n (%)	24 (96)
Longstanding persistent AF, n (%)	1 (4)
AF history, months (mean, SD)	35 ± 32.9
Diameter left atrium, mm (mean, SD)	54.5 ± 5.7
Renal disease, n (%)	2 (8)
Coronary artery disease, n (%)	7 (28)
Arterial hypertension, n (%)	20 (80)
Diabetes mellitus, n (%)	3 (12)
CHA_2DS_2-Vasc-Score (mean, SD)	2.6 ± 1.08

SD: standard deviation, AF: Atrial fibrillation, BMI: Body mass index, LVEF: Left ventricular ejection fraction.

Table 2
Stability sorting: *t*-test velocity and variability.

Stability: high/low		Velocity: high/low		Variability: low/high	
97.1	20	21	10.9	1.02	7
73.1	19.7	20.3	17.6	1.66	15.7
58.8	18.1	18.5	12.9	0.7	15.3
44	17.1	12.6	13.1	0.06	24.2
43	16.4	11.3	6.3	8.2	27
41	16	22.6	11.4	1.81	26
39.3	15.6	16.6	8.7	2.68	38.2
39	13.7	18.3	24.7	2.65	12.9
37	12.2	23.6	11.4	0.12	11.7
36.8	11.9	22.8	7.2	10.3	12.3
35.9	11.6	8.6	12.3	16.3	18.7
34.1	10.9	18.4	7.2	5.12	36.1
			$p = 0.004$		$p = 0.0002$

have often a low velocity in the center. We observe the velocity only by taking 2 × 2 electrodes around the source. Centripetal (potentially passive) rotors often don't have this low velocity core and are therefore a bit faster on average.

Velocities of the sources of the left atrium were on average 13.8 ± 4.9 el/s. Velocities of sources of the right atrium were on average 13.8 ± 4.5 el/s. These results show no statistical difference. Four out of 25 patients presented in sinus rhythm at the beginning of the procedure and AF was induced with programmed atrial stimulation. Likewise, there were no significant differences in the four induced patients regarding the velocity of AF sources (13.4 ± 5.3 el/s). However, there was a weak correlation between left atrial diameter and the leading source velocity, which was 13.0 ± 6.2 el/s in atria with a diameter of 50 mm and less and 15.6 ± 4.0 el/s in atria with a diameter of 57 mm and more ($p = 0.18$). No correlation to specific anatomical regions was identified regarding SV, SST and TS.

4. Discussion

This study is the first to evaluate the correlation between velocity of EGF around a respective AF source and its spatial variability and stability.

The main findings of this study are:

1) Less stable AF sources with high spatial variability identified by EGF showed reduced excitation propagation velocity
2) Very stable AF sources as identified by EGF displayed a high average velocity in their vicinity.
3) If sources identified by EGF were targeted by ablation this generally affected their velocity and their temporal and spatial stability.
4) When ablation was performed, this caused an average decrease of temporal stability by 47% and of velocity by 27% while spatial variability more than doubled.

4.1. Stability and velocity of AF sources

Various hypothesis regarding the temporospatial stability of AF sources have been proposed recently. Whereas some investigators report on AF sources with high spatiotemporal stability [9,17,18] in animal models and in vitro studies using optical mapping technologies or in clinical settings using phase mapping [9] a meandering behavior of rotors has been advocated [19,20]. Human data show that sources come and go, and may process but not meander much from optical mapping [21] and clinical mapping [13]. This phenomenon will be addressed with EGF in future analyses. In the present study, a substantial number of AF sources with high temporospatial stability have been found in humans during AF ablation procedures using EGF. However, also more unstable scenarios were identified by the EGF mapping technology including some atria without any clearly stable AF source. We believe, that these findings support both, the idea of stable AF drivers and AF sources and situations where either no AF sources outside the PVs are present or slowly meandering AF sources can be observed. This has to be determined in larger ablation studies where EGF is used.

Dominant frequency and propagation velocity have been described recently to play a major role in the characteristics of AF sources [22–25]. Previously, dominant frequencies of AF sources have been shown to be high in animal studies [17,18,23]. In line with these findings, there has been shown a close relationship between the cycle length of AF sources and the region of interest for catheter ablation. In early studies using optical mapping the importance of the dominant frequency of AF sources in particular within the left atrium has been addressed [24] with higher frequencies in the region of interest, although interatrial regional disparities have been described [24]. In addition, several parts of the RA or LA have been identified to harbour regions with high frequency areas detected by different AF source identification tools [21]. In particular the cycle lengths of left atrial sources determined the dominant frequency in a study provided by Skanes et al. [26,27].

The results of our study support the hypothesis of the leading AF source with a high propagation velocity in its nearest proximity. In all stable AF sources identified by EGF in patients with persistent AF the propagation velocity was higher as compared to the velocity in more unstable sources (Table 2, Figs. 1 and 2). However, no significant differences between drivers within the LA or RA were observed.

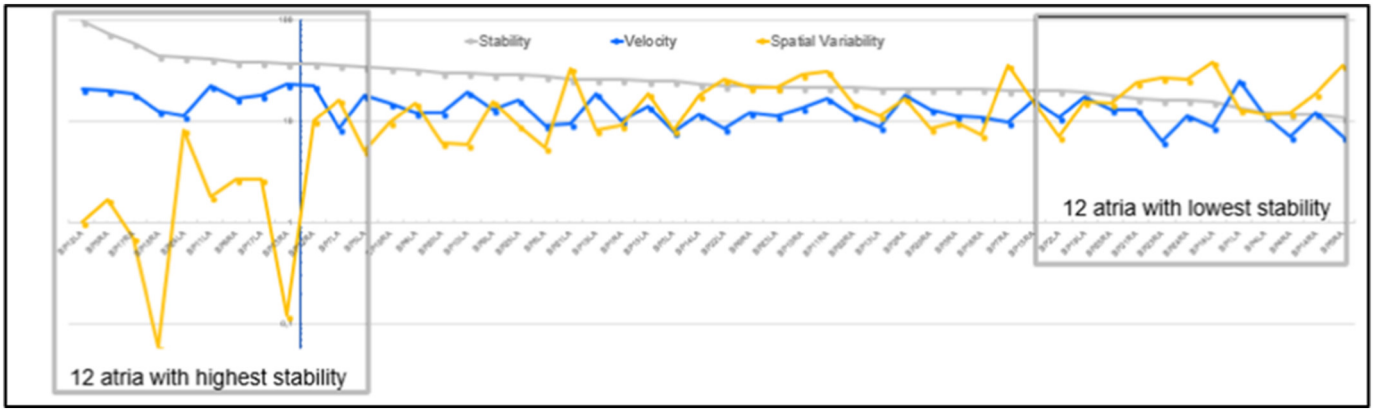

Fig. 1. 50 atria of 25 patients were sorted according to stability, ranging from 97% to 11%. Spatial variability was high in those where temporal stability was low and vice versa ($p < 0.01$). Velocity values measured in one electrode distance around a source were larger in the 12 most stable sources (18 ± 4.8 el/s) than in the 12 least stable sources (12 ± 5.1 el/s; *t*-test $p = 0.004$).

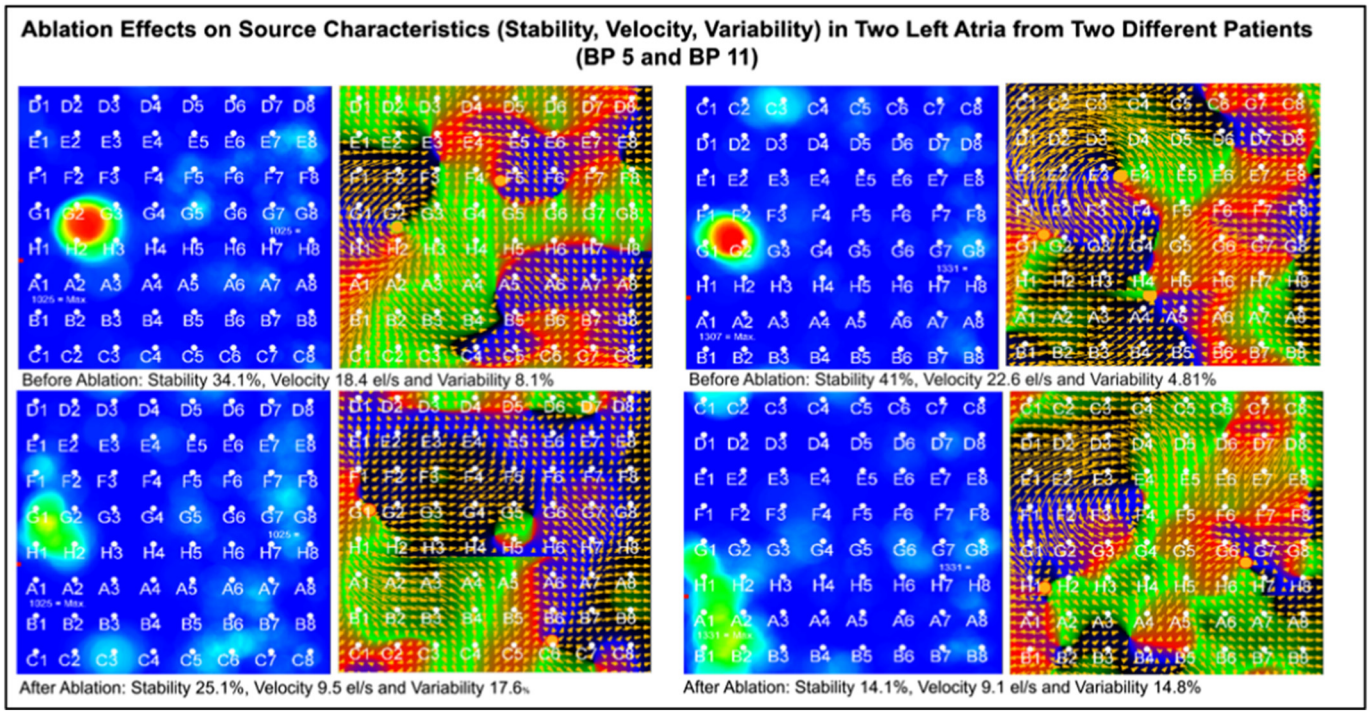

Fig. 2. Examples of ablation effects on source characteristics (stability, velocity, variability).

4.2. Impact of catheter after ablation on propagation velocity

High frequency sites of AF might be significantly influenced by catheter ablation [22]. In general, the velocity of high frequency sites during AF is reduced after catheter ablation in the targeted regions [22]. This has been further illustrated by Lim et al. in a study using a 3-dimensional model and they could show, that successful elimination of AF sources is depending on conduction velocity [28]. This is supported by the findings of our study. After catheter ablation of the regions with stable AF sources identified by EGF displaying a high propagation velocity generally a significant change has been observed with a reduced temporal and spatial stability and reduced velocity within these regions if sources were targeted by ablation. In the 11 atria where ablation was performed, ablation caused an average decrease of temporal stability by 47% and of velocity by 27% while spatial variability more than doubled suggesting a high relevance of these parameters in guidance for catheter ablation (Table 2, Fig. 2).

4.3. Limitations

Although this was a thoroughly planned prospective study, evaluation of EGF was performed after FIRM guided ablation. Thus, a limitation is the retrospective nature of the data analysis. The results did not influence the ablation strategy. For this reason, the patient's outcome is difficult to assess. Therefore further studies with EGF guided ablation are necessary in the future. Another limitation is that so far only one basket catheter has been used. Perhaps the combination of multipolar mapping catheters could provide even more accurate data.

5. Conclusion

Less stable AF sources with high spatial variability showed reduced excitation propagation velocity while very stable AF sources displayed a high average velocity in their vicinity. Catheter ablation reduced stability of sources and velocity indicating that these parameters are not linked through measurement conditions.

Conflicts of interest

AR received travel grants from Biosense, Hansen Medical, St. Jude Medical, EP Solutions and Medtronic and lecture fees from St. Jude Medical and Boehringer Ingelheim, proctorship fees from Medtronic, consultant fees from Ablacon and participated at the Boston scientific EP-fellowship. BB participated at the Boston scientific EP-fellowship. TL received a clinical fellowship from EHRA, travel grants from Biosense Webster, St. Jude Medical, Bayer and Topera Inc., and Speakers honoraria from Servier and Boehringer. PR is the CEO of Ablacon™ Inc. VT received travel grants from Biotronik, Biosense Webster, St. Jude Medical and a sponsored EP and Devices-fellowship from Biotronik. PN received travel grants, lecture fees or compensations for Advisory Board activities from Biotronik, Boehringer-Ingelheim and ZOLL CMS and participated at the Boston scientific EP-fellowship. MR received travel grants, lecture fees or compensations for Advisory Board activities from Bayer Healthcare, Berlin Chemie, Biotronik, Boston Scientific, Medtronic, Pfizer, Sanofi, St. Jude Medical and ZOLL CMS. UL has received advisory board honoraria from St Jude Medical.

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