Annals of Case Reports & Reviews

Case Report

doi: 10.39127/2574-5747/ACRR:1000181.
Vassallo F, et al. Annal Cas Rep Rev: ACRR-181.

Validation of Complex Fractionated Electrograms Mapping in The Identification of Vagal Ganglionated Plexux During Cardioneuroablation

Fabricio Vassallo[1,2*], MD, Edevaldo da Silva[3], BSC, Eduardo Serpa[1,2], MD. Aloyr Simões Jr.[1,2], MD, Hermes Carloni[1,2], MD, Christiano Cunha[1,2], MD, Lucas Luiz Meigre[1], BSC, Carlos Alexandre Lovatto[1,2], MD, Rafael Zeni[3], BSC, Anderson Barcelos[3], BSC

[1]Instituto de Cardiologia do Espirito Santo-Vitoria/ES-Brazil.
[2]Santa Rita Cassia Hospital-Vitoria/ES-Brazil.
[3]St Jude Medical / Abbott-Brazil.

*__Corresponding author:__ Fabricio Sarmento Vassallo, MD: Electrophysiologist - Coordinator of Electrophysiology of Instituto de Cardiologia do Espirito Santo. Rua Taciano Abaurre n. 225. 7 and 8th floors. Enseada do Sua. Vitória - Espirito Santo,Brazil. ZIP code: 29050-470. Phone: (+55) 27 33571200; Mobile: (+55) 27 992318545; Email: fabricio@arritmiaes.org

Citation: Vassallo F, da Silva E, Serpa E, Simões Jr. A, Carloni H, et al. (2020) Validation of Complex Fractionated Electrograms Mapping in The Identification of Vagal Ganglionated Plexux During Cardioneuroablation. Annal Cas Rep Rev: ACRR-181.

Received Date: 05 December 2020; **Accepted Date:** 10 December 2020; **Published Date:** 17 December 2020

Introduction

The subject was a symptomatic 59-year-old female with no comorbidity, presenting with new symptoms of general sweating, blurred vision, dizziness, fainting and syncope. Admitted to Emergency Room evaluated and discharged after full recovery and no abnormalities on exams performed. Two weeks later the patient presented another event of syncope while she was walking with head trauma and new admission at hospital. After a positive Tilt-Table Test patient was submitted to a cardioneuroablation (CNA) with success.

Keywords: Cardioneuroablation, Electroanatomical Mapping, Syncope, Sinus Bradycardia, Fractionated Signals.

Case Report

A 59-year-old female patient with history of hypercholesterolemia treated with statin therapy presented with recurrent syncope since her youth. Episodes were preceded by prodrome (e.g.; transient visual blurring) typically occurring during menstruation or blood draws. To exclude sinus node dysfunction amongst other causes of syncope, extensive work up was performed including a stress treadmill test, 24-hour Holter monitor and tilt-table test. Polysomnography was also obtained with documentation of mild obstructive sleep apnea and an apnea-hypopnea index of 8.6 events per hour. Treatment with daily use of a mandibular advancement plate was started with good clinical result.

More than the recurrence of the dysautonomia symptoms a diagnosis of sick sinus syndrome must be discarded because of the age of the patient and the presentation of the events. This approach is essential since the treatment of the two diseases are different and may impact in the quality of life of our patients. The patient achieved submaximal heart rate in exercise treadmill test and had lower heart rates on Holter without the medication (table 1). Tilt-table test showed cardioinhibitory response with sinus bradycardia and pause of 2.8 seconds at the time of syncope. Based on the above information, we decided to perform in September 30th 2020 a cardioneuroablation (CNA).

EXAMS	NO-THEOPHYLLINE	THEOPHYLLINE
TREADMILL TEST (MAX HR – BPM)	135 BPM	143 BPM
24-HOUR HOLTER (MIN-MEDIAN-MAX HR – BPM)	36 – 51 – 98 BPM	42 – 61 – 109 BPM

Table 1: Treadmill Test and 24-hour Holter with and without use of medication before cardioneuroablation.

We performed CNA [1] on an anatomic basis using indirect spectral analysis and Fast Fourier Transformation (FFT) by the recording system (EP Tracer recording system - CARDIOTEK, the Netherlands), to target the ganglionated plexi located in the right and left atria as well as the coronary sinus. A baseline electrophysiologic study (EPS) was performed prior to ablation along with high frequency stimulation along right and left internal jugular veins to demonstrate a vagal response. The EPS findings were normal pre and post-ablation and atrioventricular effective refractory period was achieved with a basal cardiac cycle length of 600mseg (Table 2).

ELECTROPHYSIOLOGICAL PARAMETERS	Pre-CNA	Post-CNA	Normal Values
Heart Rate	42bpm	81bpm	-
Atrioventricular Wenckebach	430ms	380ms	
Atrioventricular Effective Refractory Period	390ms	330ms	

Table 2: Electrophysiologic parameters before and after cardioneuroablation.

After this an endocardial bipolar 3D anatomical was performed with Ensite Velocity 5.0 (St Jude Medical Abbott-USA) and a circular mapping catheter with 20 poles (AFocus II Abbott-USA) used to create a voltage map of left and right atrial to prove the presence of a normal tissue and the parameters to define scar tissues were a voltage bellow 0.5mV and normal tissue above 1.5mV. The CFE map was analyzed during sinus rhythm and parameters were standardized at internal and external projections of 8 mm, interpolation of 8 mm, and low-voltage identification of 0.1 mV. Map was created using combinations of width of 10 msec, refractory time of 30 msec, roving sensitivity of 0.1 mV, and fractionation threshold of 3. The map color scale was set to color areas at or above the fractionation threshold of 3 as white and these areas were accepted as potential GP sites exactly by the high fractionated signals found at those sites. Finally, at this point we started the ablation procedure with the use of a contact force-sensing catheter Tacticath™ with a power of 40Watts and a flow irrigation pump of 35ml/min and the mapping catheter was the AFocus II Double-Loop. Electrical targets for ablation were high frequency, and long fractionated signals were seen in the distal and proximal catheter dipoles and at abnormal FFT signals. We saw that the CFE map correlated with anatomical sites that were identified as potential targets and appropriate vagal response was noted during ablation.

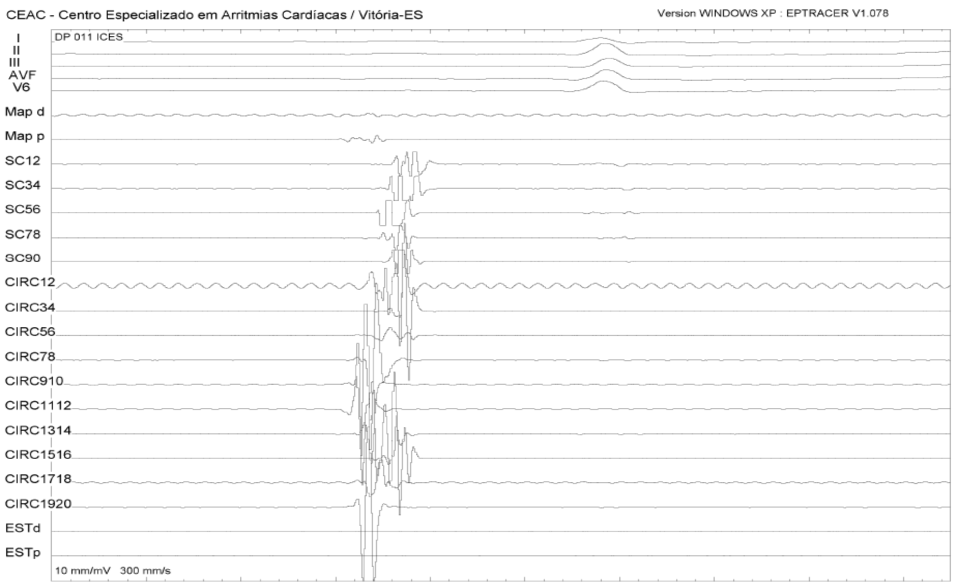

Figure 1: Circular mapping (CIRC) catheter showing the fragmental signal at a GP site (tracing speed of 300ms/s).

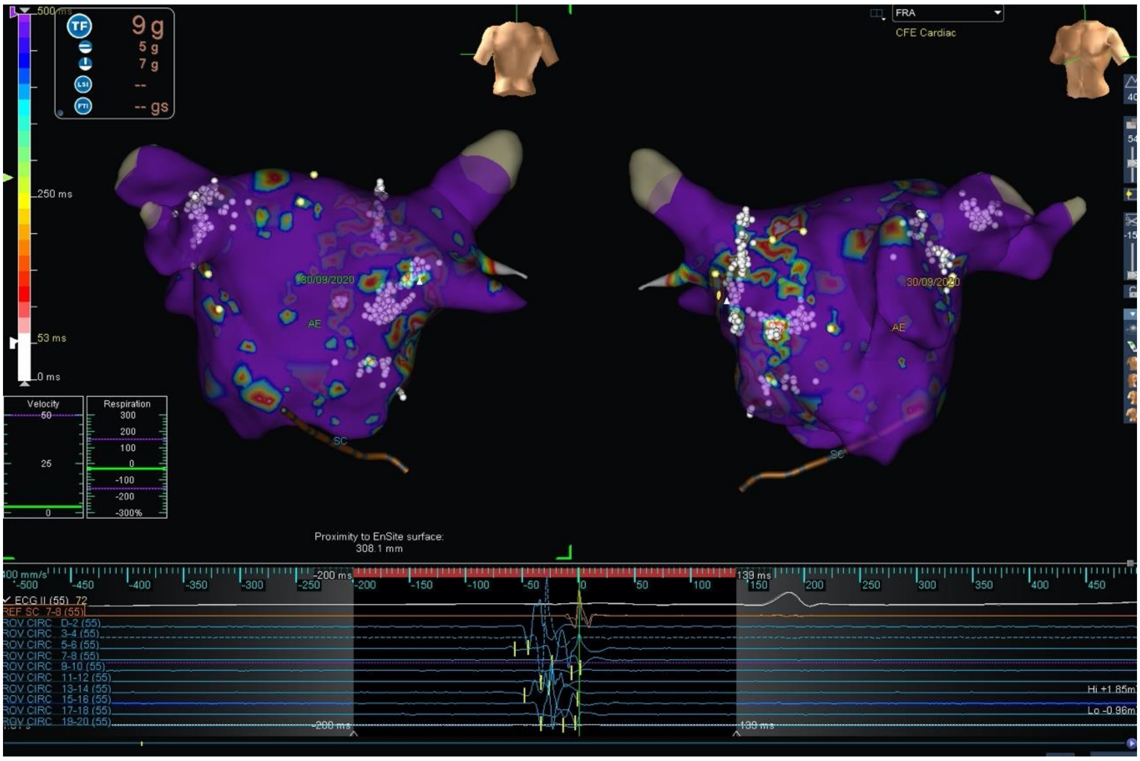

Figure 2: At top left atrial CFE Map and anatomical GP site and RF application. The CFE Map showing GP sites as white colors and RF application in white dots. At bottom in the ROV CIRC we see a tracing fractionated signal identifying a GP site (tracing speed of 400mm/s).

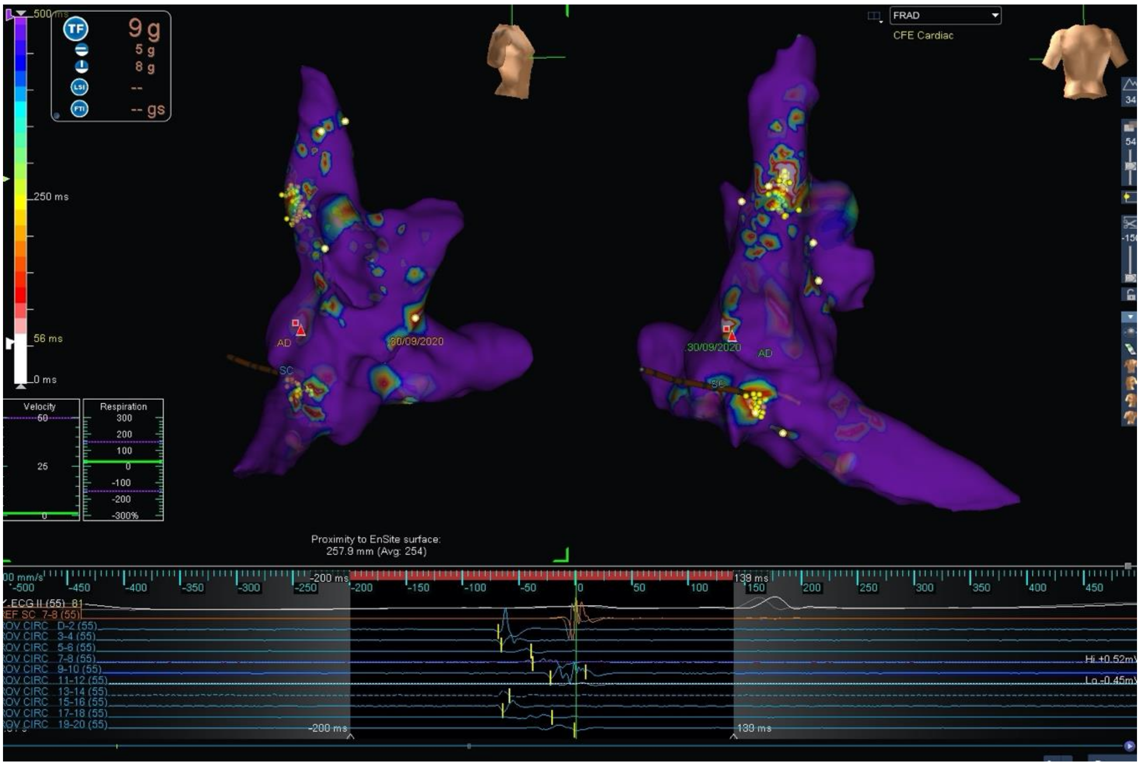

Figure 3: At top right atrial CFE Map and anatomical GP site and RF application. The CFE Map showing GP sites as white colors and RF application in white dots. At bottom in the ROV CIRC we see a tracing fractionated signal identifying a GP site.

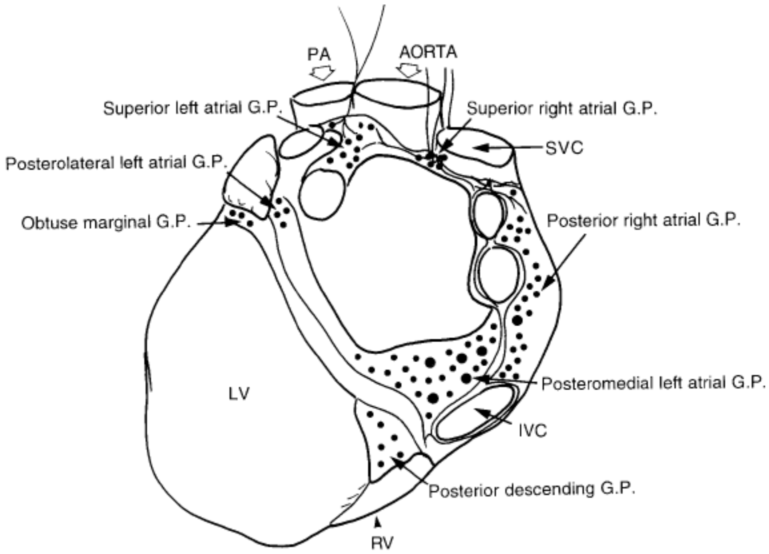

Figure 4: Major and minor ganglionated Plexus associated on atrial cardiac innervation (from Armour et. al. on Gross and Microscopic Anatomy of the Human Intrinsic Cardiac Nervous System).

Before the CNA the heart rate of 42bpm and at the end it was 81bpm. The infusion of atropine 2mg before and after an EPS study at this point, showed no heart rate increase, no difference in atrioventricular Wenckebach and atrioventricular effective refractory period demonstrating a reduction of the parasympathetic cardiac effect.

Discussion

Anatomical study of intact human heart by Armour et al. [2] identified five major atrial location of GPs. They have been given specific names that are related to their locations: 1) ganglionated plexus identified on the posterior superior surface of the right atrium adjacent to the superior vena cava and right atrium junction (nominated superior right atrium ganglionated plexus); 2) collection of ganglia on the posterior surface of left atrium between the pulmonary veins (nominated superior left atrial ganglionated plexus); 3) ganglionated plexus on the posterior surface of right atrium adjacent to interatrial groove (nominated posterior right atrial ganglionated plexus); 4) ganglionated plexus located on posterior medial surface of left atrium (posteromedial left atrial ganglionated plexus) and 5) a small atrial ganglionated plexus on the posterior lateral surface of left atrium base, on the left side of the atrioventricular groove (nominated posterolateral left atrial ganglionated plexus). The posterior atrial ganglionated plexus fused and extend anteriorly into the interatrial septum to form the interatrial septal ganglionated plexus. They observed that the largest number of ganglia was associated with the two major ganglionated plexus on the posterior surface of the two atria.

Pachón et al. [1,3] were the first to report CNA through catheter ablation guided by FFT analysis as an alternative treatment for functional high-degree AV block. In 7 of the 21 patients included in their study, the diagnosis was intermittent high-degree AV block. The procedural end-point was normalization of AV conduction. In three patients, the procedure was performed only via the RA, and one of these patients still experienced nocturnal Mobitz type I AV block after the procedure. Long-term follow-up results presented in another study [4] concluded that endocardial RF ablation of neurally mediated reflex syncope via both atria has excellent results in some patients and may prevent the need for pacemaker implantation. Anatomical mediated CNA has been increasingly used to treat severe vagal-related arrhythmias worldwide [1,4-7].

Although guidelines indicate pacemaker implantation for cases of symptomatic bradycardias or AV block [8], when patients are mostly young and otherwise healthy individuals, we encourage a conservative approach. Pacemaker implant in patients with vasovagal syndrome has been a controversial topic and official guidelines and statement have approached it with the same caution. In vasovagal syncope studies did not support the role of pacemaker except in select patients with syncope without clear provocation or provoked with a pause of more than 3 seconds, asymptomatic pause of more than 6 seconds. Furthermore, in the past there was a understanding that cardiac pacing was more likely to help older patients with concurrent SND. Recently more cases of older patients with more than 50 years-old treated with CNA have been described worldwide. Despite these good results with CNA we cannot forget that recurrence may occur because of an intrinsic cardiac nervous system forms a complex neural network composed of the ganglia plexus and interconnecting axons. Larger ganglia are observed close to the pulmonary vein and serve as autonomic integration centers, modulating cardiac excitability. This widely distributed structure cannot be entirely targeted. A comprehensive and selective approach is required and meant to promote attenuation instead of total vagal blockade, and a step by step test with extracardiac vagal stimulation can be a much wiser management during this kind of procedure.

Targeting all the GPs could be a risk if continuously monitoring by extracardiac vagal stimulation is not done because AV block can get more severe if you denervate only the sinus node with the HR increase, so an individualized approach to ensure the objective and success of the CNA is mandatory.

The aim of this case report is to disseminate and encourage other colleges to perform the CNA and the use of the CFE Map was to help the identification of the anatomical sites of parasympathetic ganglia. The role of fractionation mapping software of Ensite system was investigated to detect localization of GP during sinus rhythm. Distribution of white areas which is suggestive for fragmented EGMs demonstrated a high similarity with visually selected ablation points. Potential importance of fragmented EGMs during sinus rhythm for the identification of GPs was firstly studied by Lellouche et al**.** [11] They found that fragmentation of EGMs was the best single predictor of vagal response during radiofrequency ablation. Fractionation mapping software was previously used to detect localization of GP and critical substrate for continuity of AF by Asku et al. [12]. In the present work, fractionation mapping software during sinus rhythm demonstrated a GP distribution pattern which is suitable with anatomical localization. It might be a promising method in detection of GPs to avoid potential low reproducibility of visual methods by low-experienced operators. However, in this technique, mapping parameters like width, refractory time, roving sensitivity, and fractionation threshold should be standardized because based on these parameters, the algorithm assigns each EGM a fractionation score. The use of the CFE Map software was developed to be used during AF for detection of critical AF substrate [9,10] the use to define localization of GP sites [11] should need some validation in further randomized controlled studies with the use of high frequency stimulation or potentially by nuclear imaging. Therefore, in the present study, ablation points were selected based on previously validated visual method and latter compared the localization of these anatomical sites with the CFE map.

At the LA the CFE Map were able to identify 7 places of supposed GP site and the anatomical localization of this sites occurred only in 5, that were also anatomical sites of GP, radiofrequency application reproduced vagal response. At the other 2 site the attempt of RF application had no vagal response nor with sinus tachycardia or bradycardia suggesting that these locations were not GP sites. At the RA we identified 3 locations of GP sites in the CFE Map and 2 anatomical GP locations with the same response during RF application observed at the LA. With this information we can claim that the CFE Map at left atrial had a sensitivity of 87.5%, specificity of 78.57%, positive predictive value of 70% and negative predictive value of 91.66%.

At the 7 and 14-day follow up the patient presented with a rest electrocardiogram with heart rate of 86 and 82 bpm, respectively. At 30 days patient stayed asymptomatic and a 24-Hour Holter monitoring was performed and showed a lower, median and maximum heart rate of 68, 84 and 108bpm (Table 3) respectively, with a SDNN of 77 and a PNN< 50 of 0.08.

HOLTER	HR – Lower (bpm)	HR – Medium (bpm)	HR – Max. (bpm)	Longer Pause (sec)	1st Degree Block	2nd Degree Block	High Degree Block	SDNN	PNN>50
Pre-Ablation	45	68	101	1,33	YES	NO	NO	144	8.76
30 days post-ablation	68	84	108	0,88	NO	NO	NO	77	0,08

Table 3: Pre and post-ablation 24-hour Holter monitoring (HR= heart rate / Max.= Maximum).

Conclusion

As in other authors' series cases, results for cardioneuroablation for the treatment of functional sinus bradycardia and AV blocks are encouraging and excellent. This case showed us that the use of CFE Map matched with anatomical GP sites and is very useful and a helpful tool for groups that are starting the cardioneuroablation.

Learning Objectives

1) Cardioneuroablation can be reproduced in electrophysiology labs in selected patients with good results.
2) The use of the CFE Map software is a useful tool for helping the identification of GP sites and is a good reference in localizing anatomical GP.

Financial support: This study has no financial support source.

All authors declare no conflicts of interest.

Bibliographic references

1. Pachón JC, Pachón EI, Pachón JC, et al. "Cardioneuroablation"-New treatment for neurocardiogenic syncope, functional AV block and sinus dysfunction using catheter RF-ablation. Europace 2005; 7:1–13.
2. Armour JA, Murphy DA, Yuan BX, Macdonald S and Hopkins DA. Gross and Microscopic Anatomy of the Human Intrinsic Cardiac Nervous System. The Anatomical Record 247:289-298 (1997).
3. Pachón MJC, Pachón MEI, Lobo TJ, et al. Syncopal high degree AV block treated with catheter RF ablation without pacemaker implantation. Pacing Clin Electrophysiol 2006; 29:318–325.
4. Rivarola E, Hardy C, Sosa E, Hachul D, Furlan V, Raimundi F and Scanavacca. Selective atrial vagal denervation guided by spectral mapping to treat advanced atrioventricular block. Europace 2016; 18:445–449.
5. Aksu T, Golcuk E, Yalin K, Guler TE, Erden I. Simplified cardioneuroablation in the treatment of reflex syncope, functional AV block, and sinus node dysfunction. Pacing Clin Electrophysiol. 2016; 39:42–53.
6. Yao Y, Shi R, Wong T, et al. Endocardial autonomic denervation of the left atrium to treat vasovagal syncope: An early experience in humans. Circ Arrhythm Electrophysiol. 2012; 5:279–286.
7. Fukunaga M, Wichterle D, Peichi P, Aldhoon B, Cihak R, Kautzner J. Differential effect of ganglionic plexi ablation in a patient with neutrally mediated syncope and intermittent atrioventricular block. Europace 2017;19(1):119–126.
8. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, et al. 2012 ACCF/AHA/HRS focused update incorporated into ACCF/AHA/ HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2013;61: e6–75.
9. Aksu T, Guler TE. Electroanatomical mapping-guided ablation during atrial fibrillation: a novel usage of fractionation mapping in a case with sinus bradycardia and paroxysmal atrial fibrillation. J Interv Card Electrophysiol 2020; 57: 331–332.
10. Aksu T, Guler TE, Bozyel S, Yalin K. Usage of a new mapping algorithm to detect possible critical substrate for continuity of atrial fibrillation: fractionation mapping in preliminary experience. J Interv Card Electrophysiol. 2020;58(1):29-34.
11. Lellouche N., Buch E., Celigoj A. et al. Functional characterization of atrial electrograms in sinus rhythm delineates sites of parasympathetic innervation in patients with paroxysmal atrial fibrillation. J Am Coll Cardiol. 2007; 50: 1324-1331.
12. Aksu T, Yalin K and Gopinathannair R. Fractionation mapping software to map ganglionated plexus sites during sinus rhythm. First published online: 20 September 2020. https://doi.org/10.1111/jce.14753.