Inverse Solution Mapping of Epicardial Potentials: Quantitative Comparison To Epicardial Contact Mapping.

Running title: Sapp et al.; Inverse Solution Epicardial Mapping

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Abstract:

Background - Catheter ablation of ventricular tachycardia (VT) is still one of the most challenging procedures in cardiac electrophysiology, limited in part by unmappable arrhythmias which are non-sustained or poorly tolerated. Calculation of the inverse solution from body surface potential mapping (BSPM) has shown tremendous promise, and can rapidly map these arrhythmias, but we lack quantitative assessment of its accuracy in humans. We compared inverse solution mapping with CT-registered electroanatomic epicardial contact catheter mapping to study the resolution of this technique, the influence of myocardial scar, and ability to map VT.

Methods and Results - For 4 patients undergoing epicardial catheter mapping and ablation of VT, 120-lead BSPMs were obtained during implantable defibrillator pacing, catheter pacing from 79 epicardial sites, and induced VT. Inverse epicardial electrograms computed using individualized torso/epicardial surface geometries extracted from CT images were compared to registered electroanatomic contact maps. The distance between estimated and actual epicardial pacing sites was 13 ± 9 mm over normal myocardium with no stimulus-QRS delay, but increased significantly over scar (p=0.013) or very close to scar (p=0.014). Contact maps during right ventricular pacing correlated closely to inverse solution isochrones. Maps of inverse epicardial potentials during 6 different induced VTs indicated areas of earliest activation which correlated closely with clinically identified VT exit sites for 2 epicardial VTs.

Conclusions - Inverse solution maps can identify sites of epicardial pacing with good accuracy, which diminishes over myocardial scar, or over slowly-conducting tissue. This approach can also identify epicardial VT exit sites, and ventricular activation sequences.

Key words: ablation; electrocardiography; electrophysiology mapping; mapping; ventricular tachycardia
Introduction

Catheter ablation of scar-related ventricular tachycardia (VT) is still one of the most challenging procedures in clinical cardiac electrophysiology. The majority of these arrhythmias are poorly hemodynamically tolerated, may be difficult to induce and frequently transform to other tachycardias during catheter mapping. Three-dimensional substrate mapping has added substantial capability and insight to catheter ablation of VT, but the procedure is restricted by the limitations of point-by-point catheter mapping. Methods for rapidly identifying VT circuit and exit sites are needed to facilitate the procedure.

Body surface potential mapping (BSPM), the acquisition of electrocardiographic recordings from multiple thoracic sites, can be combined with patient-specific geometry to estimate, by inverse solution, epicardial electrical events from body-surface recordings. This methodology, also known as ECG imaging, elegantly described by Rudy et al, has been correlated to biventricular pacing, to sites of successful ablation of accessory pathways, to open-chest mapping, to spontaneous ventricular ectopy in a case report, and in a series of patients who subsequently underwent electrophysiologic (EP) study with catheter mapping.

ECG imaging shows tremendous promise, although its spatial accuracy in humans has not yet been completely determined. We quantitatively assessed the accuracy of BSPM with inverse solution mapping to localize paced epicardial sites of activation by comparing it to simultaneously acquired CT-registered three-dimensional electroanatomic epicardial contact maps created during catheter mapping/ablation procedures for patients with VT. Then, we applied the technique to gain insight into the tachycardia circuit and exit sites.

Methods

Four consecutive consenting patients undergoing epicardial catheter mapping and ablation of VT
were enrolled. In a protocol approved by the institutional research ethics board, BSPM was performed during the clinical procedure. Patients underwent CT scanning prior to the procedure for correlation with electroanatomic mapping and generation of patient-specific geometry, and surface electrodes were applied on the patient torso according to our previously published methodology.

Clinical Methods

BSPM electrodes were applied prior to the procedure, which was performed using standard techniques.4 The pericardial space was entered percutaneously17 and mapped using an electroanatomic non-fluoroscopic system (Carto, Biosense Webster, Inc., Diamond Bar, CA). Point-by-point epicardial and endocardial mapping was performed using an irrigated 3.5 mm tip deflectable electrode catheter (Navistar Thermocool, Biosense Webster Inc., Diamond Bar, CA) during sinus or paced rhythm. Pacing was performed with stable catheter position at multiple epicardial sites at minimum pacing output (< 10 mA) to ensure consistent focal myocardial capture. BSPM recordings were acquired during pacing at each site. The location of each pacing site provided by the electroanatomic mapping system was noted for later off-line comparison.

Body Surface Potential Mapping and Computed Tomography

Body surface electrodes (Foxmed, Idstein, Germany) were applied immediately prior to beginning the clinical procedure using our previously published schema.16 Consistent lead position was assured by the use of bony landmarks and prefabricated electrode strips with fixed interelectrode spacing of 50 mm. Recordings were made using a 128-channel acquisition system with 1000-Hz sampling rate (Mark 6, BioSemi, Amsterdam). Axial computed tomography (0.8 – 3 mm) was performed within 24 hours prior to the procedure (Siemens Sonata, Erlangen,
Germany) and images were analyzed to create patient-specific torso and epicardial surfaces using commercial software (Amira 4.1, Mercury Computer Systems, Chelmsford, MA).

**Modeling and Data Processing Methods**

The bioelectric problem was modeled based on the epicardial potential approach. \(^{16,18,19}\) The linear model relating epicardial potentials (\(\Phi_H\)) and measured body-surface potentials (\(\Phi_B\)) through the transfer matrix \(A\) at every time instant can be expressed by the equation:

\[
A\Phi_H = \Phi_B
\]  

(1)

Transfer coefficients of matrix \(A\) were calculated using a homogeneous isotropic realistic torso model and constant interpolating functions between triangle centroids. The ill-posed system of equations was solved for epicardial potentials (\(\Phi_H\)) using Tikhonov regularization \(^{20}\) according to:

\[
\min \{ |A\Phi_H - \Phi_B|^2 + \lambda^2 |\Phi_H|^2 \}
\]  

(2)

where \(|.|\) denotes the \(l_2\) norm, \(\lambda\) is the regularization (smoothing) parameter and \(B\) is the regularizing operator. Second-order (Laplacian) operator \(^{21}\) was used and the regularization parameter was determined using the \(L\)-curve method. \(^{22}\) BSPM signals were processed to interpolate leads with considerable noise or missing data in order to produce a single averaged ECG complex for each recorded lead. Computational routines were implemented in MATLAB\(^{\text{TM}}\) (The Mathworks Inc., Natick, MA) for processing and analysis of data. MAP3D visualization software \(^{23}\) was used to display and inspect potential distributions on heart and torso surfaces.

**Data Analysis**

The electroanatomic (Carto) epicardial map was registered to the CT and points were projected to the nearest nodes of the discretized CT epicardial surface and utilized as the localization gold...
standard. The Carto map was registered manually to the CT data (Figure 1) to permit quantitative comparison of pacing sites with sites of earliest activation identified by the inverse solution map. As a measure of accuracy, the Euclidean (shortest 3D) distance was calculated for each recording between the earliest computed potential minimum and the actual pacing site projected on the epicardial surface. In addition, the geodesic distance (the shortest path connecting the two points along the surface) was estimated by solving for the shortest path on the discretized epicardial surface.\(^{24}\) For analysis of pacing-site localization, the sites were grouped into categories based on anatomic substrate at the pacing location: sites were characterized as “scar”, “scar margin”, or “no scar”, based upon filtered (50 – 400 Hz) bipolar signal amplitude.\(^{2}\) Sites with bipolar peak-to-peak signal amplitude < 1.5 mV were classified as “scar”, while sites within 10-mm Euclidean distance of a point with signal amplitude < 1.5 mV were classified as “scar margin”. Sites were also classified by the presence or absence of delay greater than 40 ms between stimulus and QRS onset.

Electroanatomic (Carto) pacing sites were compared to the centroid of areas of calculated early negative potentials. The centroid was identified visually within the earliest discrete area of calculated negative isopotentials by investigators blinded to the corresponding electroanatomic maps. In three cases, recordings were also made during pacing from the endocardial right-ventricular apex using the ICD lead. This site was easily localized on the CT scan providing a readily-identifiable pacing site for comparison. For two of these, epicardial point-by-point activation mapping was performed in order to qualitatively compare patterns of activation identified by contact mapping with those identified by ECG imaging. Local activation was determined from the inversely computed electrograms at the point of steepest descent (minimum \(dV/dT\)) during depolarization. Epicardial potential distributions of VTs for which an exit site
was identified were computed. Epicardial isochrones were calculated as described above. Sites of early calculated potential minima were compared qualitatively with isochronal maps and sites of successful ablation.

**Statistical Analysis**

Statistical analysis was performed with the SAS package (SAS Institute Inc., Cary, NC) taking into account the relationship among the 6 groups of measurements—each characterized by delay factor and scar factor—incorporating these factors into the model. Because data is unbalanced and correlated within subjects, the GEE approach was used (the GLIMMIX Procedure of SAS), with the natural logarithm of the Euclidean distance as the outcome variable. From the GLIMMIX Procedure options, within-subject analysis was chosen, with a constant correlation between all pairwise repeated measurements (referred to as Compound Symmetry or CS model). The significance level was $p < 0.05$; post hoc analysis used Sidak protected $p$ values for multiple pairwise comparisons. For all groups of measurements, we calculated the least squares mean values with standard error and 95% confidence intervals for natural logarithm of Euclidean distance, as well as back-transformed geometric mean values and their 95% confidence intervals. Differences of least squares means of natural-logarithm values (ratios of back-transformed values) were tabulated and their significance was assessed by Sidak $p$ values, adjusted for multiple comparisons.

**Results**

Four patients, all male, age 60 ± 20 years, with scar-related VT were included (Table 1). Inverse solution maps created from recordings during pacing at epicardial sites demonstrated an initial negative potential surrounding the pacing site. Figure 2 illustrates a typical example of both recorded body surface potentials and calculated epicardial potentials at multiple time instants.
following pacing at a basal inferior epicardial site. An early minimum potential correlates with
the site of pacing. During early repolarization a maximum appears in close proximity to the
pacing site.

**Accuracy of Localization of Pacing Sites And Influence of Myocardial Scar**

Comparison of computed inverse solution sites of activation to registered electroanatomic maps
yielded good accuracy when pacing at sites without scar, and without stimulus-QRS delay. The
results of pacing site localization in relation to the anatomic substrate are summarized in Table 2
and Figure 3. The 6 groups in Table 2 and Figure 3 are not independent, but each is defined by
two factors: presence of delay (ND/D) and presence or proximity to scar (NS/SM/S). The test of
fixed effects showed that there is no significant interaction between these factors and that the
delay factor is not statistically significant ($p=0.467$). Figure 3 graphically depicts the differences
between the groups. The greatest accuracy is at sites where there is neither stimulus-QRS delay,
nor local scar. The presence of nearby scar significantly reduces the accuracy of the technique.
The significance of differences of least-squares means of natural logarithm of Euclidean distance
(ratios of back-transformed values) was assessed by $p$-values adjusted for multiple comparisons
as follows: NS vs SM ($p=0.014$); NS vs S ($p=0.013$); SM vs S ($p=0.076$).

Euclidean distances $\leq 50$ mm were closely matched by geodesic distances (distances over
the curvature of the heart surface). There were no differences in estimates of surface alignment
(registration of electroanatomic to CT surface) accuracy among the groups.

In the three cases for which maps were created during pacing from the patient’s ICD an
area of positive potentials was observed early over the right-ventricular apex (thought to
represent endocardial to epicardial spread), followed by a potential minimum which increased in
negative magnitude throughout the depolarization phase. The calculated distances between the
RV apical pacing lead tips and the centroids of the areas of earliest negative potentials were 12, 25 and 24 mm, respectively, for the three cases. Inverse solution mapping of RV endocardial pacing is illustrated in Fig. 4.

**Ventricular Activation Sequence: Contact Mapping vs. Inverse Solution**

Contact mapping of the epicardium during pacing from the right-ventricular apical endocardium revealed activation patterns which were highly congruent with inverse solution maps (see Fig. 5). The site of earliest activation was accurately identified by both techniques at the right-ventricular epicardium over a relatively large area of epicardial breakthrough. In case 3, breakthrough was at the anterior RV apex, from which activation spread radially over the right-ventricular free wall, with latest activation at the basal inferior left ventricle. This pattern was very nearly replicated by inverse solution mapping. The area of late activation at the basal inferior wall of the left ventricle correlated very closely with a large area of endocardial scar, which was only minimally represented on the epicardial contact map (not shown). In case 4, the site of epicardial breakthrough was identified by both techniques at the apical inferior wall of the right ventricle.

Activation spread across the inferior wall, with late activation occurring at the basal anterolateral left ventricle. This patch of late activation was identified as being more inferiorly distributed on inverse solution maps, while it was more superolateral on the Carto map. The site of late activation correlated with a large basal lateral infarction scar where late, fragmented, low amplitude signals were recorded from the endocardium.

**Localization of VT Exit Sites**

VT ablation or exit sites were localized clinically for 6 VTs (see Table 1), of which two were epicardial. VT1 was recorded from a 30-year-old male with nonischemic cardiomyopathy.

Epicardial contact mapping revealed a confluent patch of posterior and lateral basal low-
amplitude signals. This VT appeared to exit from the superior margin of the basal lateral scar, and was successfully ablated at a site proximal to the superior scar margin (noted by asterisk in Fig. 6, first row). The successful ablation site was within scar, where a late potential was recorded, and where pacing resulted in stimulus-QRS delay and a morphologic match for VT; near-match without delay was observed pacing higher on the posterobasal LV epicardium. This correlated with an area of early epicardial potential minimum on the inverse solution map.

Computed epicardial isochrones suggested a basal superior origin, with propagation across the basal anterior wall, constrained by a line of slow conduction (crowding of isochrones) along the basal mid-anterior wall, with breakout just superior to the site of successful ablation. VT2 was recorded in patient 2, a 70-year-old male with prior inferior myocardial infarction. Computed epicardial potential maps are shown in Fig. 6, second row, at two time instants during ventricular activation in VT: 40 ms after QRS onset an early minimum potential is recorded at the mid-inferolateral left ventricle. This area of negative potentials intensifies and enlarges by mid-QRS (77 ms after QRS onset). The site of early minimum correlates approximately to the site of successful ablation (which was an isthmus site within scar, not at the breakout site). Computed isochronal maps are highly consistent with these findings, demonstrating earliest activation at the mid-inferolateral left ventricle, followed by propagation across the inferior wall, constrained by a line of slow conduction surrounding infarct scar (represented by isochronal crowding), with breakout over the apical junction of the two ventricles.

**Discussion**

**Localization of Epicardial Pacing Sites**

The accuracy of the inverse solution has been previously reported using canine heart preparations in a torso-shaped tank, and in humans with implanted pacing devices. It has also
been compared in clinical cases to identify an epicardial focus, and more recently, clinical ventricular ectopy and origins of VT. We are not aware of previous studies comparing simultaneous BSPM with epicardial three-dimensional contact mapping, nor of closed-chest human studies quantitatively comparing contact mapping to inverse-solution mapping. The inverse solution calculates epicardial potentials, and thus performing BSPM during epicardial catheter mapping/ablation procedures represents an ideal circumstance to estimate the accuracy of this technique to identify sites of epicardial activation. The Carto system provides excellent and reproducible positional localization, and thus supplied a good “gold standard” against which to compare localization by inverse solution mapping. We compared epicardial pacing sites localized by Carto with computed localization using inverse solution maps generated from body surface potential maps, registering the cardiac surface mapped using Carto with the epicardial surface determined from a pre-procedure CT scan, which was also used to provide patient-specific torso and cardiac geometry for performing the inverse solution.

We found that epicardial pacing from sites which were not within or very close to myocardial scar, in the absence of significant stimulus to QRS delay, was accurately mapped using BSPM with inverse solution computation. The mean distance between sites of earliest activation determined by Carto and those determined by the inverse solution was only 13 ± 9 mm. This accuracy is markedly reduced, however, in the presence of myocardial scar, which increased the estimated discrepancy to 28 ± 27 mm, or the presence of nearby scar, which was associated with a discrepancy of 43 ± 11 mm. The reasons for this detraction in localization accuracy are not completely clear, but there are several likely contributors. The presence of myocardial scar was not factored into the calculation of epicardial potentials by the inverse solution, and the inhomogeneity of myocardial substrate may thus significantly violate the
assumptions used to calculate epicardial potentials. Pacing from within myocardial scar, even in
the absence of substantial stimulus-to-QRS delay, may result in relatively early activation of
myocardium which is not immediately below the pacing catheter, but rather within the
ventricular wall or on the endocardial side, so that the usual pattern of epicardial activation (early
potential minimum with radial spread of activation) is not seen. Likewise, because scar is a
three-dimensional structure, it is likely that the scar margin identified by contact mapping of the
epicardial surface does not accurately identify the full extent of myocardial scar, possibly
contributing to the reduced accuracy seen when pacing near myocardial scar.

Stimulus to QRS delay was defined as that which exceeded 40 ms, in keeping with
clinical practice. Latency between stimulus and QRS onset is typically thought to represent
activation of a “channel” or isthmus, usually within scar, which is too small to generate a
significant representation on the surface ECG. The duration of the delay is determined by the
distance from the pacing site to a larger volume of myocardium (the “breakout” site) which
generates the earliest portion of the QRS, as well as the conduction velocity within the isthmus.
Sites with delay may exit close to the pacing site if local conduction velocity prior to breakout is
very low, but may also exit remotely. Indeed this was reflected in our data, in which the
presence of stimulus-to-QRS delay increased the variability of distances assessed (see Figure 3).
It is interesting to note that we observed clustering of calculated early potential minima sites
when pacing within scar or near scar-margin in the presence of stimulus-QRS delay. In case 1,
the early minima clustered at the high anterobasal left ventricle (5 sites) and high basal-lateral
segments (6 sites), possibly correlating with exit from the margins of scar which was mapped to
this area. In case 2, clustering occurred at the mid-inferior left ventricle (7 sites) correlating with
the basal inferior scar. In case 3, clustering occurred on the high basal lateral left ventricle (5
sites) and in case 4, three disparate pacing sites within the inferior scar resulted in calculated early potential minima clustered at the mid inferior left ventricle at the margin of scar. It is possible that this clustering represents activation of myocardial isthmuses with common exits at the scar margin, although this can not be confirmed from the available data. It is intriguing, however, that sites of clustering of calculated early activation correlate moderately well with sites where VT was successfully ablated.

Ventricular Activation Sequence: Contact Mapping vs. Inverse Solution

Qualitative comparison of the activation sequence determined by point-by-point contact mapping with that determined by inverse solution mapping yielded very similar patterns, including the demonstration of areas of slow conduction or functional block where isochronal crowding was observed. Because of the complexity of the analysis and the small sample size we did not attempt quantitative comparisons. We used the minimum $dV/dT$ of the calculated epicardial potential to identify local activation. This has been used in unipolar contact mapping and is supported by experimental and theoretical studies.$^{26}$ The derivative calculated from a few successive samples is vulnerable to measurement noise in body-surface potentials, or to slight changes in the regularization parameter that controls the amount of smoothing in the inverse calculation. This problem was partially mitigated by spatial smoothing of inverse electrograms using moving-average spline interpolation. Rapid activation over large regions and lines of abrupt “jumps” in the calculated activation time, suggesting lines of conduction delay/block, have also been observed in figures published by other investigators.$^{7,13,8}$ Differences in overall activation time between contact maps and calculated epicardial activation maps were observed (see Fig. 5). These discrepancies may be due in part to limitations of the inverse solution method used, which can only produce “unipolar-like” electrograms, which inherently have reduced...
ability to resolve changes in activation time with respect to neighboring sites, and which contain superposition of both near- and far-field potentials (epicardial and transmural contributions) in comparison with contact bipolar recordings. Not surprisingly, contact mapping had better ability to resolve very low amplitude late potentials, seen in Fig 5, Case 4 at the high postero-basal left ventricle.

Localization of VT Exit Sites

This study attempts to correlate sites of early activation during epicardial VTs determined by BSPM and inverse-solution calculation with sites of myocardial break-out or critical isthmuses identified during catheter ablation procedures. This comparison is necessarily limited by a number of important factors: the site of successful ablation may be remote from the site of epicardial exit; diastolic components of VT are not mappable using this methodology; and myocardial scar is 3-dimensional, but is mapped on the endocardial and epicardial surfaces only using catheter techniques. Despite these challenges, BSPM with inverse solution mapping approximately co-localized the site of earliest epicardial activation with the site of successful ablation in the two VTs which were mapped to the epicardium. The exact activation sequence during VT was not mapped using contact catheters because of hemodynamic instability, or for clinical expediency; thus the location of VT exit was inferred and not necessarily precisely located for all cases. Computed isochronal maps of VT showed earliest activation in the region at or close to the site where the early potential minimum was identified. Similar to the recordings during apical right ventricular pacing, regions of isochronal crowding were observed, suggesting sites of functional block. Not surprisingly, sites of conduction block were seen at similar locations during both right-ventricular apical pacing and VT in cases 3 and 4 (data not shown). Our findings confirm prior modeling studies performed in canines, as well as human
studies,\textsuperscript{28,29,30} which have demonstrated the ability of this technique to delineate cardiac activation.\textsuperscript{15}

\textit{Study Limitations}

Geometric inaccuracies in the representation of the heart surface have been identified as contributing the most substantial errors to estimates of epicardial potentials.\textsuperscript{31,32,33} We attempted to minimize these inaccuracies by constructing customized torso and cardiac geometries for each patient from CT scans obtained the day before the procedure, and with the use of the \textit{L}-curve method for identification of a regularization parameter, which has been thought to be more robust in the presence of geometric errors.\textsuperscript{34} It is possible that differences in body position, intravascular volume, or other factors may have changed the geometry between the imaging and mapping studies. Likewise, we were unable to control error introduced by respiration (which may change both thoracic conductance and relative cardiothoracic position) or other changes in patient position during the procedure, nor was it possible to control for error introduced by cardiac motion during ventricular activation, particularly during VT. These potential inaccuracies may have affected both the inverse solution map and the “gold standard” electroanatomic map, artificially increasing discrepancies between the two. The challenges of epicardial contact mapping include the confounding effect of epicardial fat\textsuperscript{35} as well as higher pacing thresholds. In our study, this resulted in stimulus-QRS delay and reduced signal amplitude at multiple sites. While these factors place some constraints on the ability of our methodology to fully assess the potential accuracy of inverse solution mapping, epicardial contact mapping likely still represents a physiologically relevant comparator. This study was limited by its small sample size. Potential future clinical applicability of these techniques would require substantial automation to accomplish real or near-real time imaging; processing and
analysis was time-consuming and complex within the study.

Perhaps the most important limitation to inverse solution mapping of cardiac activation in this study is the lack of exact localization of body surface recording electrodes on the torso. Incorporation of this data in calculation of the inverse solution may have increased the accuracy of the technique, but would have required placement of the electrodes (with radio-opaque markers) prior to performance of the CT scan, all accomplished immediately prior to the procedure to avoid loss of electrode integrity. Accomplishing this posed logistic hurdles which we were unable overcome in the clinical context. We therefore attempted to minimize this potential source of error by using skin electrodes with defined interelectrode distances and using strictly defined bony landmarks while affixing electrode strips. It is possible that the spatial resolution achieved in this study would be higher if body surface electrode position were more accurately identified.

The boundary element transfer matrix was calculated based on constant basis functions assuming a homogeneous isotropic torso, as supported by earlier work. Mapping of myocardial scar was performed using only contact electroanatomic mapping in this study. Proximity of pacing sites to myocardial scar was assessed from epicardial maps only, not endocardial maps. Endocardial and mid-myocardial scar were thus not assessed, and may have contributed to greater discrepancy in site localization at scar margin sites. Cardiac MRI was precluded by the presence of ICDs, and we did not endeavor to incorporate scar location data from echocardiography or other imaging modalities.

Finally, we noted discordant findings between contact mapping and inverse solution mapping for VT4, which had myocardial breakout in the LV septum. Inverse solution maps calculate epicardial potentials. Further study is required to understand patterns generated when
the septum is activated early.

**Conclusions**

This study provides human, closed-chest validation that inverse solution maps derived from body surface potential maps can identify sites of epicardial pacing with very good accuracy, which diminishes when pacing is performed over myocardial scar, or over a slowly conducting isthmus. This modality can also be applied to map myocardial activation sequences, both during ventricular pacing and during VT. BSPM can be performed during catheter ablation procedures; the performance of inverse solution calculations in real-time may aid catheter ablation of VT, or other cardiac interventions.

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**Conflict of Interest Disclosures:** John Sapp has received research support from St. Jude Medical, Biosense Webster and Philips Healthcare and received consultant reimbursement or honoraria from Biosense Webster, Boston Scientific, and Boehringer-Ingelheim. Milan Horacek has received research support from Philips Healthcare.

**References:**


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Table 1: Description of VT recordings for the 4 patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Etiology</th>
<th># Pace Sites</th>
<th>Mapped VT</th>
<th>VT Exit/Ablation Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>30</td>
<td>NICM</td>
<td>23</td>
<td>VT1</td>
<td>epicardial basal lateral LV</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>70</td>
<td>ICM</td>
<td>23</td>
<td>VT2</td>
<td>epicardial basal inferior LV</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>65</td>
<td>ICM</td>
<td>22</td>
<td>VT3</td>
<td>endocardial basal inferior LV</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>65</td>
<td>ICM</td>
<td>11</td>
<td>VT5</td>
<td>endocardial basal lateral LV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VT6</td>
<td>endocardial basal superior LV</td>
</tr>
</tbody>
</table>

ICM, Ischemic cardiomyopathy; NICM, Non-Ischemic cardiomyopathy

Table 2: Localization of epicardial pacing sites: cumulative results for all 4 cases

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (NS-ND)</th>
<th>Group 2 (SM-ND)</th>
<th>Group 3 (S-ND)</th>
<th>Group 4 (NS-D)</th>
<th>Group 5 (SM-D)</th>
<th>Group 6 (S-D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inverse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euclidean distance</td>
<td>13 ± 9</td>
<td>43 ± 11</td>
<td>28 ± 27</td>
<td>28 ± 26</td>
<td>50 ± 47</td>
<td>67 ± 37</td>
</tr>
<tr>
<td>Median (range)</td>
<td>10 (30)</td>
<td>44 (33)</td>
<td>22 (87)</td>
<td>16 (77)</td>
<td>24 (97)</td>
<td>63 (115)</td>
</tr>
<tr>
<td>Minimum time</td>
<td>27 ± 15</td>
<td>58 ± 36</td>
<td>31 ± 11</td>
<td>46 ± 21</td>
<td>76 ± 24</td>
<td>68 ± 29</td>
</tr>
<tr>
<td>Alignment distance</td>
<td>3 ± 3</td>
<td>3 ± 2</td>
<td>4 ± 2</td>
<td>5 ± 4</td>
<td>3 ± 6</td>
<td>7 ± 5</td>
</tr>
</tbody>
</table>

Measured

|                  |                |                 |                |                |                |               |
| Delay time       | 30 ± 10        | 25 ± 12         | 32 ± 9         | 57 ± 15        | 71 ± 26        | 73 ± 28       |
| Bipolar signal amplitude | 4.2 ± 2.8  | 2.2 ± 0.9  | 0.9 ± 0.4  | 4.1 ± 1.7  | 2.0 ± 0.4  | 0.8 ± 0.4 |

NS/SM/S, pacing sites with ‘no scar’/in scar margin/within scar region; D/ND, pacing producing delay/no delay; Minimum time, time (ms) when the first discernible minimum appears in calculated epicardial potential distribution; Euclidean distance, 3-D distance (mm) between pacing site and estimated location of that pacing site; Alignment distance, distance (mm) between actual CARTO point and point projected onto the epicardial surface (registration error); Delay time, time (ms) from stimulation spike to the earliest QRS onset of surface ECG; Bipolar signal amplitude, peak-to-peak bipolar signal amplitude (mV) measured by CARTO system at pacing site during sinus rhythm; values with ± sign indicate mean ± standard deviation.

Figure Legends:

Figure 1: Body surface, CT and CARTO image fusion. The electrodes were positioned in standardized locations shown in yellow. Left: The CT-derived torso and epicardial surfaces are
registered with the electroanatomic epicardial map, shown in anterior (left top) and lateral (left, bottom) views. Right: Registration of electroanatomic map with CT.

**Figure 2:** Epicardial and body-surface potential maps for epicardial pacing. **Top row:** inferior view of the patient-specific epicardial surface with the calculated epicardial potential maps for time instants 25, 37, 59, and 180 ms after pacing at an inferior left ventricular site (pink disk). The calculated epicardial potential at the site of pacing is shown in green. The region of early minimum potentials, shown in the first panel, correlates closely with the pacing site. **Bottom row** anterior view of the patient-specific torso surface with recorded potential maps that were used to calculate epicardial potentials at four time instances, as above. The body surface signal recorded at the site of the precordial lead V2 (pink disk) is shown in green; the bar on the right margin indicates color coding of potentials.

**Figure 3:** Box plot of natural logarithm of Euclidean distances between sites of pacing as identified by CARTO electroanatomic maps and sites of early negative potentials identified from epicardial inverse-solution maps, grouped by presence or absence of stimulus-QRS delay > 40 ms, and by whether pacing was over myocardial scar (signal amplitude <1.5 mV), within 1 cm of scar (scar margin), or over myocardium with normal signal amplitude. Heavy line indicates median, boxes represent interquartile ranges, and error bars represent range.

**Figure 4:** Right ventricular apical pacing. Top: CT-derived epicardial surface and site of right ventricular apical pacing lead. Bottom: Inferior views of calculated epicardial maps demonstrating an area of positive potentials over the site of the pacing leads (left panel), possibly
representing endocardial to epicardial spread, which rapidly becomes an area of negative potentials 6 msec after the pacing impulse. Subsequent maps showed propagation of negative amplitude away from the pacing site.

**Figure 5:** Contact electroanatomic epicardial activation isochronal maps (left panels) and computed inverse solution epicardial isochronal maps (right panels) for case 3 (top row) and case 4 (bottom row) during right ventricular endocardial pacing. Activation spreads radially from RV pacing site to LV postero-lateral wall. Qualitatively similar patterns of activation are reconstructed by the inverse solution. Contact mapping was more sensitive to very late, low amplitude potentials, demonstrating later activation in the superobasal LV segment in case 4 than was detected by the inverse solution map.

**Figure 6:** Inverse epicardial potential maps and isochrones of activation for cases 1 and 2 during VT1 and VT2. Asterisk (*) indicates the ablation site that terminated VT, or the clinically identified VT exit site. On left are calculated epicardial isopotential maps at time instants after QRS onset as shown, with views as noted. On right are calculated epicardial isochronal maps of the entire QRS with views as noted. **First row VT1:** An early minimum potential is seen at the mid superolateral left ventricle; isochronal maps demonstrate propagation from the superobasal left ventricle across the anterior wall. **Second Row VT2:** Inferior views of potential maps at 40 msec and 77 msec after QRS onset are shown. An early inferolateral minimum potential is seen just apical to the ablation site which was within myocardial scar. Isochronal maps are consistent with myocardial breakout near this site, and propagation across the inferior wall. *See more detailed discussion in text.*
2 msec post-pacing

6 msec post-pacing
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