Comparison of Electroanatomic Contact and Noncontact Mapping of Ventricular Scar in a Postinfarct Ovine Model With Intramural Needle Electrode Recording and Histological Validation

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Background—Substrate-based ablation is useful for nonhemodynamically tolerated postinfarct ventricular tachycardia. We assessed the accuracy of the CARTO contact and EnSite noncontact systems at identifying scar in a chronic ovine model with intramural plunge needle electrode recording and histological validation.

Methods and Results—Scar mapping was performed on 8 male sheep with previous percutaneous-induced myocardial infarction. Up to 20 plunge needles were inserted into the left ventricle of each animal in areas of dense scar, scar border, and normal myocardium. A simultaneous CARTO map and EnSite geometry were acquired using a single catheter, and needle electrode locations were registered. A dynamic substrate map was constructed using ratiometric 50% peak negative voltage. The scar percentage around each needle location was quantified histologically. Analysis was performed on 152 plunge needles and corresponding histological blocks. Spearman correlation with histology was 0.690 ($P<0.001$) for needle electrode peak-to-peak voltage (PPV), 0.362 ($P<0.001$) and 0.492 ($P<0.001$) for CARTO bipolar and unipolar PPV, and 0.381 ($P<0.001$) for EnSite dynamic substrate map ($\leq$40 mm from array). The area under the receiver operator characteristics curve ($\leq$50% and $\geq$50% scar) was 0.896 for needle electrode PPV, 0.726 and 0.697 for CARTO bipolar and unipolar PPV, and 0.703 for EnSite dynamic substrate map ($\leq$40 mm from array).

Conclusions—Both the CARTO contact and EnSite noncontact systems were moderately accurate in identifying postinfarct scar when compared with intramural electrodes and confirmed with histology. The EnSite dynamic substrate map was comparable to the CARTO contact bipolar PPV when points $>40$ mm from the array were excluded. (Circ Arrhythmia Electrophysiol. 2008;1:363-369.)

Key Words: arrhythmia ■ electrophysiology ■ mapping ■ myocardial infarction

Selected use of radiofrequency ablation is an emerging adjunctive therapy for postinfarct ventricular tachycardia (VT).1,2 Current indications are expanding from patients experiencing multiple implantable cardioverter defibrillator shocks to possible prophylactic therapy before clinical arrhythmia.3–6

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Current strategies for postinfarct VT ablation involve isolation of critical pathways within the VT re-entrant circuit. These circuits involve bundles of viable myocardium in the border zones of infarct scar.7 Entrainment of VT allows identification of various parts of the reentrant circuits but is limited to hemodynamically stable arrhythmias.8,9 Substrate-based ablation, aided by pace mapping, is an alternative for the majority of postinfarct VT, which is not hemodynamically tolerated.4,6,10–12

Accurate identification of ventricular scar is critical during VT ablation procedures as the exit sites of postinfarct VT are associated with scar border zones.13 Contact mapping using the CARTO system allows ventricular scar to be identified by measuring the voltage of bipolar electrograms during sinus rhythm.4,5,14,15 Virtual reconstructions of endocardial electrograms using the EnSite noncontact mapping system allows single beat mapping of stable and unstable VT but does not accurately identify areas of scar.16–20 A newer dynamic substrate mapping algorithm is more accurate than noncontact mapping in sinus rhythm at identifying postinfarct left ventricular scar.21,22

The purpose of this study was to assess and directly compare the accuracy of electroanatomic contact (CARTO) and noncontact (EnSite) systems for scar mapping, using...
intramural plunge needle electrode recording and tissue histology for validation, in a chronic ovine postinfarction model.

**Methods**

All procedures were performed in the Westmead Hospital vivarium with approval from the institutional animal ethics committee.

**Myocardial Infarction Induction**

Myocardial infarctions were induced via a closed chest method in 11 male sheep (Merino). Each animal was fasted overnight and then premedicated with intramuscular xylazine 2 mg. Anesthesia was induced with intravenous propofol 200 mg via a 7F sheath inserted under aseptic technique in the left external jugular vein. Each animal was intubated with an 8.0 endotracheal tube and anesthesia maintained with 2.5% inhaled isoflurane. Throughout the procedure, the ECG, oxygen saturation, end tidal CO2, and invasive arterial pressure were monitored. A 7F AL1 or AL2 guide coronary catheter was engaged in the left main coronary artery via a retrograde aortic approach from the right common femoral artery. A 0.014-inch coronary angioplasty wire was selectively passed into the homonymous artery (ovine left anterior descending artery equivalent). A 3.0×20 mm coronary angioplasty balloon was deployed midway in the homonymous artery equivalent for 3 hours as described by Reek et al. After balloon deflation, each animal was observed on the anesthetic table with full hemodynamic monitoring for 1 hour. After this, all sheaths were removed and the animal recovered and observed for a further 1 to 3 hours, and given analgesia with 0.3 mg IM buprenorphine.

**Scar Mapping Procedure**

A scar mapping procedure was performed in surviving sheep. Each animal was premedicated, anesthetized, and monitored with the same regimen as per the myocardial infarction induction procedure. Bilateral femoral arterial and venous vascular access was obtained via the wire Seldinger technique with the animal in the supine position.

The sheep was then rolled into a right decubitus position. A thoracotomy was performed through the third or fourth intercostal space. The pericardial sac was incised and opened. Up to 20 in-house electrodes were inserted in normal left ventricular tissue. The MEA (Multi-Electrode Array) was then advanced from the left femoral artery by a D-curve catheter was then advanced by a retrograde transaortic approach from the right femoral artery into the left ventricle.

The NaviStar catheter was used to simultaneously acquire an EnSite 3-dimensional geometry and a CARTO (Biosense Webster) 3-dimensional electroanatomic voltage map, ensuring the same catheter contact positions were compared on both systems.

The EnSite system had a sampling rate of 1.2 kHz with filter settings 0.1 to 300 Hz. The CARTO system recorded bipolar electrograms between the first and second tip electrodes of the NaviStar catheter. The interelectrode spacing was 1 mm. Unipolar filtering was set at 0.05 to 400 Hz, and bipolar filtering set at 30 to 400 Hz. Wilson central terminal was assigned as the unipolar reference electrode. Local electrograms during sinus rhythm were recorded at each stable catheter point, the bipolar and unipolar peak-to-peak voltage (PPV) amplitude was automatically calculated by the CARTO system. A bipolar PPV <0.5 mV was considered dense scar, and >1.5 mV normal myocardium, and a corresponding voltage color range, was applied to the geometry.

Mapping points were collected on both systems, including pacing points, until the entire chamber had been sampled. Key anatomic structures such as the mitral and aortic valves and the left ventricular apex were annotated. High density mapping was performed around regions of low bipolar voltage.

A mean of 10±1 points were used to perform pacing for construction of dynamic substrate maps (DSMs) using the EnSite system. Pacing points encompassed all aspects of the left ventricle including basal, lateral, anterior, and septal walls. Pacing was also performed from the right ventricular apex. All pacing was delivered at twice the local diastolic threshold at a cycle length of 400 ms. After geometry completion, from a recording of sinus rhythm and from each pacing site a zone of low electrogram voltage, <50% of the peak negative electrogram voltage (PNV), was marked. Scar was defined on the DSM as an area where the low voltage zones overlapped.

The position of the intramural plunge needles were annotated on both systems. On the EnSite system, this was done by connecting each electrode to the Enguide locator, and 3-D labeling each electrode on the EnSite geometry. On the CARTO system, the plunge needle positions were annotated by moving the NaviStar catheter to the endocardial fluoroscopic projection of each needle, or by using the NaviStar catheter to mark the epicardial needle entry site on a separate epicardial CARTO map.

The distance of each point from the center of the MEA was automatically calculated by the EnSite system. Intracavitary points on the CARTO system were manually identified and excluded from the geometry to improve accuracy.

All data from the Prucka Cardiolab recording system and EnSite system was analyzed off-line on customized software developed with Matlab V7.0 (Mathworks). Needle electrode PPV and PNV, and EnSite virtual PNV and PNV were measured at each point over the same sinus beat. The CARTO bipolar and unipolar PNV were exported after being automatically measured within the CARTO system.

**Histological Analysis**

At the end of the procedure, each animal was euthanized by inducing ventricular fibrillation with rapid right ventricular pacing. Each heart was immediately excised with the plunge needles in situ. The needles were then replaced with markers and the heart was stored in formalin for 3 weeks. Blocks of myocardium (1 cm×1 cm) were excised around each needle marker and dehydrated with 100% ethanol. Sections from each block were stained with Gomori trichrome for histological analysis. Each slice of myocardium from endocardium to epicardium was examined to calculate scar percentage. This was done by digitally scanning histological slides and importing the images into Scion Image software (Version 1.62c, Scion Corporation). All areas of scar (stained blue with Gomori trichrome) were measured at five arbitrary sites around each needle marker and dehydrated with 100% ethanol. Blocks of myocardium (1 cm×1 cm) were excised around each needle marker and dehydrated with 100% ethanol. Sections from each block were stained with Gomori trichrome for histological analysis. Each slice of myocardium from endocardium to epicardium was examined to calculate scar percentage. This was done by digitally scanning histological slides and importing the images into Scion Image software (Version 1.62c, Scion Corporation). All areas of scar (stained blue with Gomori trichrome) were measured at five arbitrary sites around each needle marker.
To better differentiate areas of partial and densely scarred myocardium, 2 histological classifications were used: (1) <50% and ≥50% scar was used to differentiate dense scar from partial scar/normal myocardium, and (2) ≥10% and >10% scar was used to differentiate partial/dense scar from normal myocardium.

The accuracy of the needle electrode unipolar PPV and PNV, CARTO contact bipolar and unipolar PPV, EnSite DSM percentage PNV, and virtual electrogram unipolar PNV, were compared with histopathology at each needle site. Analysis was repeated on the EnSite data excluding points >40 mm from the equator of the MEA.

**Statistical Analysis**

All analysis was performed using the Statistical Package for the Social Sciences (SPSS) for windows (Release 14.0, SPSS Inc). ANOVA was used to compare mean values, or Kruskall-Wallis tests were used for continuous variables when normal distribution was not present. Spearman rank correlation between scar percentage and each mapping measure were calculated for all data points and for each sheep. The average of these rank correlations and its standard deviation were used to summarize within sheep observations. Receiver operating characteristic (ROC) curves were constructed to assess sensitivity and specificity. A 2-tailed P<0.05 was considered significant.

**Statement of Responsibility**

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

**Results**

**Myocardial Infarction Induction**

A 20.0×3.0 mm balloon was inflated at 6 atmospheres for 3 hours in 11 sheep. The median percentage of homonymous left anterior descending artery occluded was 45%. The survival rate of the myocardial infarction induction was 73% (8 of 11).

**Scar Mapping Procedure**

The median time from myocardial infarction to scar mapping procedure was 6 (range, 2–32) months.

At thoracotomy, the epicardial visualized scar involved the left ventricular apex, anterior wall, and extended across the interventricular groove to involve the anterior wall of the right ventricle. Patchy scar was noted at the scar borders. The first sheep had 12 plunge needles inserted, the others had 20. There were a total of 152 intramural plunge needles available for analysis (Figure 1).

For each animal, a mean of 216±35 (range, 150–273) CARTO endocardial electrograms were recorded, including needle position markers. 10±1 pacing sites per animal were used for construction of DSM maps. An example of corresponding CARTO bipolar PPV and EnSite DSM percentage PNV maps is shown in Figure 2, with right and left anterior oblique equivalent views.

Correlations between scar percentage and each needle electrode, CARTO, and EnSite mapping measure are presented in Table 1, expressed as the correlation coefficient for all animals and the average rank correlation between animals. The EnSite DSM percentage of maximal PNV and virtual unipolar PNV correlations improved when points >40 mm from the equator of the MEA were excluded. The best correlations were seen with needle electrode unipolar PNV and PPV. Figure 3 shows examples of transmural histology at sites of normal myocardium (<10% scar), partial scar (10% to 50% scar), and dense scar (>50% scar).

A separate correlation was performed between CARTO bipolar PPV and EnSite percentage PNV for all animals. This correlation was weak, r=0.100 (P=0.233). There was better correlation between CARTO bipolar PPV and CARTO unipolar PPV, r=0.569 (P<0.001).

The calculated area under the curve for each mapping measure and each scar classification ROC curve are presented in Table 1. The largest area under the curve was seen with the plunge needle electrode unipolar measures (PPV and PNV). The CARTO bipolar PPV was better at differentiating dense scar ≥50% (0.726 versus 0.665), although the CARTO unipolar PPV was better at differentiating all scar >10% (0.789 versus 0.697). The EnSite DSM was equivalent for both categories of scar (0.703 versus 0.700). The EnSite DSM area was comparable to the CARTO bipolar area when points >40 mm from the equator of the MEA were excluded.

The electrogram characteristics for each mapping measure according to percentage of scar are presented in Table 2. With the exception of EnSite virtual PNV, there was a significant difference between the mean values with all assessed mapping measures.

For CARTO points with bipolar PPV ≤0.5 mV, the median percentage of histological scar was 84%. At points with CARTO bipolar PPV >1.5 mV, the median percentage of scar was 0%, and at points with bipolar PPV 0.5 to 1.5 mV, the median was 10% (P<0.001).

**Discussion**

This is the first study that has directly compared the accuracy of the CARTO contact and EnSite noncontact systems at identifying scar defined by histological analysis at plunge needle reference points. By using a single catheter and the same catheter movements to generate both geometries simultaneously, direct comparisons between both systems could be made. By annotating individual needle points on both the
EnSite and CARTO systems, and obtaining histopathology at these precise points, the risk of alignment error (by using areas) was minimized. The accuracy of both systems to identify scar was compared using histology of the myocardium surrounding each needle. Both contact and noncontact mapping were comparable at differentiating normal and densely scarred myocardium in this study. The EnSite DSM was comparable to CARTO contact measures (ROC curves) once distances >40 mm from the array were excluded, a known limitation of the noncontact system.

The use of intramural plunge needles allowed up to 152 points of reference when comparing the CARTO and EnSite systems with histology, as well as providing an independent reference unipolar electrogram at each site. It has been shown that plunge needles do not alter myocardial activation, structure, or function.24 The use of plunge needles in this study would not have affected pacing wavefronts for construction of dynamic subtate maps or altered contact unipolar and bipolar voltages.

Reentrant circuits are not limited to the endocardium, and pathways can course through all layers of myocardium. Local reconstructed noncontact endocardial electrograms are known to be a summation of transmural activation at that point.25 Quantification of histology with a transmural (endocardium to epicardium) approach at each point allowed direct comparison of the local measured electrogram (contact and

| Table 1. Correlations Between Measured Percentage of Histological Scar and Each Mapping Measure and Averaged Within Animals; Calculated AUC for ROC Curves for Both Histological Classifications |
|---------------------------------|-----------------|-----------------|-----------------|
|                                | Spearman Correlation (All Animals) | Average Rank Correlation (Within Animals) | ROC AUC |
|                                | r | P Value | r=SD | P Value | Classification 1 | Classification 2 |
| Needle electrode unipolar PNV  | 0.550 | <0.001 | 0.477±0.334 | 0.153 | 0.767 | 0.802 |
| Needle electrode unipolar PPV  | 0.690 | <0.001 | 0.665±0.220 | 0.002 | 0.896 | 0.874 |
| CARTO bipolar PPV              | 0.362 | <0.001 | 0.401±0.270 | 0.138 | 0.726 | 0.665 |
| CARTO unipolar PPV             | 0.492 | <0.001 | 0.522±0.131 | <0.001 | 0.697 | 0.789 |
| EnSite DSM (% maximum PNV)     | 0.292 | <0.001 | 0.366±0.418 | 0.382 | 0.667 | 0.650 |
| EnSite DSM (% maximum PNV) ≤40 mm | 0.381 | <0.001 | 0.433±0.366 | 0.236 | 0.703 | 0.700 |
| EnSite unipolar PNV            | 0.238 | 0.003 | 0.297±0.415 | 0.474 | 0.615 | 0.616 |
| EnSite unipolar PNV ≤40 mm     | 0.301 | 0.001 | 0.393±0.439 | 0.371 | 0.643 | 0.646 |

PNV indicates peak negative voltage; PPV, peak-to-peak voltage; DSM, dynamic substrate map; ROC, receiver operator characteristic; AUC, area under the curve; Classification 1, <50% and ≥50% scar used to differentiate dense scar from partial scar/normal myocardium; Classification 2, ≤10% and >10% scar used to differentiate partial/dense scar from normal myocardium.
noncontact) with the underlying transmural source and was not limited to endocardial histopathology.

The only other study that has performed simultaneous comparison of CARTO and EnSite systems was by Abrams et al., as they used simultaneous contact and noncontact mapping to identify abnormal endocardium in the right atrium in patients late after Fontan procedure. Using a DSM <30% PNV, the noncontact system could not reliably define areas of low-voltage endocardium compared with the contact bipolar electrogram reference. The authors clarified that the noncontact system accuracy was limited by the dilated chamber and a large proportion of abnormal endocardium noncontact system accuracy was limited by the dilated bipolar electrogram reference. The authors clarified that the areas of low-voltage endocarium compared with the contact atrium in patients late after Fontan procedure. Using a DSM/H11021 30% PNV, the noncontact system could not reliably define (bottom) to epicardium (top).

Table 2. Electrogram Characteristics and Calculated Histological Scar Percentage

<table>
<thead>
<tr>
<th>Scar Category</th>
<th>Needle Electrode Unipolar PNV, mV</th>
<th>Needle Electrode Unipolar PPV, mV</th>
<th>CARTO Bipolar PPV, mV</th>
<th>CARTO Unipolar PPV, mV</th>
<th>Ensite DSM, % Maximum PNV</th>
<th>Ensite DSM ≤40 mm, % Maximum PNV</th>
<th>EnSite Unipolar PNV, mV</th>
<th>EnSite Unipolar PNV ≤40 mm, mV</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10% Scar</td>
<td>5.03±3.67</td>
<td>8.34±5.75</td>
<td>2.38±1.72</td>
<td>7.63±4.30</td>
<td>71±24</td>
<td>74±21</td>
<td>5.85±4.07</td>
<td>6.39±4.37</td>
</tr>
<tr>
<td>11–49% Scar</td>
<td>2.16±1.85</td>
<td>3.44±3.19</td>
<td>1.84±1.07</td>
<td>3.82±1.79</td>
<td>65±18</td>
<td>66±15</td>
<td>4.49±2.49</td>
<td>4.68±2.52</td>
</tr>
<tr>
<td>≥50% Scar</td>
<td>1.37±0.79</td>
<td>1.49±0.91</td>
<td>1.18±0.96</td>
<td>4.37±3.42</td>
<td>58±19</td>
<td>58±19</td>
<td>4.51±3.36</td>
<td>4.58±3.49</td>
</tr>
<tr>
<td>P Value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.012</td>
<td>0.001</td>
<td>0.079</td>
<td>0.040</td>
</tr>
</tbody>
</table>

PNV indicates peak negative voltage; PPV, peak-to-peak voltage; DSM, dynamic substrate map.

Figure 3. Trichrome Gomori stained myocardium at representative points showing (A) normal myocardium (<10% scar), (B) partial scarring (10% to 50% scar), and (C) dense scarring (>50% scar). Slices are shown from endocardium (bottom) to epicardium (top).
near perfect correlation ($r=0.99$) between calculated patho-
anatomic infarct mass and MRI measured infarct mass in
fox-hounds. Infarct size was also correlated using DSM (PNV
34%) compared with MRI measurements and again was near
perfect ($r=0.99$). Both correlations in that study used only 4
data points (4 animals), and the accuracy of noncontact
mapping was not directly compared with histopathology.\textsuperscript{22}
Although there was no difference in scar area in these 2
noncontact mapping studies, the accuracy of the noncontact
DSM method remained unclear as the low voltage points on
DSM were not directly correlated with scar on histop-
thology. Further, direct comparison to the CARTO contact
system had not been performed.

The CARTO bipolar voltage measurements were most
accurate at differentiating dense ($>50\%$) scar (ROC area
under the curve 0.726), whereas the CARTO unipolar voltage
measurement was best at differentiating normal ($<10\%$ scar)
myocardium (ROC area under the curve 0.789). Both histo-
logical classifications are relevant for identifying scar border
regions, the likely exit site of re-entrant VT. Contact bipolar
PPV has been shown to correlate better with areas of
infarction, as measured by endocardial scar, than unipolar
PPV.\textsuperscript{27} The limitation with unipolar electrograms is the
presence of far field signals, although this can be partially
overcome with high pass filtering.\textsuperscript{28} With the noncontact
system, this limitation of unipolar electrograms is overcome
by using multiple pacing wavefront angles to construct an
overlapping DSM. Unexpectedly, in this study, the best
correlation with histological scar percentage was seen with
the CARTO unipolar electrograms. Contact bipolar electro-
grams have varying orientations of the bipole to the wave-
front. This limits the accuracy of the bipolar electrogram
because it is dependent on the angle of wavefront propoga-
tion. The difference in unipolar and bipolar filtering on the
contact system may have also contributed to the difference in
accuracy. The selected filtering was recommended by the
manufacturers for substrate mapping.

For large dilated or aneurismal chambers, as often occurs
with VT postmyocardial infarction, the accuracy of the
EnSite system is limited by endocardial proximity to MEA
equator. Careful positioning of the MEA is required to
accurately map substrate and arrhythmias. This study has
demonstrated that the EnSite DSM has similar scar discrimi-
atory capability to the CARTO contact system in a chronic
ovine model when points $>40$ mm from the MEA were
excluded. The CARTO contact system does not have the
spatial limitations of the EnSite system and only requires 1
mapping catheter, potentially making it safer. However, the
EnSite noncontact system has the advantage of being able to
create accurate substrate maps for scar-related VT plus the
capacity for single beat activation mapping of nonsustained
VT, as well as VT causing hemodynamic compromise—a
limitation of sequential point-to-point mapping with the
CARTo system. Both systems each have their own advan-
tages, and the choice will ultimately be determined by
individual patient electrophysiological requirements.

Study Limitations
In this model, the region of scar was confined to the apex,
apical septum, and apical anterior wall. In each animal, the

MEA was positioned with the pigtail part of the catheter in
the left ventricular apex. The accuracy of the EnSite system is
known to decrease at the polar regions of the MEA. However,
the study was performed using the orientation of the MEA
used clinically in the left ventricle. The study has demon-
strated that even with this limitation, the EnSite DSM was
equivalent to the CARTO contact electrograms in discrimi-
ating scar.

For construction of DSMs, $10\pm1$ pacing sites were used
per animal in this study. To the best of our knowledge, the
precise number of pacing sites required for DSM has not been
defined. We are currently performing a separate study ad-
dressing the optimum requirements for DSM.

This study was performed in an ovine model, and it is not
clear whether similar correlations would be present in hu-
mans. However, direct correlation of both systems to histol-
ogy would not be possible in humans. Further, the chronic
postinfarct ovine model of ventricular scarring is considered
a good representation of what occurs clinically in humans.\textsuperscript{29}

Conclusions
This study demonstrated that dynamic substrate mapping
using the EnSite noncontact system, for sites within 40 mm of
the array, is comparable to the CARTO contact system in
differentiating normal myocardium and scar in a chronic
ovine model using a rigorous method of direct comparison
with transmural histology at plunge needle sites.

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biomedical statistician.

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None.

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