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Statistical guidance of VT ablation

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Ventricular tachycardia (VT) is a major cause of sudden cardiac arrest, recurrent discharges in individuals with implantable defibrillators, and may contribute to cardiomyopathy.¹

Catheter ablation has evolved as an effective therapy for VT,² yet success rates are suboptimal^{3,4} due to many factors. One of the major limitations in VT ablation is targeting critical areas, traditionally performed by detailed contact mapping or more recently by noninvasive methods,⁵ which remains challenging in many cases and a major bottleneck for improving both the efficacy and efficiency of VT ablation procedures.

In this issue of the *Journal*, Zhou et al.⁶ report a novel ECG signal processing method to rapidly and noninvasively localize VT exit sites during a procedure. In patients undergoing epicardial (n = 4) or endocardial (n = 3) VT mapping, the authors applied a statistical technique (multiple linear regression, MLR) to 12-lead ECG during multisite pacing, compared with the simultaneous inverse solution from 120 body surface electrodes. MLR constructs regression equations specific for each patient, deriving ECG coefficients while pacing at 10–15 sites at mapped 3D coordinates. The inverse solution in this study uses complex equations that fuse 120 surface electrodes with anatomy from preprocedural CT.⁷ Remarkably, the authors found that ECG-MLR produced smaller localization errors than the inverse solution for both epicardial (10.6 vs. 27.3 mm) and endocardial (7.7 vs. 17.1 mm) sites. When applied to sites of successful VT ablation in 2 patients, MLR retained its superior localization accuracy. The authors conclude that this approach may facilitate rapid real-time localization of VT-exit sites during catheter ablation.

This study addresses several important aspects of VT mapping. Among these are the ability of pace-mapping to accurately identify VT ablation sites, the relative accuracy of the 12-lead ECG versus 120 electrode body surface maps to localize ablation targets, and the utility of mapping using procedural data alone without the need for preprocedural imaging.

1| ACCURACY OF PACE-MAPPING FOR VT

MLR is based on the premise that pacing close to a VT exit site produces ECGs similar to clinical VT, i.e., that the activation sequence of cardiac tissue approximates VT more closely as the pacing site nears the VT exit. To do this, the authors create a linear regression model

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using paced ECGs as inputs, and ECG parameters in VT as reference. This concept has strengths and limitations.

1. Pace-mapping has adequate accuracy for focal VT but is less accurate in reentrant VT, in which ablation targets critical isthmuses rather than just exit sites. Pacing introduces retrograde capture and fusion that may alter ventricular activation.⁸ Accordingly, a closely matched ECG may arise even if pacing some distance from critical sites, while pacing near true critical sites may generate an ECG that differs from VT.⁹
2. Pace-mapping is more accurate in patients with normal hearts, who constituted the N = 3 patients mapped endocardially this series, and may be less accurate in patients with structural abnormalities.¹⁰ In the presence of abnormal tissue, interpretation of in pace-maps may be confused by different tissue conductance and activation paths, which also vary with rate and may not match those in VT. Conversely, in normal tissue, pacing from a wide area may produce ECGs similar to those in VT, although MLR technique may improve this lack of specificity.
3. Pace-mapping from up to 15 sites achieved highest accuracy in this study, which may not be feasible clinically due to limited accessibility of sites, selection of optimal sites that span the parameter space to arrive at optimum MLR coefficients, as well as other factors not explored in this preliminary study.

2| STRENGTHS AND LIMITATIONS OF SURFACE ELECTROCARDIOGRAPHIC SOLUTIONS IN VT

This study again shows the strength of the ECG to provide meaningful information for detailed mapping and ablation in VT.¹¹ However, the optimal quantitative method for ECG analysis remains undefined. Historical studies used multiple body surface electrodes (up to 62) without structural data, which provided modest localization accuracy.¹²

Electrocardiographic imaging (ECGI), codeveloped by an author of the present study,^{7,13} fuses ECG with detailed torso anatomy from CT, and uses assumed tissue conductivities to noninvasively reconstruct epicardial (and potentially endocardial) electrical activity.¹⁴ The application of this approach is wide, yet its accuracy of reconstruction is still being defined, and in a recent calibration study was ~1–2 cm distant from sites of ventricular pacing.¹⁵ ECGI has had notable successes,⁵ but given the large number of ECGI approaches applied to different arrhythmias,¹⁶ it would be useful to compare methods head-to-head to ensure that they are identifying similar mechanisms and locations.

3| WHAT STRUCTURAL INFORMATION SHOULD BE INTEGRATED TO GUIDE VT LOCALIZATION?

MRI or CT clearly identify ventricular infarct scar and fibrosis,⁹ but this may not provide sufficient functional information to identify critical VT sites. Ideally, ECGI or reduced ECG-based approaches such as that presented by Zhou et al.⁶ would identify not just potentially critical sites, but ranges of voltages, potential (and not just realized) isthmuses, scar areas,¹⁷ and other functional measures of arrhythmic vulnerability.^{18,19}

However, the optimal set of structural data needed to reconstruct cardiac electrical activation in this way is undefined. A major unresolved issue is to provide direct measures of conductivity and their potential rate dependence (restitution) of different tissues within the thorax, which should improve the inverse solution. On the other hand, recent work suggests that under certain algorithmic conditions these factors may be less critical than anticipated.²⁰ Accordingly, reduced-dataset ECGI methods are under development that, with specific algorithms, may be applicable without structural data.²¹ The relative accuracy and efficiency of such solutions remains to be determined relative to alternatives such as the current statistical ECG MLR method in clinical studies, and must be referenced to endpoints such as VT termination and long-term arrhythmia freedom by ablation, rather than by surrogates such as localizing sites of pacing.

4| OTHER APPLICATIONS OF NONINVASIVE ARRHYTHMIA LOCALIZATION

Noninvasive localization has been applied to channelopathies such as Brugada syndrome,²² to guide cardiac resynchronization therapy to identify epicardial sites of latest activation,²³ and to identify localized rotational and focal circuits for VF²⁴ referenced to contact mapping.^{25,26} Noninvasive localization is also applied to guide ablation of atrial fibrillation²⁷ with similar issues of resolution and preprocedural imaging and may identify critical sites for AF²⁸ using approaches to ECGI including reduced electrode methods and without pre-procedural imaging.^{21,29} Such work continues to expand.

5| CONCLUSIONS

Zhou et al.⁶ should be congratulated for providing proof-of-concept that critical targets for VT ablation may be identified rapidly from the 12-lead ECG by combining novel statistical analyses with multisite pacing, potentially with greater accuracy than the 120-lead inverse solution. Studies in larger populations are needed to confirm this approach, and more generally to establish the relative merits of noninvasive versus invasive mapping or when they should be combined, the optimal use of multisite pacing, and establish those features ideally extracted from structural imaging. With ongoing studies in these areas, arrhythmia mapping is likely to enable major changes in arrhythmia therapy in coming years.

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REFERENCES

1. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A report of the American College of Cardiology/American Heart Association

Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2017;S1547–5271:31249–3.

2. Reddy VY, Reynolds MR, Neuzil P, et al. Prophylactic catheter ablation for the prevention of defibrillator therapy. N Engl J Med. 2007;357:2657–2665. [PubMed: 18160685]
3. Stevenson WG, Wilber DJ, Natale A, et al. Multicenter Thermocool VT Ablation Trial Investigators. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: The multicenter thermocool ventricular tachycardia ablation trial. Circulation. 2008;118:2773–2782. [PubMed: 19064682]
4. Tung R, Vaseghi M, Frankel DS, et al. Freedom from recurrent ventricular tachycardia after catheter ablation is associated with improved survival in patients with structural heart disease: An International VT Ablation Center Collaborative Group study. Heart Rhythm. 2015;12:1997–2007. [PubMed: 26031376]
5. Cuculich PS, Schill MR, Kashani R, et al. Noninvasive cardiac radiation for ablation of ventricular tachycardia. N Engl J Med. 2017;377:2325–2336. [PubMed: 29236642]
6. Zhou S, Sapp JL, AbdelWahab A, Stovicek P, Horacek M. Localization of ventricular activation origin using patient-specific geometry: Preliminary results. J Cardiovasc Electrophysiol. 2018;29:10.1111/jce.13622.
7. Horacek BM, Clements JC. The inverse problem of electrocardiography: A solution in terms of single-and double-layer sources on the epi-cardial surface. Math Biosci. 1997;144:119–154. [PubMed: 9258003]
8. Dukkipati SR, Koruth JS, Choudry S, Miller MA, Whang W, Reddy VY. Catheter ablation of ventricular tachycardia in structural heart disease: Indications, strategies, and outcomes-part II. J Am Coll Cardiol. 2017;70:2924–2941. [PubMed: 29216988]
9. deChillou C, Groben L, Magnin-Poull I, et al. Localizing the critical isthmus of postinfarct ventricular tachycardia: The value of pace-mapping during sinus rhythm. Heart Rhythm. 2014;11:175–181. [PubMed: 24513915]
10. Arenal A, del Castillo S, Gonzalez-Torrecilla E, et al. Tachycardia-related channel in the scar tissue in patients with sustained monomorphic ventricular tachycardias: Influence of the voltage scar definition. Circulation. 2004;110:2568–2574. [PubMed: 15492309]
11. Kuchar DL, Ruskin JN, Garan H. Electrocardiographic localization of the site of origin of ventricular tachycardia in patients with prior myocardial infarction. J Am Coll Cardiol. 1989;13:893–903. [PubMed: 2926041]
12. Sippensgroenewegen A, Spekhorst H, van Hemel NM, et al. Value of body surface mapping in localizing the site of origin of ventricular tachycardia in patients with previous myocardial infarction. J Am Coll Cardiol. 1994;24:1708–1724. [PubMed: 7963119]
13. Ramanathan C, Ghanem RN, Jia P, Ryu K, Rudy Y. Noninvasive electrocardiographic imaging for cardiac electrophysiology and arrhythmia. Nat Med. 2004;10:422–428. [PubMed: 15034569]
14. Wang L, Gharbia OA, Horacek BM, Sapp JL. Noninvasive epicardial and endocardial electrocardiographic imaging of scar-related ventricular tachycardia. J Electrocardiol. 2016;49:887–893. [PubMed: 27968777]
15. Cluitmans MJM, Clerx M, Vandersickel N, Peeters RLM, Volders PGA, Westra RL. Physiology-based regularization of the electrocardiographic inverse problem. Med Biol Eng Comput. 2017;55:1353–1365. [PubMed: 27873155]
16. Figueroa C, Suarez-Gutierrez V, Hernandez-Romero I, et al. Regularization techniques for ECG imaging during atrial fibrillation: A computational study. Front Physiol. 2016;7:466. [PubMed: 27790158]
17. Cuculich PS, Zhang J, Wang Y, Desouza KA, Vijayakumar R, Woodard PK, Rudy Y. The electrophysiological cardiac ventricular substrate in patients after myocardial infarction: Noninvasive characterization with electrocardiographic imaging. J Am Coll Cardiol. 2011;25:1893–1902.
18. Zhang J, Cooper DH, Desouza KA, Cuculich PS, Woodard PK, Smith TW, Rudy Y. Electrophysiologic Scar Substrate in Relation to VT: Non-invasive High-Resolution Mapping and Risk Assessment with ECGI. Pacing Clin Electrophysiol. 2016;39:781–791. [PubMed: 27197804]

19. Horacek BM, Wang L, Dawoud F, Xu J, Sapp JL. Noninvasive electrocardiographic imaging of chronic myocardial infarct scar. *J Electrocardiol.* 2015;48:952–958. [PubMed: 26415018]
20. Rodrigo M, Climent AM, Liberos A, et al. Highest dominant frequency and rotor positions are robust markers of driver location during non-invasive mapping of atrial fibrillation: A computational study. *Heart Rhythm.* 2017;14:1224–1233. [PubMed: 28408329]
21. Rodrigo M, Climent AM, Liberos A, et al. Solving inaccuracies in anatomical models for electrocardiographic inverse problem resolution by maximizing reconstruction quality. *IEEE Trans Med Imaging.* 2018;37:733–740. [PubMed: 28541896]
22. Chaykovskaya M, Rudic B, Tsyanov A, Zaklyazminskaya E, Yakovleva M, Borggreffe M. The use of noninvasive ECG imaging for examination of a patient with Brugada syndrome. *Heart Rhythm Case Rep.* 2015 5 6;1:260–263.
23. Bear LR, Huntjens PR, Walton R, Bernus O, Coronel R, Dubois R. Cardiac electrical dyssynchrony is accurately detected by non-invasive electrocardiographic imaging. *Heart Rhythm.* 2018;S1547–5271:30135–8.
24. Ho G, Villongco CT, Yousefian O, et al. Rotors exhibit greater surface ECG variation during ventricular fibrillation than focal sources due to wavebreak, secondary rotors, and meander. *J Cardiovasc Electrophysiol.* 2017;28:1158–1166. [PubMed: 28670858]
25. Nash MP, Mourad A, Clayton RH, et al. Evidence for multiple mechanisms in human ventricular fibrillation. *Circulation.* 2006;114:536–542. [PubMed: 16880326]
26. Krummen DE, Hayase J, Morris DJ, et al. Rotor stability separates sustained ventricular fibrillation from self-terminating episodes in humans. *JAm Coll Cardiol.* 2014;63:2712–2721. [PubMed: 24794115]
27. Rodrigo M, Guillem MS, Climent AM, et al. Body surface localization of left and right atrial high-frequency rotors in atrial fibrillation patients: A clinical-computational study. *Heart Rhythm.* 2014;11:1584–1591. [PubMed: 24846374]
28. Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel WJ, Miller JM. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. *JAm Coll Cardiol.* 2012;60:628–636. [PubMed: 22818076]
29. Rodrigo M, Climent AM, Liberos A, et al. Minimal configuration of body surface potential mapping for discrimination of left versus right dominant frequencies during atrial fibrillation. *Pacing Clin Electrophysiol.* 2017;40:940–946. [PubMed: 28586103]