Automated functional substrate mapping further hurdles to be cleared

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EDITORIAL COMMENT

Automated Functional Substrate Mapping

Further Hurdles to Be Cleared*

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Ventricular tachycardia (VT) ablation after myocardial infarction remains challenging. Only a minority of patients have VTs that are reproducibly inducible and hemodynamically tolerated, allowing for delineation of the re-entrant circuit. Three-dimensional electroanatomical substrate mapping and ablation during stable rhythm have been shown to be superior to a strategy targeting only mappable VT (1). "VT substrates" have a complex geometry. Bundles of viable myocardium of variable size separated by fibrosis give rise to near-field abnormal (local abnormal ventricular activity), fractionated, split, or late potentials (LP). These "surrogates" for VT substrates are defined based on their general aspect (sharp, high-frequency), amplitude, duration, and timing, with LPs usually inscribed after QRS. Manual annotation of the components is prone to interpretation bias. Of importance, local "LP" may inscribe within QRS, and their near-field component may be even buried within the far-field electrogram (EGM) (2).

Changing the activation wave front from sinus rhythm (SR) to right ventricular (RV) pacing and mapping with small, narrow spaced (multi)electrodes can help to separate near-field from far-field activation (3). However, there is increasing evidence that critical parts of VT circuits are formed by functional rather than fixed line(s) of block (4). Regions of functional conduction slowing or block may not be evident during SR or pacing at commonly used pacing rates. Accordingly, mapping strategies to identify functional components of VT circuits without the need for VT induction have been proposed. During mapping of decrement-evoked potentials (DEEP), a RV pacing train (600 ms) with one short-coupled extrastimulus (S2) is delivered whenever LP are recorded. If the LP further delay in response to S2, the site is annotated as DEEP, which is more specific for isthmus sites than LP (5). During evoked delayed potential mapping, S2 is applied after a drive train (500 ms), independent from the local EGM during SR, thus also unmasking poorly coupled near-field potentials that are hidden by far-field potentials and not recognized during SR (6,7). Targeting all sites that delay in response to S2 has improved ablation outcomes in patients with small/nontransmural scars (6).

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The study by Srinivasan et al. (8) in this issue of *JACC: Clinical Electrophysiology* provides further evidence of the importance of functional substrate mapping during stable rhythm. The authors included 30 consecutive post-myocardial infarction patients with a remarkably low mean left ventricular ejection fraction of 25 ± 10%; 57% were on amiodarone. Mapping was performed with the EnSite Precision Mapping system (Abbott Inc., Abbott Park, Illinois). coupled with the 16-electrode (4 mm center-to-center spacing, 1 mm electrodes) Advisor HD Grid sensor enabled catheter (Abbott Inc.) to create a map of LP, defined as isolated, high-frequency local EGMs inscribing after the QRS offset, during SR (SR-LP).

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While constructing the SR-LP map, one short-coupled extrastimulus from the right ventricle was applied after every fifth sensed SR beat to change the activation wave front and evoke conduction delay simultaneously. After completing the map, the authors used the TurboMap feature allowing retrospective creation of a second map, consisting only of the extrastimulus based on the paced morphology. The "latest deflection" was used to automatically annotate the "sensed-paced" evoked LP within the diastolic interval (SP-EP).

The high-density wave ("HD wave") algorithm was used for bipolar voltage (BV) mapping, selecting the largest signal from orthogonal bipoles for each point (8). The dense scar was unexpectedly small (mean 38.2 mm^2) compared with prior mapping studies using conventional catheters (6). This may be explained by the applied 0.5 mV threshold, as BV recorded from the same site with small electrodes are significantly larger than BV using conventional catheters (7). Interestingly, the dense scar area was similar after changing wave front direction (from SR to RV pacing), suggesting that the HD wave algorithm may compensate for the wave front direction dependency of BV.

The region containing LP during SR was only 6 mm^2 (9% of the dense scar) and 3 times smaller than the region with SP-EP (19 mm^2, 38% of the dense scar) (8). After substrate mapping, activation/entrainment mapping could be performed in 21 of 30 patients. Of note, all 30 patients were inducible for VT, and 75 VTs could be entrained (n = 45) or pace-mapped (n = 30). The co-localization of critical VT sites and regions with SR-LP and SP-EP was analyzed.

Although Srinivasan et al. (8) unfortunately did not provide further details about how large the critical VT area was, nor how the co-localization analysis was performed, the true positive predictive value of SR-LP regions for VT-critical sites was already high (78%). This is higher than in previous studies (9,10), suggesting that in this cohort, HD mapping during SR was already very helpful in characterizing the substrate for the mappable VTs. With SP-EP mapping, the positive predictive value further increased to 87%. Of note, 35% of sites with SR-LP were not related to VT, in contrast to only 4% of SP-EP sites, supporting previous observations that evoked conduction delay is more specific for substrates of mappable VT than LP.

Ablation targeted all sites with best entrainment/pace map and all LP as defined by their mapping strategy and local abnormal ventricular activity (8). Nonclinical VTs were not targeted. Acute and long-term results were excellent in this population with a low ejection fraction in whom VT-free survival rates are usually poor. Noninducibility from 2 RV sites was achieved in 29 of 30 patients. After a median of 12 months, 63% of patients had no VT recurrence, and the VT burden was reduced from a median of 30 (interquartile range [IQR]: 12 to 47.5) to 2 (IQR: 1 to 4.75) and implantable cardioverter-defibrillator shocks from a median of 2 (IQR: 1 to 4.75) to 0 (IQR: 0 to 0). Despite the semi-automated determination of an SP-EP area of <2 cm^2, ablation time (median 32 min) and procedure time (mean 4 h 6 min) were still long, probably because of the attempt to identify VT-related sites for study purposes.

Automated annotation of near-field EGMs during SR, RV pacing, and extrastimulus (ES) and ideally, real-time visualization of evoked local activation delay, is desirable; the authors (8) should be congratulated for their important contribution toward automated mapping. However, for accurate automated annotation, applicable to all ischemic scars, there are still hurdles to be cleared and methodological limitations that need to be recognized. First, setting the window of interest is crucial. The authors' (8) definition and automated annotation of SR-LP excluded those LP inscribing within the QRS, more likely for early activated regions (e.g., the septum [11] and nontransmural scars [7]). Second, distinguishing late activated regions from evoked local delay is necessary. Applying single RV ES during SR to avoid the negative effects of RV pacing in patients with poor left ventricular function is appealing. However, separating a near-field from the far-field EGM does not prove local activation delay if one simultaneously changes the activation sequence and the coupling interval. This is in contrast to DEEP/evoked delayed potential mapping, which requires a short RV pacing drive but allows for the direct determination of the local delay by keeping the wave front direction constant. This local evoked delay, for which we suggest the term "evoked potential (EP)," has been directly linked to the mechanism of initiation and maintenance of VT (5). It could reliably identify the viable layer separated by fibrosis, validated by histology also for large tip electrodes (7). The main disadvantage of EP mapping is the need for manual calculation and annotation.

Any effort to simultaneously and automatically annotate and display LP and EP during substrate mapping in the current era of HD multielectrode mapping is desirable. A standardized and objective approach to delineate all fixed and functional components of VT substrates without the need for VT induction is likely to further improve ablation outcome for post-myocardial infarction VTs across centers.

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AUTHOR DISCLOSURES

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