

Noninvasive Electrocardiographic Mapping: Are We Ready for Prime Time?

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Noninvasive electrocardiographic imaging through body surface potential (BSP) mapping and mathematical *inverse* procedures represents a novel and emerging technology that enables estimation of myocardial depolarization and repolarization. As such, this mapping approach offers the possibility of not only facilitating therapeutic catheter interventions for a variety of cardiac arrhythmias, but also of helping to define the underlying electrophysiological mechanisms of certain cardiac arrhythmias and to perhaps even guide cardiac resynchronization therapy and optimization.^{1,2} Although this mapping strategy merely estimates the time course of unipolar epicardial potentials, the latter is capable of providing substantial information regarding intramyocardial activation.^{3,4} The currently available BSP mapping systems allow incorporation of data using a greater number of electrodes than before, yielding preprocedural arrhythmia localization using only a few or a single heartbeat. The mean resolution of the currently used noninvasive electrocardiographic imaging techniques is ≈ 1 to 2 cm, though some investigators have reported better results.^{2,5} Aside from their noninvasive feature and ability to be applied at bedside, current BSP mapping technologies also permit 3-dimensional integration with computed tomography or magnetic resonance imaging modalities. The initial experiences using this innovative mapping approach have demonstrated improved efficacy and reduced procedural duration.^{6–8} Furthermore, a noninvasive electrocardiographic imaging system (ECVUE; Cardiolsight Technologies, Inc) was recently approved for

clinical use in Europe. Yet, despite multiple encouraging reports and experiences, this imaging technique has not quite evolved into daily clinical practice, perhaps due to limited data availability, insufficient validation, and complexity of the mathematical models underlying the applied inverse procedures.

The initial recording of human BSPs was reported by Waller in 1887, with a capillary electrometer that he used to systematically investigate the potential distribution associated with the beating heart.⁹ Subsequently, Einthoven published the first surface ECG in 1903, constructed using the string galvanometer.¹⁰ Nearly a century later, alternative configurations based on the recording of potentials from a large number (32 to 256) of torso electrodes using a multielectrode vest were proposed¹¹. However, the latter has not been systematically incorporated into daily clinical practice due to uncertainty surrounding its clinical utility. In the meantime, much experience has been gained with interpretation of the 12-lead ECG, which remains the gold standard in clinical cardiac electrophysiology. Nevertheless, there are inherent limitations to the use of the 12-lead ECG. Multiple electrocardiographic algorithms have been proposed to predict the activation site of various cardiac arrhythmias, but accuracy and consistent reproducibility have been lacking. A major limitation has to do with the spatial resolution afforded by the 12-lead ECG. Also, alterations in the heart's anatomy and orientation within the chest with variable precordial lead placements can yield conflicting results. Therefore, a definitive diagnosis typically requires an invasive approach.

In contrast, the recent development of robust inverse procedures has kindled renewed interest in utilization of BSP mapping. Although the *forward* problem of electrocardiography refers to the estimation of BSPs from those measured on the surface of the heart, the inverse problem implies the contrary.¹² Through an inverse procedure, the potentials on the epicardial surface and myocardial activation times are estimated using the recorded BSPs as source data. To determine cardiac activation times, the potentials generated by cardiac electrical activity within the torso volume need to be modeled. Unlike the forward problem, which may be solved uniquely, the inverse problem is not unique with regard to

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sources.¹³ Various source configurations can correspond to the same BSP, even in the setting of noise- and error-free data. These different sources are termed *equivalent sources* because they are capable of generating the same potentials on the surface of the body, thus the inverse problem is said to be *ill-conditioned*. In other words, the desired solution is unstable and can vary significantly with the slightest noise or perturbations in BSP. To circumvent this conundrum, investigators have developed several regularization methods that impose significant constraints on the outcome.¹⁴ These, in turn, have become a subject of ongoing debate. Meanwhile, most inverse procedures use a combination of 2 models: a biophysical source model and a volume conductor model (VCM). In a biophysical source model, the heart muscle is simply represented as an electrical current generator, whereas the VCM attempts to reproduce the influences of different tissue types within the thoracic cavity on the potential waveforms. To reproduce such an effect, a detailed anatomical model of the patient's chest incorporating the conductive properties of thoracic structures is, in fact, required. Such anatomical data can be derived from a computed tomography or magnetic resonance scan.

In this issue of the journal, Bhagirath et al¹⁵ reported their findings on noninvasive electrocardiographic imaging (inverse potential mapping using 62 recording electrodes) guided by magnetic resonance-derived VCMs, creating both homogeneous and nonhomogeneous models. It should be pointed out that the principal difference between homogeneous and nonhomogeneous models consists of the latter additionally taking into account the specific conductivity values for the lungs (0.04 S/m). The most commonly used noninvasive mapping technique typically uses a homogeneous VCM, and other investigators have shown sufficient accuracy associated with the use of computed tomography-derived models^{16,17}. However, in their study, Bhagirath et al emphasized the significance of magnetic resonance-guided nonhomogeneous VCMs. The authors advocated for integration of adjacent organs and their specific impedances, particularly in those with a high body surface area, myocardial infarction, or pulmonary edema. As such, they argued that the aforementioned circumstances can meaningfully influence BSPs and, consequently, the data due to alterations in conductivity and resistivity. Briefly, their study included 3 healthy volunteers and 8 symptomatic patients with frequent ventricular ectopy. Using this approach, it was possible to estimate—with great accuracy—the locations of the sinoatrial node and/or ventricular arrhythmia foci using a single ectopic beat. Although this study was based on a small sample size, the authors illustrated a difference in accuracy with inverse potential mapping using homogeneous versus nonhomogeneous VCMs, in favor of the latter. In 2 of 8 patients, there was no difference in localization between homogeneous and

nonhomogeneous VCMs. However, homogeneous VCM was associated with a notably greater difference (≥ 2 mm) in localization in 5 patients, whereas in another patient, the focus could not even be identified. It should be emphasized that these differences were judged exclusively by the site of ablation as marked on the 3-dimensional electroanatomical mapping system (EnSite, St. Jude Medical, Inc), which itself could have inherent inaccuracies. Nonetheless, this study provides important and relevant insights into the clinical implications and applicability of magnetic resonance-guided inverse potential mapping in patients with idiopathic ventricular arrhythmias. The findings of this study suggest that implementation of such an approach may offer several crucial benefits including improved ablation planning as a result of preprocedural identification of the arrhythmia focus, reduction of procedural duration and radiation exposure, and possibly improvements in ablation efficacy among patients presenting with reduced arrhythmia burden and/or multifocal arrhythmias.

Although certain advancements such as real-time panoramic mapping and improved signal processing will likely help enhance the current state of this technology, a potential weakness of this approach is that it derives its diagnostic information from reconstructed electrograms on the epicardial surface of the heart. Although a recent report¹⁸ has shown a close correlation, the endocardial sequence of activation will not always be identical to the epicardial activation sequence. Furthermore, because the septum is not an epicardial structure, direct mapping of the septum is also not possible. Instead, localization of a septal focus would have to be deduced through indirect analysis and timing of the epicardial breakthrough activation sequence. Lastly, suboptimal detection of arrhythmia activation from the corresponding cardiac chamber needed for accurate analysis can also pose a source of limitation with regard to noninvasive electrocardiographic mapping. This becomes relevant in situations in which the atrial activation may be obscured within the inscription of the ventricular activity, as in the case of an atrial tachycardia with 2-to-1 conduction to the ventricles. To effectively permeate into the clinical cardiac electrophysiology arena, the physical validity of the simulations and the strength of the methodologies must be undisputed. To satisfy this condition, additional knowledge about the challenges regarding the use of inverse potential mapping seems imperative. In addition, high-resolution imaging techniques and improved inverse algorithms should be developed and further integrated.

In summary, noninvasive electrocardiographic mapping of cardiac excitation has recently become the primary focus of active and ongoing research. Although this technology holds great promise and will likely evolve to complement the conventional mapping techniques currently used in cardiac electrophysiology, it has not yet emerged as a clinical tool

that is usable in day-to-day practice. This has largely been due to technical challenges in recording, processing, and interpreting the data. Moreover, clinical validation with respect to various arrhythmia mechanisms is still needed. The study by Bhagirath et al greatly exemplifies critically needed research to further enhance noninvasive electrocardiographic imaging and to help create utility for such a technology in clinical practice.

Disclosures

None.

References

- Rudy Y. Noninvasive electrocardiographic imaging of arrhythmogenic substrates in humans. *Circ Res*. 2013;112:863–874.
- Han C, Pogwizd SM, Killingsworth CR, Zhou Z, He B. Noninvasive cardiac activation imaging of ventricular arrhythmias during drug-induced QT prolongation in the rabbit heart. *Heart Rhythm*. 2013;10:1509–1515.
- Oster HS, Taccardi B, Lux RL, Ershler PR, Rudy Y. Electrocardiographic imaging: noninvasive characterization of intramural myocardial activation from inverse-reconstructed epicardial potentials and electrograms. *Circulation*. 1998;97:1496–1507.
- Hutchinson MD, Gerstenfeld EP, Desjardins B, Bala R, Riley MP, Garcia FC, Dixit S, Lin D, Tzou WS, Cooper JM, Verdino RJ, Callans DJ, Marchlinski FE. Endocardial unipolar voltage mapping to detect epicardial ventricular tachycardia substrate in patients with nonischemic left ventricular cardiomyopathy. *Circ Arrhythm Electrophysiol*. 2011;4:49–55.
- Lee K, Lv W, Ter-Ovanesyan E, Barley ME, Voysey GE, Galea AM, Hirschman GB, Leroy K, Marini RP, Barrett C, Aroundas AA, Cohen RJ. Cardiac ablation catheter guidance by means of a single equivalent moving dipole inverse algorithm. *Pacing Clin Electrophysiol*. 2013;36:811–822.
- Shah AJ, Hocini M, Xhaet O, Pascale P, Roten L, Wilton SB, Linton N, Scherr D, Miyazaki S, Jadidi AS, Liu X, Forclaz A, Nault I, Rivard L, Pedersen ME, Derval N, Sacher F, Knecht S, Jais P, Dubois R, Eliaoutou S, Bokan R, Strom M, Ramanathan C, Cakulev I, Sahadevan J, Lindsay B, Waldo AL, Haissaguerre M. Validation of novel 3-dimensional electrocardiographic mapping of atrial tachycardias by invasive mapping and ablation: a multicenter study. *J Am Coll Cardiol*. 2013;62:889–897.
- Cakulev I, Sahadevan J, Arruda M, Goldstein RN, Hong M, Intini A, Mackall JA, Stambler BS, Ramanathan C, Jia P, Strom M, Waldo AL. Confirmation of novel noninvasive high density electrocardiographic mapping with electrophysiology study: implications for therapy. *Circ Arrhythm Electrophysiol*. 2013;6:68–75.
- Jamil-Copley S, Bokan R, Kojodjojo P, Qureshi N, Koa-Wing M, Hayat S, Kyriacou A, Sandler B, Sohaib A, Wright I, Davies DW, Whinnett Z, Peters NS, Kanagaratnam P, Lim PB. Noninvasive electrocardiographic mapping to guide ablation of outflow tract ventricular arrhythmias. *Heart Rhythm*. 2014;11:587–594.
- Waller AD. A demonstration on man of electromotive changes accompanying the heart's beat. *J Physiol (Lond)*. 1887;8:227–234.
- Einthoven W. The galvanometric registration of the human electrocardiogram, likewise a review of the use of the capillary-electrometer in physiology. *Pflügers Arch Ges Physiol*. 1903;99:472–480.
- Donnelly MP, Finlay DD, Nugent CD, Black ND. Lead selection: old and new methods for locating the most electrocardiogram information. *J Electrocardiol*. 2008;41:257–263.
- van der Graaf AW, Bhagirath P, Ramanna H, van Driel VJ, de Hooge J, de Groot NM, Götte MJ. Noninvasive imaging of cardiac excitation: current status and future perspective. *Ann Noninvasive Electrocardiol*. 2014;19:105–113.
- Van Oosterom A. Source models in inverse electrocardiography. *Int J Bioelectromagn*. 2003;5:211–214.
- Shou G, Jiang M, Xia L, Wei Q, Liu F, Crozier S. A comparison of different choices for the regularization parameter in inverse electrocardiography models. *Conf Proc IEEE Eng Med Biol Soc*. 2006;1:3903–3906.
- Bhagirath P, van der Graaf M, van Dongen E, de Hooge J, van Driel V, Ramanna H, de Groot N, Götte M. Feasibility and accuracy of cardiac MRI based whole-heart inverse potential mapping of sinus rhythm and idiopathic ventricular foci. *J Am Heart Assoc*. 2015;4:e002222 doi: 10.1161/JAHA.115.002222.
- Erkaptic D, Greiss H, Pajitnev D, Zaltsberg S, Deubner N, Berkowitsch A, Möllman S, Sperzel J, Rolf A, Schmitt J, Hamm CW, Kuniss M, Neumann T. Clinical impact of a novel three-dimensional electrocardiographic imaging for non-invasive mapping of ventricular arrhythmias—a prospective randomized trial. *Europace*. 2015;17:591–597.
- Sapp JL, Dawoud F, Clements JC, Horáček BM. Inverse solution mapping of epicardial potentials: quantitative comparison with epicardial contact mapping. *Circ Arrhythm Electrophysiol*. 2012;5:1001–1009.
- Wang Y, Cuculich PS, Zhang J, Desouza KA, Vijayakumar R, Chen J, Faddis MN, Lindsay BD, Smith TW, Rudy Y. Noninvasive electroanatomic mapping of human ventricular arrhythmias with electrocardiographic imaging. *Sci Transl Med*. 2011;3:98ra84.

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